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Temperature Reactions in Dogs to Inoculation with Ferret Passage Distemper Virus.

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Serial passage through ferrets of a distemper virus virulent for dogs, foxes, and ferrets results in a modification¹ of the virus tending toward higher virulence for the ferret and lower virulence for foxes and dogs. Within this zoologic modification related to animal species, additional modifications of the virus may be accomplished by the consistent selection of a single tissue, such as skin, brain, or spleen, for use as transmission virus. The histologic modifications effected by selection of tissue seem to produce viruses that have distinct abilities to invade to a greater or lesser extent the various types of susceptible cells. The study of temperatures induced by these viruses was stimulated by the observation that, upon injection into dogs, smaller doses of the ferret-passage virus appeared to excite more marked clinical reactions than did larger doses. In utilizing various doses of ferret-passage virus furnished by us, Stader and Slauchenhaupt² noted milder reactions in dogs from

15 mg of virus than from 2.5 mg. Similar observations were made by Schlotthauer.³

Dogs from 8 to 12 weeks old were selected for these experiments but were chosen without special consideration as to their weight. Although they varied considerably in the latter respect, the variation in weight was much smaller proportionally than the variation in the doses of virus used. The differences in weight were minimized by the division of litters to put as nearly as possible an equal number of littermates in each group. The dogs were housed in small kennels in outdoor yards. The temperatures were taken during the afternoon, usually at 3:30.

Two ferret-passage viruses of 54 and 63 serial transfers, respectively, were studied with regard to the temperature reactions they induced in dogs when injected subcutaneously in a small dose and in a large dose. The virus was prepared by subcutaneous injection of spleen tissue and the subsequent collection of

* Aided by funds and facilities furnished by Fromm Laboratories, Grafton, Wisconsin.

¹ Green, R. G., *J. Am. Vet. Med. Assn.*, 1939, **95**, 465.

² Stader, Otto, and Slauchenhaupt, R. R., *No. Am. Vet.*, 1942, **23**, 782.

³ Schlotthauer, Carl F., *J. Am. Vet. Med. Assn.*, 1943, **103**, 290.

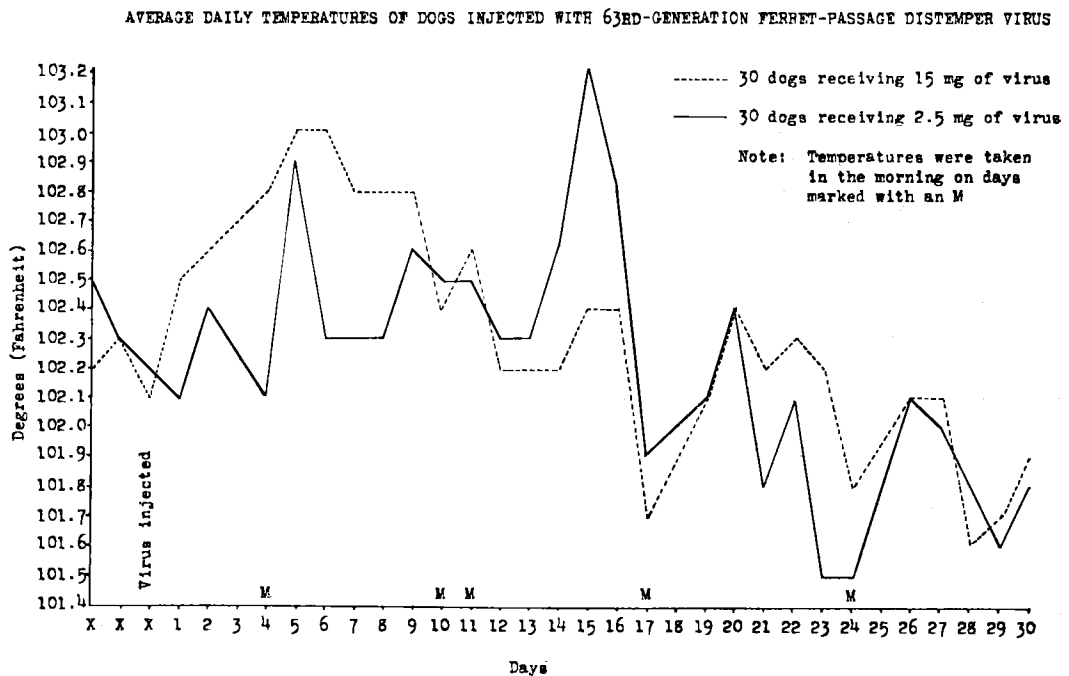


FIG. 1.

spleen tissue for virus. The 54th-generation virus was injected in doses of 2.5 and 15 mg into 25 dogs each. The 63rd-generation virus was injected in doses of the same sizes into 30 dogs each. The results obtained from inoculation of the 110 dogs included in these experiments would seem to demonstrate that, as determined by average daily temperatures, ferret-passage distemper virus of 63 generations shows somewhat of an inverse relationship between dose and degree of temperature reaction.

