

castrate condition. Thus the anomalous situation presents itself of a precociously matured rat, in oestrus at time of sacrifice, possessing what appears to be a typical castration pituitary. The most obvious interpretation appears to be that, although the implanted gonads effected a release of secretion from the pituitary, the time interval before sacrifice was not sufficient for the gonads to induce correction of the castrate picture. None of the grafts were allowed to remain over 16 days. Thus the time required for a complete return to normal would appear to lie between 16 and 30 days, Haterius and Nelson⁴ having reported a complete correction to have occurred at the latter figure. This point is now being studied in animals carrying grafts over a longer period.

Successful grafts were characterized by the presence of enormous cystic follicles, the walls of which were becoming markedly luteinized. In some instances very large luteal masses were present, comparing very favorably with the histological picture of ovaries from animals subjected to anterior lobe administration.

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Experimental Poliomyelitis: Evidence of Early Involvement of Central Nervous System.

S. D. KRAMER AND G. C. PARKER. (Introduced by A. J. Goldforb.)

From the Laboratories of the Infantile Paralysis Commission and Department of Neuropathology, the Long Island College of Medicine, Brooklyn, N. Y.

The epidemic of poliomyelitis in New York and New England in 1931 presented an opportunity for controlled studies^{1, 2} to determine the value of convalescent and other immune serums, administered in the preparalytic stage of the disease. In these reports the authors were unable to present statistical evidence that such serums were of value, either in reducing the death rate or in preventing paralysis. Since experience with virus diseases indicates that little is to be expected from the use of immune serums, once the disease has become established in the organism, it becomes important to determine the extent of involvement, particularly of the central nervous system, in the preparalytic stage of poliomyelitis.

⁴ Haterius, H. O., and Nelson, W. O., *J. Exp. Zool.*, 1932, **61**, 175.

¹ Kramer, Aycock, Solomon and Thenaby, *N. Eng. G. of Med.*, 1932, **206**, 432.

² Park, William H., *Transactions Assn. Physicians*, 1932, **47**, 123.

In this study, an effort was made to determine the early pathology in the experimental disease, following intranasal instillations of the virus. The close analogy between experimental poliomyelitis and the human disease should make any findings in the former significant in their application to the latter.

We have recently succeeded in obtaining a nasal strain of virus* which has successfully infected every animal. This mode of infecting the experimental animal is the probable mode of infection in man, and eliminates the trauma incident to intracerebral inoculation.

Method. Six *Macacus rhesus* were simultaneously inoculated intranasally on 3 successive days with a 10% centrifuged suspension of cord in distilled water. 1 cc. of the suspension was instilled into each nostril. Temperatures were taken twice daily and the animals observed for evidence of illness. They were sacrificed in the following order: The first animal 24 hours after the third instillation, and one animal each day thereafter until the 6 had been killed. The animals were killed with chloroform and autopsies performed immediately. The brains and cords were removed *in toto* and fragments from different levels and areas fixed in 10% neutral formalin, Zenker's solution and 95% alcohol. Sections were also taken from the abdominal and thoracic viscera and from peripheral nerves. The present report gives the results of histologic findings in the brains and cords, using hemotoxylin eosin and Nissl stains. One additional animal that did not receive the intranasal instillations, was sacrificed to serve as a control. This animal was not entirely normal inasmuch as it was suffering from a prolapsed rectum.

The first two animals sacrificed had no elevation of temperature and showed no evidence of illness. The third animal showed no signs of illness, but had an elevation of temperature for several hours before it was killed. The fourth had a temperature for 24 hours, a mild tremor which became evident only after severe exertion, and no evidence of paralysis. The fifth animal presented all the classical findings of the experimental infection, elevation of temperature, tremor, ruffled fur, staccato cry and ataxic gait, but no paralysis. The animal could climb but preferred to crouch quietly. The sixth and last animal presented all the findings of the fifth, and in addition, had flaccid paralysis of the left shoulder and arm.

* This virus was obtained through the kindness of Mr. M. Schaeffer of the Department of Bacteriology, New York University.

