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Serial Transmission of Virus of Infectious Papillomatosis in Domestic Rabbits.

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It was reported[1] that the virus of infectious papillomatosis produced warts which were readily transmissible in its natural host, the wild cottontail rabbit. However, warts which it regularly induced in domestic rabbits were not transmissible serially in either wild or domestic rabbits. A similar situation as regards the transmission of Rous Sarcoma 1 to turkeys, guinea fowls, and pheasants has been described.[2, 3]

The purpose of the present paper is to report the successful transmission of the virus of infectious papillomatosis serially in domestic rabbits. Warts from domestic rabbits, infected with papilloma virus of wild rabbit origin in the usual fashion,[1] were removed at various intervals, ground with sand, suspended in physiological saline and the resulting suspension used in attempts to infect other domestic rabbits. The technique of infection was the same that had been used unsuccessfully in earlier experiments. Thirty-two attempts to carry the virus beyond its first domestic rabbit passage have been made since the 26 fruitless efforts first reported.[1] Of these, 13 were successful, the domestic rabbits of the second serial passage developing one or more papillomas over the area of skin inoculated. Efforts to maintain the virus in domestic rabbits beyond its second serial passage were made in 7 instances and, of these, 4 were successful. Two series were carried through their fifth domestic rabbit passage and then discontinued. The remaining 2 series are still being passed; one has reached its 6th and the other its 10th domestic rabbit passage.

The individual papillomas developing in rabbits infected with the domestic rabbit-passaged virus are identical in all respects with those resulting following similar infection with virus obtained from wild rabbit warts. The incubation period following infection with the domestic rabbit virus, however, ranges from 13 to 30 days as contrasted to a 6 to 12-day incubation period following infection with

[1] Shope, R. E., *J. Exp. Med.*, 1933, **58**, 607.

[2] des Ligneris, M. J. A., *Am. J. Cancer*, 1932, **16**, 307.

[3] Andrewes, C. H., *J. Path. and Bact.*, 1932, **35**, 407; 1933, **37**, 17.

wild rabbit virus. Also the extensive confluent folded mass of papillomatous tissue resulting from infection with wild rabbit virus is seldom seen even following a heavy infection with the domestic rabbit virus; rather the papillomata induced by the latter virus tend to be more isolated and discrete over the area of skin inoculated. Similar isolated papillomata developing after a prolonged incubation period result when rabbits are infected with very dilute wild rabbit virus. These 2 differences are thus probably quantitative and merely indicate that the wild rabbit papillomata contain a higher concentration of available virus than do those from domestic rabbits.

No fact has been yet brought to light to explain why, in certain instances, domestic rabbit papillomata prove transmissible in series and in other instances non-transmissible. That the degree of maturity of the warts in domestic rabbits at the time that attempts were made to transmit them was not a determining factor is indicated by the fact that the ages of those that proved transmissible ranged from 7 to 377 days, while warts ranging in age from 1 to 116 days have proven non-transmissible. The breed of rabbit used seems also to be immaterial. Preliminary experiments suggest that the age of the rabbit may be of some importance, for warts taken from rabbits over 2 years old have proven serially transmissible more frequently than warts taken from rabbits 2 to 4 months old. It seems likely that, in determining whether or not a domestic rabbit wart will prove transmissible at least 2 factors are involved; the concentration of the inciting agent in the papillomata used as the source of infection, and the natural threshold of resistance, to the virus, of the animal to be infected. A successful passage of the disease in series from one domestic rabbit to the next, on this basis, can be visualized as the result of a fortunate and unpredictable coincidence in which the papillomata of the rabbit serving as the source of infection are especially rich in virus and the natural threshold of resistance, to the virus of the animal to be infected is unusually low. Factors determining these 2 conditions are not yet understood. Experiments with the domestic rabbit-passaged virus make it appear likely that, after 3 or 4 serial passages through domestic rabbits, transmission from animal to animal is more easily effected and that, in fact, an actual adaptation to the new host is in process. But even during these serial passages a rabbit is occasionally encountered whose warts fail to infect. In such instances it is necessary to revert to glycerol-stored material from an earlier passage in order to carry the series on.

This is a preliminary report published only to correct the con-

ception created by an earlier paper[1] that the virus of infectious papillomatosis was never serially transmissible in domestic rabbits. Experiments attempting to determine accurately the conditions necessary for the regular serial transmission in domestic rabbits are in progress.

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Attempts to Produce Poliomyelitis in Refractory Laboratory Animals.*

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Since the successful transmission to monkeys of the virus of poliomyelitis by Landsteiner and Popper,[1] many attempts have been made to produce the disease in the other laboratory animals. This work has been adequately reviewed by Shaughnessy *et al.*[2] and Harrington.[3] Experiments concerned with transmission of the virus to any animal other than the monkey have given only negative results. In this work, the passage and multiplication of the virus of poliomyelitis was attempted in mice, rats, guinea pigs and rabbits. It was thought possible to overcome the factors which make these animals naturally resistant to the virus, by using very young animals, by lowering their resistance and by passing the virus serially in the hope of adapting it to the new host.

First, to determine the time of survival of the virus in the brains of these animals, they were injected intracerebrally and after various intervals of time, the site of inoculation was removed, emulsified and injected into monkeys to determine the presence of virus. Rabbits received 0.3 cc., guinea pigs 0.2 cc., rats 0.1 cc., and mice 0.03 cc. of virus suspension. Table I indicates the time of removal of

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[1] Landsteiner, K., and Popper, E., *Z. f. Immunitätsforsch. und exp. Therap.*, 1909, **2**, 377.

[2] Shaughnessy, H. J., Harmon, P. H., and Gordon, F. B., *J. Prev. Med.*, 1930, **4**, 59, 89.

[3] Poliomyelitis, International Committee, 1932, p. 101. Williams and Wilkins, Baltimore, 1932.