6615

Neurotropism of Vesicular Stomatitis Virus.

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The virus of vesicular stomatitis is peculiarly epitheliotropic (dermotropic) in the guinea pig: only the pad tissue of the dermal surface is uniformly susceptible.[1, 2, 3]

Through the kindness of Dr. W. E. Cotton, samples were sent us of Indiana and New Jersey strains of virus propagated in guinea pig pads for several years. After 20 consecutive transmissions of the experimental disease in pads, both strains were filtered through Seitz' discs and were inoculated intracerebrally in respective guinea pigs.* The amount injected was 0.15 cc. of filtrate, derived from 1:10 suspensions of affected pad tissue ground in hormone broth at pH 7.5. Both the New Jersey and the Indiana materials produced a striking reaction.

From 2 to 5 days after injection, the animals exhibited first weakness, then paresis of both posterior extremities, which became progressively more marked and reached, within 2 to 3 days, the stage of complete flaccid paralysis. No other signs of disturbance, including fever, were detectable. About 60% of the animals died during the paralytic stage. The survivors either recovered partially, showing merely an ataxic gait, or were left with paralyzed legs. To the present, 6 brain to brain passages have been made in the guinea pigs. Practically all of the animals proved susceptible to intracerebral inoculations and, after several such passages, the action of the virus became regular.

Microscopic study of the organs removed at the height of reaction revealed changes only in the cerebrospinal system. The meninges and choroid plexus showed only invasion by few mononuclear cells. The brain itself exhibited general edema, slight perivascular mononuclear infiltration, and inconspicuous, diffuse, monocytic reaction, together with mild increase of glia nuclei. Many ganglion cells revealed various stages of degeneration and occasional neurono-

[1] Olitsky, P. K., *J. Exp. Med.*, 1927, **45**, 969; Olitsky, P. K., Traum, J., and Schoening, H. W., *Technical Bull.*, No. 76, U. S. Dept. of Agriculture, 1928, 172.

[2] Hoffman, D. C., *J. Exp. Med.*, 1931, **53**, 43.

[3] Wagener, K., *J. Am. Vet. Med. Assn.*, 1932, **80** (N. S. **33**), 39.

* All operative procedures were carried on under ether anesthesia.

phagia. The spinal cord was the seat of corresponding changes; the membranes, except for slight mononuclear cellular infiltration, were normal. The cord itself was edematous and the nerve cells were degenerated. The nuclei of many of the nerve cells contained an acidophilic, granular material. Inclusion bodies were not detected.

The identification of the neurotropic nature of the vesicular stomatitis virus is based first on the characteristic local lesions following, invariably, the injection of pads with active brain tissue. These reactions are more marked than those obtained with ordinary pad virus, thus indicating a greater activity of the neurotropic virus. The second means of identification depends on cross-immunity, that is, animals recovered from a brain inoculum are immune to the original vesicular stomatitis virus injected in their pads, and conversely, guinea pigs recovered from pad inoculation of original virus develop resistance in their pads and in their central nervous system against active cerebral tissue.

Brain material retained its neurotropism after storage for at least 32 days in 50% glycerol. It was also found to be active in the cerebrospinal system of rabbits and white mice. Experiments with mice are still in progress.

In conclusion, a neurotropic strain of vesicular stomatitis virus has been described, which may prove of value when bacteria-free, yet unfiltered, active material is desired—heretofore unobtainable with pad virus.

6616

Further Studies on Neurotropism of Vesicular Stomatitis Virus.

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In a preceding report[1] we have shown that intracerebral inoculation of guinea pigs with the virus of vesicular stomatitis of horses induces characteristic degenerative lesions in the organs of the central nervous system, and after the virus had become fixed by

[1] Cox, H. R., and Olitsky, P. K., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 653.