RISE IN TEMPERATURE PRECEDING THE APPEARANCE OF SYMPTOMS IN EXPERIMENTAL POLIOMYELITIS*

By S. D. KRAMER, M.D., K. H. HENDRIE, AND W. L. AYCOCK, M.D.

(From the Department of Preventive Medicine and Hygiene, Harvard University Medical School, Boston, and the Research Laboratory of the Vermont Department of Public Health, Burlington)

(Received for publication, March 31, 1930)

In the main the clinical manifestations and pathological lesions of experimental poliomyelitis in the monkey represent a faithful reproduction of the human disease.

The clinical course of the experimental disease is fairly uniform. The first symptoms vary somewhat in time of appearance. This depends largely on the strain of virus used, the extent to which the virus has been modified either by temperature (1), by chemical agencies (2), or by the addition of convalescent serum (3). When a 7- or 8-day unmodified virus is inoculated intracerebrally the monkey remains normal in appearance (after the effect of the operation and anaesthetic has worn off) until the seventh or eighth day. The first symptoms to appear are tremor of the head and the extremities (more easily noticed in the upper extremities), the ruffled coat and some awkwardness and stumbling when the monkey attempts to climb. Within a few hours these symptoms are followed by paralysis of varying severity and in most instances by complete prostration and death. When the disease does not terminate fatally the animal goes through a convalescent period of several weeks' duration, after which except for the residual paralysis it seems quite normal.

In one respect, however, the experimental disease had been considered as differing from the human form in that a phase of the disease analogous to the preparalytic stage of the human disease was lacking. As is pointed out in this paper this view is not justified. The preparalytic stage of the disease in human beings is now well established.

* This work was supported by the Harvard Infantile Paralysis Commission, a fund privately donated to the Vermont Department of Public Health and a gift from the International Committee for the Study of Infantile Paralysis.
TEMPERATURE IN EXPERIMENTAL POLIOMYELITIS

(4), lasting 2 or 3 days before the onset of paralysis and consisting of a syndrome of fever, headache, vomiting, stiff neck and back and a coarse tremor. These symptoms are regularly associated with an increase in the cell count and in the globulin of the spinal fluid. In the experimental disease paralysis follows the earliest symptoms so rapidly that a division comparable to the human preparalytic stage has not previously been often made. On account of the lack of an obviously preparalytic stage there is a question whether certain procedures applied to the inoculated monkey are applicable to the human disease in the preparalytic stage. This uncertainty has been felt particularly in experiments dealing with the effects of convalescent serum therapy on the course of the disease.

In an attempt to determine if there are some earlier detectable manifestations in the experimental disease comparable to the preparalytic stage of the human form, we undertook a series of studies on monkeys inoculated in the course of our work. These studies dealt with the temperature, formed blood elements, spinal fluid, and blood chemistry. Similar studies made on a group of normal monkeys served as controls.

The present communication devotes itself to temperatures observed in normal monkeys and in monkeys infected with the virus of poliomyelitis. Rectal temperatures were used throughout. It was noted early that the administration of ether causes an immediate, though transient, drop in the temperature, so that temperatures were not taken at such times.

The temperature of the normal monkey is about 103°F., varying to some extent, however, without apparent reason in the same monkey both on the same day, and from day to day. Fluctuations of 1° and occasionally 1.5° between the maximum and minimum temperatures are not uncommon, but variations of more than 1° from the average mean temperature are rare. The average of 1301 readings on 46 monkeys over a period of several months was 102.9°F. A number of the monkeys showed a temperature consistently higher than 103°F., several ranging between 104° and 105°. The reason for these exceptions was not always clear, although some animals developed diarrhea, and in several instances where the monkeys came to autopsy a generalized tuberculosis was found. In others, however, there was no such explanation.
Graph I is a composite curve of 11 intranasally inoculated animals that resisted infection. The average temperature of 147 readings on these monkeys was 102.9°F., with a maximum plus deviation of 0.5°F., and a maximum minus deviation of 0.6°F. from the average.
Graph II is a similar composite curve of 42 intracerebrally inoculated animals that did not succumb to the disease. The average temperature of 470 readings on these monkeys during the "normal" period was 103.1°. The maximum plus and minus deviations were 0.6° and
Experimental Poliomyelitis - Temperature

Positive Intracerebral Inoculation

Graph V

S. D. KRAMER, E. H. HENDRIE, AND W. L. AYCOCK
0.4°F, respectively. With the exception of the transient rise following intracerebral inoculation the two curves are identical. The preliminary rise of 1° to 2° following the operation was regularly observed in monkeys inoculated intracerebrally and usually did not last beyond the first 24 hours. This rise was absent in those monkeys in which the virus was instilled into the nostrils.

The temperatures of the monkeys which succumbed, however, showed constant and characteristic alterations from the normal. Graphs III, IV, and V show the temperature curves of a number of intracerebrally inoculated animals that developed the disease. These graphs show the preliminary rise, already referred to, followed by a varying period of "normal" temperature, followed in turn by an abrupt rise which reaches its maximum about 24 hours before the onset of the earliest symptoms. This interval of "normal" temperature has at times lasted 18 to 21 days, as in the instances of prolonged incubation period illustrated in Graph V. This type of curve occurred in about two-thirds of the animals that succumbed. In the remaining animals, however, the second rise was more gradual, although the temperature, as in the other animals, reached its maximum about 24 hours before the onset of symptoms.

* On this and subsequent charts the date of appearance of symptoms is indicated by an arrow.
Graph VI* is a composite temperature curve of 9 monkeys successfully inoculated intranasally. These animals did not show the early preliminary rise noted in Graphs III, IV, and V, but the temperature rise preceding the manifestation of symptoms appeared in a manner identical to that observed in the intracerebrally inoculated animals.

Coincident with this preparalytic rise in temperature, spinal fluid changes were observed similar to those in preparalytic human poliomyelitis. Details of these findings will be published in a later communication.

The trend of the temperature curve after the monkey is paralyzed and prostrated is illustrated in Graph VII.* With the appearance of the usual symptoms of the experimental disease the temperature is already declining. Within 24 hours after the appearance of paralysis it has usually become subnormal. When paralysis is extensive and the prostration marked the temperature has in several instances dropped as much as 10°F. That this pronounced drop in temperature is due in part to external factors is indicated by the fact that it was possible to avoid such an extreme drop by keeping the animal warm. The return of the temperature to the normal range in surviving monkeys seemed to depend considerably on the degree of prostration as well as the temperature of the environment. Several such monkeys were carefully nursed for a number of weeks and Graph VII shows the gradual return of the temperature to the normal range as the monkey's general condition improved.

SUMMARY

The data presented in this paper offer a means of earlier recognition of experimental poliomyelitis in the monkey. The early appearance of the temperature rise (1 to 3 days before the onset of the usual recognizable symptoms) associated with spinal fluid changes suggests that there is a stage in the experimental disease corresponding to preparalytic human poliomyelitis.

* Since some of these animals had been given repeated intranasal instillations of the virus, the incubation period was not ascertainable. Hence, the temperature readings are expressed in days preceding the onset of symptoms.
REFERENCES