Centrifugal propagation of virus from the CNS into peripheral nerves is a well established phenomenon in at least two neurotropic infectious diseases, rabies (1) and endemic encephalomyelitis of horses, cattle, and sheep (Borna disease) (2), and in the former is probably related to viral excretion. In poliomyelitis, centrifugal spread from the CNS into peripheral nerve ganglia is known to occur (3), but its dissemination into the more distal portions of the peripheral nervous system has been questioned, notably by Sabin and Ward (4) on the basis of negative tests in certain human tissues, including the salivary glands, adrenals, and cervical sympathetic ganglia. These investigators did not, however, test peripheral nerves themselves for virus. On the other hand, Bumet and Jackson (5) in 1940 obtained positive tests from vagus, sciatic, and sympathetic nerves of two *cynomolgus* monkeys paralyzed after intracerebral and intracocular inoculations with the Mar and MV strains respectively, but, for reasons that are not clear from their protocols, regarded centrifugal spread along nerves as “exceptional.” In 1950 we made a few preliminary tests on brachial, sciatic, and vagus nerves, with some positive results, to which we referred briefly in a previous paper of this series (6). The present report deals with these and with further observations. The subject has, we believe, an important bearing on the general nature of the disease and, on the mechanism of excretion and on certain clinical aspects which will be presently discussed.

We have employed two different experimental approaches to the problem. In one, virus was applied to the cut sciatic nerve on one side and its migration followed into the cord and outward through the contralateral nerve roots, ganglia, and peripheral nerves. In the other, virus was introduced into the brain and its centrifugal migration followed into various peripheral ganglia and nerves.

Observations were also made during the course of infection on the viral content of blood, muscle, nasopharyngeal washings, and intestinal contents.

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

**Virus.**—The Wis '45 strain (Type 1) was used throughout. The titer of the stock suspension was PD₅₀ 4.9. It causes infection with great regularity by a variety of routes of administration, and has been used in most of the previous papers of the present series.

**Monkeys.**—Macaca irus (cynomolgus) monkeys supplied by Okatie Farms, Pritchardville, South Carolina, were used throughout the study. They were of average weight (5 to 8 pounds; 2.3 to 3.6 kg.).

**Technic of Sciatic Nerve D/p.**—The left sciatic nerve was exposed in the lower posterior thigh, just above the bifurcation and freed as completely as possible of its connective tissue sheath. 0.1 ml. of 33 per cent virus suspension (2700 PD₅₀) was dropped on the subjacent fascia; the nerve was then divided by sharp scissors and the proximal end immediately dropped into the pool of virus. Previous experiments (7) had shown the necessity of immediate contact between virus and cut nerve ends to assure takes. After 2 to 5 minutes the excess virus was sponged off, and the wound closed. All sciatic nerve dip experiments were done under nembutal anesthesia.

**Technic of Intrathalamic Inoculations.**—The head was shaved and a burr hole made with a small trephine over the coronal suture about ½ inch lateral to the midline. A 22 gauge needle attached to a syringe was introduced perpendicular to the surface, aimed at the ipsilateral angle of the jaw and directed slightly inward to a depth of ½ inch depending upon the size of the animal. The usual amount injected into a given side has been 0.5 ml. For primary inoculations, injections have been unilateral; for subinoculations, bilateral. All intrathalamic inoculations were done under ether anesthesia.

**Removal and Preparation of Tissues for Subinoculation.**—All animals were sacrificed by exsanguination under ether anesthesia. About 125 to 150 ml. of blood was aseptically withdrawn from the heart by syringe and placed in flasks with heparin. It was prepared and subinoculated intrathalamically and intraperitoneally according to a procedure previously described (8). Individual nervous tissues were dissected aseptically, using separate instruments for each, withmeticulous avoidance of cross-contamination. When successive samples (proximal, middle, distal, etc.) of the same nerve were selected for testing, intermediate segments approximately 5 mm. in length were removed and discarded, to provide discontinuity. Nerve samples varied from 3 to 10 cm. in length, and, in the case of brachial and sciatic segments, from 133 to 370 mg. in weight. Sympathetic nerve samples were much smaller (not weighed). The weights of ganglia were: Gasserian, 42 to 65 mg.; nodose and sympathetic, 13 to 17 mg. Like specimens from the different animals in each group were pooled, stored in the deep freeze, and then prepared and inoculated by the procedures described in a previous paper (9). Preparations of ganglia were made up to a final volume of 2.5 ml. in saline; nerve preparations, of 4.0 to 5.0 ml.; and muscle preparations, of 2.5 ml. Muscle samples in 25 per cent suspension were homogenized in the Waring blender before concentration by high speed centrifugation and resuspension of pellet. The amounts of original tissue represented in the inocula injected into each test animal are shown in Table I.

