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Pathology of Experimental Vaccinal and Rabies Encephalitis.

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One of the primary infections¹ of the central nervous system of man, is termed post-vaccinal because it is most frequently found after vaccination against small pox. Yet the identical pathological changes have been described after vaccination against rabies,² complicating measles, small pox, varicella and upper respiratory infections. This, of course, does not necessarily mean that a single virus is the responsible agent. The reaction of the nervous system is more or less stereotyped and the same reaction may occur in several diseases such as is the case in Heine-Medin's disease, epidemic encephalitis, and true rabies.

In the human, post-vaccinal type of encephalomyelitis there occur disseminated foci of perivascular demyelination, especially about the veins, coalescing and extensions of the lesions to destroy the whole nerve fiber and to form true softenings composed of intra and extracellular fat. Very few or frequently no lymphocytes are found in the perivascular spaces, and meningeal exudates occur only secondary to the softenings.

¹ Grinker, R., and Bassoe, P., *Transactions Am. Neur. Assn.*, 1930.

² Bassoe, P., and Grinker, R., *Arch. Neur. and Psych.*, 1930, **23**, 1280.

Experiments to discover whether the encephalomyelitis associated with vaccination was due to the vaccine virus have given conflicting results. (McIntosh and Scarff³ and Aldershoff,⁴ Eckstein and Herzberg,⁵ McIntosh,⁶ Hurst and Fairbrother,⁷ Thompson,⁸ Pette.⁹) Many investigators contend that vaccination in the human against small pox or rabies, or the exanthematous diseases does not produce encephalitis by the introduction of a specific virus but by stimulating a latent virus to activity.

It was attempted to determine whether in the experimental animal, vaccinia encephalitis could be produced, and whether it resembled the human type. Furthermore attenuated rabies was introduced into experimental animals to determine its pathological characteristics, to compare it with vaccinia encephalitis and human post-vaccinal (rabies) encephalitis. Rabies was used particularly because it could be identified by the presence of negri bodies.

Intra-cerebral injections of an ordinary vial of calf lymph virus were made. In one guinea pig death occurred in 4 days from a severe meningo-encephalitis. One guinea pig showed no clinical symptoms but on autopsy a meningo-encephalitis was found. Further transmission of this encephalitis from the sources was unsuccessful. Intra-cerebral vaccinia injections into rabbits produced no symptoms and anatomically showed no encephalitis. Emulsions of these brains caused no encephalitis when injected intracerebrally in other animals. Intra-testicular injection of vaccine virus, however, produced in one out of 3 rabbits a fatal meningo-encephalitis which could be carried on to other rabbits by intracerebral inoculation of an emulsion of its brain. Subcutaneous inoculation of vaccine virus was unsuccessful but corneal inoculation produced a high-grade encephalitis.

Commercial rabies vaccine was used as the source of attenuated "fixed" virus. One-half cc. was injected intracerebrally into a dog and in 7 days the animal was dead after showing the typical clinical picture of rabies. An emulsion of the animal's brain was passed through several series of rabbits until by storage in glycerine and passage the time required to kill a rabbit after intracerebral inoculation was only 4 days.

³ McIntosh, J., and Scarff, R. W., *J. Path. and Bact.*, 1930, **33**, 483.

⁴ Aldershoff, H., *Acta. Path. and Microbiol. Scand.*, 1930, **3**, 9.

⁵ Eckstein, A., and Herzberg, K., *Deutsche med. Woch.*, 1930, **57**, 264.

⁶ McIntosh, J., *Brit. Med. J.*, 1928, **2**, 334.

⁷ Hurst, E. W., and Fairbrother, R. W., *J. Path. and Bact.*, 1930, **33**, 463.

⁸ Thompson, R., *Proc. Soc. Exp. Biol. and Med.*, 1929, **26**, 559.

⁹ Pette, H., *Munch. Med. Wochenschr.*, 1928, **75**, 207.

The brain and spinal cords were fixed in formalin. Sections stained by special methods to demonstrate fat, microglia, myelin sheaths, axones and the usual hematoxylin-eosin stain was also used. In no single specimen was there any evidence of demyelination, axis cylinder destruction or accumulation of fat. Thus in no manner did the vaccine virus or attenuated rabies vaccine produce a pathological change similar to the post-vaccinal encephalitis in man.

Both series showed a severe meningo-encephalitis. In the vaccinia experiments, the meningeal exudate consisted of many leucocytes mixed with histocytes while the intracerebral vessels were infiltrated with moderate numbers of lymphocytes and the adventitial cells were increased. The rabies group showed an intense lymphocytic meningeal exudate and perivascular infiltration. Negri bodies were found in every case. There was a diffuse ganglion cell degeneration and increase in microglia. Thus in both types of infection a diffuse meningo-encephalitis occurred, varying only in the predominating type of cell and intensity of reaction.

These experiments show that, in the experimental animal at least, attenuated rabies and vaccinia do not produce the pathological changes found in human post-vaccinal (cow pox and rabies) encephalitis. These findings would seem to suggest that the various types of vaccination and exanthematous diseases in man might act as a stimulant to a latent infection rather than by introducing a specific virus.

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New Technic for Roentgenographic Study of Renal Vessels.*

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Ralph Graham¹ applied the method of Hill² to the injection of the vascular tree in the human kidney. The method, involving the injection of a 25% bismuth oxychloride suspension in 10% acacia, is applicable to postmortem material. In such kidneys it demon-

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¹ Hill, E., *Bull. Johns Hopkins Hosp.*, 1929, **44**, 248.

² Graham, R., *Am. J. Path.*, 1928, **4**, 17.