The temperature reactions of dogs with distemper were first studied by Laidlaw and Dunkin,⁴ who described the biphasic temperature curve now considered typical of distemper in dogs. Usually, an initial rise in temperature occurs about the 6th day. The temperature then declines and a second rise occurs about the 14th day, following which a variable fever is maintained during the course of the disease.

In our studies, we found that both the small dose and the large dose of 54th-generation ferret-passage distemper virus produced a mild infection with a biphasic temperature reaction

such as that typical of a natural distemper infection. No marked differences were noted in the average daily temperatures produced in the dogs by the 2 different doses. However, in the dogs injected with 63rd-generation virus, the dose of 2.5 mg produced the prolonged biphasic temperature reaction while the dose of 15 mg produced only a single rise in temperature, which was followed by a gradual decline to approximately normal temperatures by the 16th day. The average daily temperatures of the 2 groups of dogs injected with 63rd-generation virus are shown in Fig. 1.

An analysis of the individual temperature records reveals that of the 30 dogs receiving the small dose, 2.5 mg, of 63rd-generation virus, 8 did not show a significant temperature reaction and did not appear to have developed an infection. A graph of the average daily temperatures of the remaining 22 dogs, which showed definite fever, does not differ materially from the curve in Fig. 1, in which the temperatures of all 30 dogs in the group were utilized. Analysis of the individual temperature records of the dogs receiving 15 mg of 63rd-generation virus shows that 23 dogs developed high initial temperatures which

⁴ Laidlaw, P. P., and Dunkin, G. W., *Vet. J.*, 1928, **84**, 600.

gradually declined. A curve of the average daily temperatures of these dogs does not differ significantly from the curve of all 30 dogs in the group as shown in Fig. 1. The other 7 dogs of this group had no significant initial rise in temperature but developed a late elevation about the 18th to 22nd day. In these 7 dogs the larger dose of 15 mg produced temperature reactions somewhat similar to those produced by the smaller dose.

Previous reports⁵ have recorded the low pathogenicity of ferret-passage virus. In the present experiments, 1 dog of the 50 injected with 54th-generation virus was destroyed on the 14th day, and 1 of the 60 injected with 63rd-generation virus was destroyed on the 15th day when they developed prolapse of the rectum. One dog injected with 63rd-genera-

tion virus died in convulsions on the 5th day, but the fatality did not seem to be related to the inoculation.

Conclusions. Ferret-passage distemper virus of 54 serial transfers, upon injection into young dogs, induced a mild infection with a biphasic temperature reaction similar to that observed in natural distemper infections. No difference in temperature reactions was observed in groups of dogs injected with 2.5 mg and with 15 mg of the ferret-passage virus. Similar mild reactions were observed following the injection of virus of 63 ferret passages. The dose of 2.5 mg produced temperature reactions which were biphasic in character. The 15-mg dose of this virus tended to produce an exaggerated initial fever which gradually declined without the production of a second rise in temperature.

⁵ Green, Robert G., *Am. J. Hyg.*, 1945, **41**, 7.

14859

The Influence of Muscle Pain on Spinal Reflexes.*

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Introduction. In a previous investigation¹ the effect of intramuscular injection of NaCl solution on the response of the motor cortex to electrical stimulation has been studied. It was shown that the effect of cortical stimulation was altered quantitatively and qualitatively under these conditions. Since evidence from our own experiments based on reflex effects, particularly on the pupil, as well as from studies of Lewis,² on man, suggested that injection of hypertonic NaCl solution caused "muscle pain," the experiments were interpreted to mean that "muscle pain" altered the effect of cortical stimulation of the motor area on the organism. The physiological mechanism involved in these reactions has not yet

been determined. As a first step in this direction experiments are reported in this paper in which the influence of "muscle pain" (*i.e.*, of stimuli known to cause muscle pain in man and to induce pupillary dilatation and vocalization in anesthetized animals) on spinal reflexes was investigated.

Method. The experiments were performed on eleven cats and one macaque. .45 cc dialurethane (Ciba)[†] /kilo was injected intraperitoneally. The knee jerk was elicited every two seconds by means of a device similar to that described by Johnson.³ The flexor reflex (tibialis ant.) was studied by means of condenser discharges applied at intervals of 2.5 seconds. In some of the animals studied the spinal cord was transected at the first lumbar level. As stimuli which result in muscle pain

* Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

¹ Gellhorn, E., and Thompson, L., *Am. J. Physiol.*, 1944, **142**, 231.

² Lewis, T., *Pain*, New York, 1942.

[†] Ciba Pharmaceutical Products, Inc., was kind enough to donate this drug.

³ Johnson, C. A., *Am. J. Physiol.*, 1927, **82**, 75.