Nasopharyngeal washings and contents of the large intestine, were concentrated by high speed centrifugation and the resuspended pellets inoculated intrathalamically, following the previously described procedure (6).

Samples of the spinal cord from animals with primary inoculations were examined histologically for lesions of poliomyelitis, and in the case of subinoculated animals similar examinations were made. In those animals not showing overt signs of infection, more complete histological examinations of the brain stem and cord were made to discover evidence of inapparent infection.

**Estimated Blood Content of Fixed Tissues.**—In interpreting the tests for virus in the various tissues examined, one must consider the possibility that positive tests may have been due
to contamination with virus-containing residual blood rather than to virus in the intrinsic tissues. While the blood was not titrated for its viral content, it should be noted that we used very large samples, 15 to 20 ml., for testing and that in our 4 day sample specimens (3A, 4A) one test was positive and one negative, suggesting that not more than one infective dose was present in that amount, or about 0.06 ID per ml. Samples of ganglia, nerves, and muscle were weighed and their content of residual blood estimated on the basis of 4 per cent of their weights, assuming that blood normally constitutes 8 per cent of body weight and that half the blood was removed at the time of sacrifice. The amounts of tissue and blood represented in individual inocula were calculated from the proportion of the final tissue suspensions.

**TABLE I**

<table>
<thead>
<tr>
<th>Individual Inocula</th>
<th>Weight</th>
<th>Blood content</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg.</td>
<td>ml.</td>
</tr>
<tr>
<td><strong>Ganglia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gasserian</td>
<td>67–89</td>
<td>0.003–0.004</td>
</tr>
<tr>
<td>Nodose</td>
<td>21–27</td>
<td>0.0008–0.001</td>
</tr>
<tr>
<td>Cervical sympathetic</td>
<td>22–26</td>
<td>0.0009–0.001</td>
</tr>
<tr>
<td><strong>Nerves</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brachial, proximal</td>
<td>296</td>
<td>0.012</td>
</tr>
<tr>
<td>“ middle</td>
<td>160–200</td>
<td>0.006–0.008</td>
</tr>
<tr>
<td>“ distal</td>
<td>150–188</td>
<td>0.006–0.008</td>
</tr>
<tr>
<td>Sciatic, proximal</td>
<td>83–166</td>
<td>0.003–0.007</td>
</tr>
<tr>
<td>“ middle</td>
<td>53–106</td>
<td>0.002–0.004</td>
</tr>
<tr>
<td>“ distal</td>
<td>89–177</td>
<td>0.004–0.007</td>
</tr>
<tr>
<td><strong>Muscle</strong></td>
<td>3300</td>
<td>0.132</td>
</tr>
<tr>
<td><strong>Blood</strong></td>
<td></td>
<td>15–20</td>
</tr>
</tbody>
</table>

* The spinal ganglia were not weighed; on inspection they appeared to be approximately the same size as the Gasserian.

Injected into each test animal. It may be noted that peripheral nerve has a relatively small blood supply and that most of the specimens appeared almost bloodless; our estimates of residual blood in them were therefore probably maximal. Excepting in muscle, the amounts of residual blood were extremely minute (Table I).

**PROTOCOLS OF INDIVIDUAL EXPERIMENTS**

**Preliminary Series**

**EXPERIMENT 1.**—2 *cynomolgus* monkeys, infected respectively by pharyngeal swabbing and intrathalamic inoculation with virus, were sacrificed 17 days after exposure, at the time of complete paralysis, and portions of the brachial and sciatic nerves were removed from which pooled suspensions of like specimens were prepared and inoculated intrathalamically into *cynomolgus* monkeys.
Results of Subinoculations.—One monkey receiving sciatic nerve suspension April 17, 1950, developed tremors on April 24 and complete paralysis on April 26. Typical lesions were found in all three levels of the cord. One monkey receiving sciatic nerve suspension and two monkeys receiving brachial nerve suspension remained well.