TABLE I.

| Monkey No. | 36 | 34 | 31 | 33 | 35 | 32 | 64 |
|--|--|--|---|---|--|--|--|
| Virus (Mixed Nasal Strain) | 1 cc. in each nostril | 1 cc. in each nostril | 1 cc. in each nostril | 1 cc. in each nostril | 1 cc. in each nostril | 1 cc. in each nostril | None |
| Dates Inoculated | 2/28/33 3/1/33 3/2/33 | 2/28/33 3/1/33 3/2/33 | 2/28/33 3/1/33 3/2/33 | 2/28/33 3/1/33 3/2/33 | 2/28/33 3/1/33 3/2/33 | 2/28/33 3/1/33 3/2/33 | — — — |
| Date Sacrificed | 3/3/33 | 3/4/33 | 3/5/33 | 3/6/33 | 3/7/33 | 3/8/33 | 5/3/33 |
| Clinical Signs | No signs of illness No elevation of temperature | No evidence of illness No elevation of temperature | Temperature elevation on day sacrificed No other sign of illness | Elevation of temperature Slight tremor Otherwise negative | Elevation of temperature Tremor Staccato cry Ataxic gait No paralysis | Elevation of temperature Tremor Ruffed fur Staccato cry Paralysis of left shoulder and arm | Prolapse of rectum Somewhat less active than normal animal |
| Outstanding Positive Pathologic Findings | Infiltration ¹ of gray matter and dorsal root ganglia Edema of cord Congestion Hemorrhage Ganglion cells: Neuronophagia (occasional) | Infiltration ² Edema of cord Pial edema and hemorrhage Congestion Hemorrhage Ganglion cells: Neuronophagia (occasional) | Infiltration ² Edema of cord Perivascular infiltration into pia and cortex of brain and gray matter of cord Ganglion cells: Chromatolysis Neuronophagia | Infiltration ² Edema of cord Perivascular infiltration into pia and cortex of brain and gray matter of cord Ganglion cells: Chromatolysis Neuronophagia | Marked infiltration ² Marked edema of cord Perivascular infiltration Congestion Hemorrhage Ganglion cells: Chromatolysis Neuronophagia | Infiltration ² Marked edema of cord Perivascular infiltration Congestion Hemorrhage Ganglion cells: Chromatolysis Neuronophagia Marked reduction in numbers | Sl. infiltration with lymphocytes Sl. edema of cord No congestion No hemorrhage No meningeal involvement Ganglion cells: showed no changes that could be considered significant |

¹ Although not clearly indicated in the table, the lesions were progressive, being more marked and extensive in successive monkeys, especially in the last three.

² This refers to a diffuse cellular infiltration by lymphocytes, plasma and glial cells and some polymorphonuclear leucocytes.

Sections of the brains and cords showed progressive involvement of central nervous system in all of the animals (Table I).

These sections therefore presented evidence of involvement of the central nervous system as early as the third day following the first intranasal instillation, at least 2 days before the appearance of temperature, and 5 days before the appearance of paralysis.

These results not only cast doubt on the therapeutic value of immune serums in paralytic poliomyelitis, but also help to explain the failure of immune serums to modify the experimental disease; and by analogy offer a similar explanation of the indifferent results of the controlled series of human cases in 1931.

The authors wish to express their thanks to Dr. William H. Park, Director of the Bureau of Laboratories, New York City, for his help and cooperation.

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Meteorological Influences on Blood pH and Cholesterol.

WM. F. PETERSEN.

From the Department of Pathology and Bacteriology, University of Illinois College of Medicine.

Among the blood chemical levels that are distinctly altered with each passing cyclonic wave are the blood pH and the cholesterol. The anoxemic stimulus to which I have previously referred is almost invariably followed by striking increase in the cholesterol level, an increase that is much greater than can be attributed to an alteration in the concentration of the serum.

When determinations are made day by day in the normal individual the fluctuations in the level of cholesterol will show a curve with a range of more than 100 mg., in the unstable person the range may be more than 300 mg.

The anoxemic stimulus results in greater liberation of acid metabolites and as might be anticipated, each cyclone is associated with an acidity which follows in its wake, the degree and duration of which is, of course, a purely individual matter. It depends on the constitutional type, on the buffering, on the season, etc. In unstable persons the fluctuations may be quite marked. While the change in the pH may be abrupt, day by day determinations reveal a distinct sequence of increasing and decreasing levels. When me-