

three to four days and no manifestations of adrenal insufficiency appeared.

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THE ENCEPHALITOGENIC PROPERTY OF HERPES VIRUS¹

MODIFICATIONS have recently been reported in the virulence of the viruses of human influenza,² vaccinia,^{3,4} infectious bronchitis of fowls⁵ and pseudorabies,^{6,7} following cultivation on the chorio-allantois of chick embryos. This communication is to describe an increase in virulence for chick embryos and a reduction in virulence for rabbits which have occurred in a neurotropic strain of herpes simplex (HF, Rockefeller Institute) during 70 serial passages on the chorio-allantois of chick embryos. The technique of establishing and maintaining membranous strains of viruses has been described elsewhere.⁸

The original HF virus on membranes metastasized rarely to the heart and brain. After the twentieth passage it regularly induced metastatic lesions in the heart, liver, lungs, spleen and kidneys of embryos. Lesions in the heart, liver and spleen are grossly visible areas of necrosis. By subinoculation of membranes, embryonic blood was shown to contain virus at 24, 48, 72 and 96 hours. There was no localization of virus in the brain from the blood stream. The lethal effect of infection has increased so that at the 75th passage embryos rarely survived 96 hours, whereas at the tenth, most embryos survived infection 6 or 7 days.

As virulence for chick embryos has increased, it has diminished for the rabbit. After the 25th passage the membranous strain no longer induced a typical keratitis in rabbits. Fifteen rabbits scarified and inoculated on the cornea at intervals between the 25th and 65th membranous generations have shown only slight lacrimation, mild inflammation of conjunctiva without supuration, no elevation of temperature and no symptoms of encephalitis. This is in contrast to an invariably fatal encephalitis which follows a suppurative keratitis induced by the original strain.

To determine whether or not this modified virus traveled along the fifth nerve from the cornea to the

brain without causing encephalitis, two rabbits were inoculated on their right corneas: one with the 50th membranous generation, the other with HF. Corneal reactions typical of each strain developed. The rabbits were killed at 96 hours. The right Gasserian ganglion and brain at the entrance of the fifth nerve were removed from each animal and inoculated onto membranes. Herpes virus transmissible in series was recovered from both the Gasserian ganglion and the brain of the HF control rabbit. Virus could not be demonstrated grossly or microscopically on membranes inoculated with material from the rabbit with the modified virus. This experiment was repeated with the same result using rabbits inoculated with the 53rd generation virus and sacrificed at 96 hours and at 7 days. Material from the medulla of one of these rabbits inoculated intracerebrally into another rabbit induced no symptom.

These experiments led to the conclusion that the HF strain of herpes virus had lost its ability to invade the central nervous system following corneal inoculation in rabbits. A second series of passages through 30 generations over a period of 6 months has not induced a similar modification. Modification of the first strain was observed at the 25th generation 11 months after initiation of the chick strain. Whether the already established modification is a repeatable *Dauer-modification* induced by prolonged passage of the virus on chick embryos or a suddenly appearing mutation remains to be determined.

To test the virulence of the modified strain following intracerebral inoculation, suspensions of HF virus (1st membranous generation) and the 62nd membranous generation in dilutions of 10^{-3} , 10^{-4} and 10^{-5} were inoculated intracerebrally into rabbits. All 3 rabbits receiving HF virus died within 5 days of herpetic encephalitis. Each rabbit receiving the modified virus had a remarkably delayed elevation of temperature. One (10^{-4}) is alive 60 days after inoculation; one (10^{-3}) died on the 20th day, and the other (10^{-5}) died on the 26th day.

Preliminary experiments indicate that corneal inoculation with the modified strain induces a stable degree of immunity to HF inoculated on the cornea.

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THE CHEMICAL COMPOSITION OF SUCKLEYA SUCKLEYANA

FOLLOWING the discovery of hydrocyanic acid in *Suckleya suckleyana* during 1937, together with the experimental work which proved its toxicity to cattle, sheep, rabbits and guinea pigs, the etiology of many of the heretofore unexplained losses in cattle and sheep in eastern Colorado was explained.¹

¹ Frank Thorp, Jr., A. W. Deem, H. D. Harrington and J. W. Tobiska, *Colo. Exp. Sta. Tech. Bul.*, 22: 1-19, 1937.

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² F. M. Burnet, *Brit. Jour. Exp. Path.*, 17: 283, 1936.

³ C. Levaditi, *et al.*, *Revue d'Immunologie*, 4: 481, 1938.

⁴ L. Molina, *Zbl. f. Bakt., I. Orig.*, 139: 493, 1937.

⁵ F. R. Beaudette (personal communication).

⁶ F. M. Burnet, Dora Lush and A. V. Jackson, *Aust. Jour. Exp. Biol. and Med. Sc.*, 17: 35, 1939.

⁷ R. E. Glover, *Brit. Jour. Exp. Path. and Med.*, 20: 150, 1939.

⁸ E. W. Goodpasture and G. J. Buddingh, *Am. Jour. Hyg.*, 21: 319, 1935.