EXPERIMENT 2.—Three cynomolgus monkeys, infected by intrathalamic inoculations of sciatic nerve, Gasserian and nodose ganglia, respectively, were sacrificed 9, 14, and 17 days after first exposure, at the time of complete paralysis; portions of the vagus, brachial, and sciatic nerves were removed and pooled suspensions of like tissues prepared and inoculated intrathalamically.

Results of Subinoculations.—Two monkeys receiving brachial nerve suspension on May 15, 1950, developed complete paralysis, one on May 24 and one on May 27. Sections of the cords of both animals showed typical lesions of poliomyelitis.

Two animals received sciatic nerve suspension on May 15, 1950. One of these died of pneumonia on May 17th. The other developed typical paralysis on May 21st; sections of the cord showed characteristic lesions.

Two animals received suspensions of vagus nerve; both remained well.

Summary of Preliminary Experiments.—By subinoculation virus was detected in both sciatic and brachial nerves of monkeys infected by pharyngeal swabbing or intrathalamic inoculation and sacrificed at the time of paralysis.

Left Sciatic Nerve Dip

EXPERIMENT 3A.—4 cynomolgus monkeys, sacrificed on the 4th day.

Results of Primary Inoculation.—No symptoms; CNS lesions in 1/4.

Results of Subinoculations.—Cord L4-S2, 2/2 positive; right spinal ganglia, L4-S2, 3/2 positive; blood, 2/2 positive. Nerves: right cord to ganglia, proximal, middle, and distal sciatic, and leg muscle all negative, 2 tests each.

EXPERIMENT 3B.—4 cynomolgus monkeys, sacrificed on the day of onset of symptoms (4, 6, 7 days after inoculation).

Results of Primary Inoculation.—Paralysis in 4/4; CNS lesions in 4/4. C7-94: onset at 4 days; complete paralysis left leg in a.m.; weakness right leg began in p.m. C7-98: onset at 6 days; paralysis both legs. C7-99: onset at 7 days; paralysis left leg, weakness right leg in a.m.; paralysis both legs in p.m. C8-00: onset at 7 days; paralysis left leg, none in right leg; paralysis both legs in p.m.

Results of Subinoculations.—Nerve roots, spinal ganglia L4-S2, middle sciatic and distal sciatic segments, and blood positive; distal sciatic segments and leg muscle negative.

EXPERIMENT 3C.—4 cynomolgus monkeys, sacrificed on the day after onset of symptoms (onset 4, 5, 5, 5 days after inoculation).

Results of Primary Inoculation.—Paralysis in 4/4; CNS lesions in 3/3 (one not examined histologically). C7-85: onset at 5 days, paralysis both legs. C7-85: onset at 5 days; paralysis both legs, more on left. C7-89: onset at 4 days; paralysis both legs. C7-91: onset at 5 days; paralysis right leg; on 6th day, paralysis both legs.

Results of Subinoculations.—Nerve roots, spinal ganglia L4-S2, middle sciatic and distal sciatic segments, leg muscle, and blood positive; proximal sciatic segments negative.

EXPERIMENT 4A.—4 cynomolgus monkeys, sacrificed 4 days after primary inoculation.

Results of Primary Inoculation.—No symptoms; CNS lesions in 1/4.
Results of Subinoculations.—Spinal ganglia, leg muscle, blood positive; nerve roots, all sciatic segments, negative.

EXPERIMENT 4a.—2 cynomolgus monkeys, sacrificed on the day of onset of symptoms (onset 5, 6 days after primary inoculation).

Results of Primary Inoculation.—Paralysis in 2/2; CNS lesions in 2/2. C8-87: onset at 6 days; paralysis left leg, right face; no paralysis right leg. C8-88: onset at 5 days; paralysis left leg in a.m.; right leg in p.m.

Results of Subinoculations.—Spinal ganglia L4-S2, distal sciatic segment, leg muscle, positive; nerve roots, proximal and middle sciatic segments, negative.

EXPERIMENT 4b.—2 cynomolgus monkeys, sacrificed on the day of onset of symptoms (onset 5, 6 days after primary inoculation).

Results of Primary Inoculation.—Paralysis in 2/2; CNS lesions in 2/2.

Results of Subinoculations.—Spinal ganglia L4-S2, distal sciatic segment, leg muscle, positive; nerve roots, proximal and middle sciatic segments, negative.

EXPERIMENT 4c.—2 cynomolgus monkeys, sacrificed the day after onset (onset 9, 7 days after primary inoculation).

Results of Primary Inoculation.—Paralysis in 2/2; CNS lesions in 2/2.

Results of Subinoculations.—Spinal ganglia, nerve roots, positive; leg muscle, positive; cervical ganglia, negative.

Primary Intrahalamic Inoculation

In the following experiments, the primary inoculation consisted of 1000 PD₅₀ of Wis '45 virus.

EXPERIMENT 5a.—2 cynomolgus monkeys, sacrificed on the day of onset of symptoms (5, 5 days after primary inoculation).

Results of Primary Inoculation.—Paralysis in 2/2. C8-31: tremors; paralysis of left leg. C8-32: ophthalmoplegia, bilateral facial paralysis, quadriplegia.

Results of Subinoculations.—Gasserian, nodose, cervical sympathetic (superior and inferior) ganglia; cervical sympathetic cord; trigeminal (maxillary and mandibular), vagus, proximal brachial nerves; heart muscle; blood; intestinal contents and nasopharyngeal washings positive. Celiac ganglia, splanchnic, middle and distal brachial, all segments of the sciatic nerves, arm and leg muscles negative.

EXPERIMENT 5b.—2 cynomolgus monkeys, sacrificed the day after onset of symptoms (onset 5, 5 days).

Results of Primary Inoculation.—Paralysis in 2/2. C8-29: paralysis both legs and right arm. C8-30: paralysis both legs and left face.

Results of Subinoculations.—Gasserian, nodose, and cervical sympathetic ganglia, proximal brachial and middle sciatic segments, blood positive. Celiac ganglia, maxillary-mandibular, vagus, splanchnic, remaining brachial and sciatic segments, arm and leg muscles, intestinal contents, and nasopharyngeal washings (NPW) negative.

EXPERIMENT 5c.—2 cynomolgus monkeys, sacrificed the day after onset, both moribund (onset 6, 6 days).

Results of Primary Inoculations.—Complete paralysis, 2/2.

Results of Subinoculations.—Gasserian, nodose, cervical, sympathetic ganglia, vagus, middle and distal brachial, proximal, middle, and distal sciatic segments, intestinal contents, and NPW positive. Celiac ganglia, maxillary-mandibular, splanchnic, proximal brachial nerves, arm, leg, and heart muscle, and blood negative.

The results of Experiments 3 and 4 are tabulated in Table II; and of Experiment 5, in Table III.
Summary of Results.—After the introduction of virus into one sciatic nerve, its centripetal migration to the cord was followed by centrifugal migration, first into the contralateral ganglia and later into the proximal, middle, and distal segments of the contralateral sciatic nerve. After intrathalamic inoculation, the most proximal (cranial) ganglia and nerves were first infected, and the more distal (brachial and sciatic) nerves last, again demonstrating centrifugal spread. The results, both positive and negative, failed to show a correlation with viremia; several negative tests with nerve tissue occurred when viremia was present and several positive tests occurred when it was absent. Moreover,

<table>
<thead>
<tr>
<th>TABLE II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sciatic Nerve Dip</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>Animals per pool</th>
<th>Days after inoculation</th>
<th>Subinoculations</th>
</tr>
</thead>
<tbody>
<tr>
<td>3A</td>
<td>4</td>
<td>4</td>
<td>+ +</td>
</tr>
<tr>
<td>4A</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>3B</td>
<td>4</td>
<td>4, 6, 7, 7</td>
<td>++ 0</td>
</tr>
<tr>
<td>4B</td>
<td>2</td>
<td>5, 6</td>
<td>++ + 0</td>
</tr>
<tr>
<td>3C</td>
<td>4</td>
<td>4, 5, 5, 7</td>
<td></td>
</tr>
<tr>
<td>4C</td>
<td>2</td>
<td>7, 9</td>
<td></td>
</tr>
</tbody>
</table>

- , positive result with paralysis; 0, negative result; --, not tested. Each + and 0 sign indicates one subinoculated monkey.

* Tibial and common peroneal nerves with some of their branches.

the estimated amounts of blood in the peripheral nervous tissues were extremely minute. In the case of muscle, some negative tests were obtained when viremia was present; but no positive tests, in its absence. In muscle, the estimated amounts of residual blood were relatively large and some of the positive tests may therefore have been due to viremia. The alternative explanation of positive tests in muscle from virus in the intramuscular nerves is not, however, excluded; in two instances, virus was detected simultaneously in leg muscle and distal segments of the sciatic. It is noteworthy that after intrathalamic inoculation, when the arm and leg muscles were negative and the blood was positive, a positive test was obtained both from the cardiac muscle and the vagus nerve, suggesting that the origin of the virus in the muscle may have been the cardiac nerve supply rather than the residual blood.
### Table III

**Intrathalamic Inoculation**

<table>
<thead>
<tr>
<th></th>
<th>Day of onset</th>
<th>Day after onset: partial paralysis</th>
<th>Day after onset: complete paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiment No.</td>
<td>5A</td>
<td>SB</td>
<td>5C</td>
</tr>
<tr>
<td>Animals per pool</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Day of onset</td>
<td>5, 5</td>
<td>5, 5</td>
<td>6, 6</td>
</tr>
<tr>
<td>&quot; &quot; sacrifice</td>
<td>5, 5</td>
<td>6, 6</td>
<td>7, 7</td>
</tr>
</tbody>
</table>

**Subinoculations**

- **Ganglia**
  - Gasserian
  - Nodose
  - Cervical sympathetic
  - Celiac

- **Nerves**
  - Trigeminal
  - Cervical sympathetic
  - Vagus
  - Splanchnic
  - Brachial
    - Proximal
    - Middle
    - Distal
  - Sciatic
    - Proximal
    - Middle
    - Distal

- **Muscles**
  - Arm
  - Leg
  - Heart

- **Blood**

- **Intestinal contents**

- **Nasopharyngeal washings**

* Maxillary and mandibular divisions.
† Mainly median, ulnar, and radial nerves: proximal segment, from axilla to middle of humerus; middle, same, to elbow; distal, same, to wrist.

The uniform absence of virus in the splanchnic nerves and celiac ganglia is interesting, and suggests that centrifugal spread from the spinal cord along these pathways encounters some difficulty and that the lesions so often found
ENTRY AND EGRESS OF POLIOMYELITIC INFECTION. VI

in the celiac ganglia are more apt to be due to centripetal spread from the
gut than to centrifugal invasion from the CNS.

The nasopharyngeal washings and the intestinal contents were positive only
when virus was demonstrated in peripheral nerves with surface connections
(trigeminal, vagus) and were negative once when the blood was positive and
positive once when the blood was negative. These findings suggest that the
excretion of virus is related to nerve infection rather than to viremia, a conclu-
sion that we reached in a previous study (9).

DISCUSSION

The demonstration of centrifugal migration of poliomyelitis virus through
the peripheral nerves into their distal (and presumably terminal) segments
places poliomyelitis in close relationship with at least two other neurotropic
viral diseases, rabies and encephalomyelitis of horses (Borna disease), in both
of which the same phenomenon occurs (1, 2). In the case of poliomyelitis, as in
rabies, it throws light on the mechanism of excretion of virus. It may also
help to elucidate in part the origin of the most frequent clinical manifesta-
tions of the disease, localized pain and tenderness (10), for which no satisfactory
explanation has hitherto been found (11).

In a previous study (12) we have shown that virus is excreted into the
pharynx and intestine within 48 hours after its initial implantation into regional
ganglia, and that this is not due to multiplication in the mucosal surface, nor
to viremia, and probably not to outflow from lymphatics to the surfaces. The
present experiments supply further evidence in support of our previous con-
tention (9) that the presence of poliomyelitis virus in the alimentary tract is
not due to primary alimentary infection nor secondary to viremia but is a
sequel of primary neural infection associated with centrifugal viral migration
in the peripheral nerves.

Viral invasion of the peripheral nerves having been demonstrated as a
frequent and apparently constant feature of poliomyelitis, the question arises
whether the virus itself could set up irritative, inflammatory, or degenerative
changes within the nerves differing qualitatively from the secondary Wallerian
degeneration that follows nerve cell damage in this disease, particularly to the
motoneurons. Certain observations on record suggest that such may be the
case.

Nicolau and his associates (13) in 1929, in 5 monkeys dying of poliomyelitis after
intracerebral inoculation, found interstitial infiltrations of nerves with lymphocytes
and polymorphonuclear cells, and some slight perivascular infiltrations. Jordi (14)
in 1931 in 17 out of 20 infected monkeys found interstitial and small perivascular
infiltrations in peripheral nerves as early as 12 hours after the onset of paralysis. In
1932, O'Leary and his associates (15) "found evidence to indicate that a difference
exists between the changes occurring in fibers corresponding to affected segments of
the cord in poliomyelitis and the course of degeneration following nerve section. In several monkeys killed during the preparalytic stage and the first days of paralysis, the threshold of the large somatic fibers in nerves and roots belonging to affected nerve segments was lowered and their refractory period shortened, that is, nerve irritability was increased. This change, absent in the stages of degeneration of severed normal nerves, can bear two interpretations: direct injury of the axons by growth of the virus within them, or a reflection in the axons of the effect of its growth within the cell." The assertion by these authors that "there is no evidence that the myoneural junction is affected before fiber degeneration, a situation that might be expected if the virus acted peripherally," is contrary to the findings of Carey and his associates (16) in their study (1944) of acute human cases, in which they noted disintegrative changes in and near the myoneural junctions, which were much more marked than the changes in the proximad portions of the nerves and were therefore indicative of centripetal spread of degeneration. These abnormalities they regarded as strikingly different from those seen in Wallerian degeneration following nerve section. Denst and Neubuerger (17) in 1950, describing the nerve changes in acute human poliomyelitis, noted swelling, fragmentation, and reduced or lost staining properties of the axis cylinders and occasional interstitial lymphocytic infiltrations in the nerve trunks. These authors, too, considered the lesions to be different from those of Wallerian degeneration.

While further investigation of the subject is desirable, there appears to be enough evidence, both virological and histological, in favor of a direct viral effect on peripheral nerves to justify a suspicion that it might be one of the factors implicated in pain and tenderness. Our detection of virus in the vagus nerve may also throw light on the electrocardiographic abnormalities not infrequently observed (18–20) during the acute and early convalescent stages of the disease, which have been interpreted as indicative of an autonomic disturbance.

The presence of poliomyelitis virus in peripheral nervous tissue must also be taken into account in interpreting such positive tests as have been occasionally obtained from various "extraneural" tissues, for example pharyngeal wall, intestinal wall, kidney, lung, and liver (4); skeletal muscle (21), and myocardium (22); all of which contain nerve fibers in abundance, and some of which (intestine, myocardium) also contain nerve cells. It is interesting to note that in rabies, which is generally regarded as a strictly neurotropic infection, virus has also been recovered from spleen, liver, and kidney (23, 24). The presence of poliomyelitis virus in lymph nodes and tonsils (25–27) may well be referable to reabsorption from the excreting surfaces or deposition from the blood stream, rather than to active proliferation.

Questions of great interest, which remain to be investigated, are how long the virus persists in peripheral nerve and whether this period extends beyond the rather brief one when it remains demonstrable in the nerve cells of the CNS and ganglia, and in the blood stream. If, as seems possible, the latter
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question were affirmatively answered, the long continued excretion of polio-
myelitis virus into the intestine and occasionally also into the pharynx might
be explained, perhaps on the basis of the slow centrifugal movement of axo-
plasm described by Weiss and Hiscoe (28).

SUMMARY AND CONCLUSIONS

We have demonstrated a progressive centrifugal migration of poliomyelitis
virus from the CNS into various peripheral ganglia and into peripheral nerves,
including their distal portions. This phenomenon appears to be a regular
occurrence in experimental animals, and is similar to that found in two other
neurotropic infections, rabies and Borna disease.

Viremia appears to be secondary to primary neural infection.

The presence of virus in the lumen of the alimentary tract appears to be
secondary to primary neural infection and not to viremia, and to be associ-
ated with the centrifugal spread of virus in peripheral nerves.

The presence of virus in "extraneural" tissues is not per se referable to in-
fected of their constituent cells but rather to infection of their supplying
nerves or, in some instances, to their content of virus-bearing blood.

The finding of virus in the vagus nerve may throw light on some of the elec-
trocardiographic changes noted in certain cases of human poliomyelitis.

The presence of virus in peripheral nerves may throw light on the etiology
of the most frequent clinical manifestations of human poliomyelitis, localized
pain and tenderness.

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