During the past two years, evidence has been accumulating that it may be possible to transmit the virus of human poliomyelitis to rodents as well as to monkeys. Armstrong (1939) has reported the transmission of the Lansing strain of virus from monkeys to cotton rats (1) and white mice (2), Toomey and Takacs (1940) the Lansing and Flexner MV and Philadelphia strains to cotton rats (3), and Jungeblut and Sanders (4-8) (1940, 1941, 1942) the SK New Haven fecal strain to cotton rats, white mice, and guinea pigs. Following preliminary unsuccessful attempts to establish the SK monkey strain in rodents (9), Toomey and Takacs (10) recently succeeded in acclimatizing the same virus in cotton rats and guinea pigs. An opportunity for studying the histopathology of the SK rodent virus infection in white mice and guinea pigs submitted by Jungeblut and Sanders has led to the following observations.

Observations on Swiss White Mice

The infection transmitted to white mice from cotton rats has continued to be passed serially. The details as to materials and methods used, and of the clinical syndrome produced in the animals by the infection have been described in detail by these investigators, and only brief reference will be made to them here. This histopathological study was carried out on a group of mice comprising approximately the 38th to the 235th generation of mice following the initial passage. Transmission was successful by intracerebral, intraperitoneal, intravenous, and subcutaneous inoculation, nasal instillation, and gavage of suspensions of infected mouse cord and brain. By the intracerebral route, dilutions of $10^{-6}$ to $10^{-8}$ were regularly infective. Somewhat larger amounts of virus, i.e. dilutions of $10^{-3}$ to $10^{-6}$, were employed for intraperitoneal, intravenous, and subcutaneous inoculation and 0.1 cc. of a 10 per cent suspension was used for nasal instillation and gavage. Within 2 to 4 days, and rarely up to 7 days, the animals became sluggish, often had roughened fur, crouched, developed flaccid paralysis of one
or both hind limbs, and less often of one or both forelimbs, at times showed
limpness of, and dragged their tails, occasionally had Jacksonian or generalized
convulsions or head tremors, evidenced respiratory difficulty, became pro-
strated, and died.

Methods.—All of the mice used for pathological examination were killed by etheri-
zation in the period between the onset of paresis in one or more limbs and the time
they became moribund. The autopsy was performed immediately after the cessation
of respiration; the spinal cord and brain were removed first and fixed in either 10 or
20 per cent formalin solution. In some instances, segments of freshly removed
spinal cord and brain were also fixed in formalin ammonium bromide solution, 95
per cent alcohol, and Zenker’s solution. Occasionally the sciatic nerves and eyes
were also removed and fixed in 10 or 20 per cent formalin solution. Specimens of
each of the other organs were fixed in Zenker’s solution in each instance. In fifteen
mice, the brain and spinal cord were removed within their boney casings, the skull
and vertebral column, and the whole fixed in 10 per cent formalin for 24 hours, the
skull being perforated and the spinal canal being opened at a number of points.
Decalcification was carried out in 1 per cent formic acid for 24 hours and the speci-
mens sectioned for embedding. Paraflin sections cut at 4 to 5 micra were used for
the majority of stains, at 10 to 18 micra for the Mahon stain, and frozen sections were
cut for the metallic glial and fat stains.

As nearly as was possible, a complete sampling of the central nervous system was
carried out, while only segments of the other organs, and occasionally sciatic nerves
and eyes were examined. The appropriate stains for the demonstration of Nissl
substance, myelin sheaths, neurofibrils, astrocytes, microglia, blood vessels, and other
connective tissues and neutral fat were carried out on the neural tissues and the
hematoxylin-eosin stain on the other organs.

In the study of the neural tissues, the findings in each animal were tabulated noting
the position and approximate severity of the lesions. The intensity of the tissue
reaction was graded roughly in the following fashion: + -- very slight, + -
slight, + mild, ++ moderate, +++ marked, and ++++ very marked. The
degree of local edema and congestion, the presence and degree of perivascular and
diffuse parenchymal infiltration by hematogenous elements, the occurrence and
extent of ganglion cell degeneration, the amount of microglial activation, the oc-
currence of astrocytic reaction, the presence of endothelial hyperplasia in the capil-
laries, and the degree of secondary leptomeningeval infiltration were all considered in
determining the severity of the lesions.

Material.—In all, fifty-six mice were studied in this fashion. Of these, nineteen
had been inoculated intracerebrally, twelve intravenously, ten intraperitoneally,
and five subcutaneously, while six had been infected by gavage and four by nasal
instillation. In general, the pathological changes produced in the central nervous
system upon inoculation of the virus by the various routes enumerated were similar
at the late stage of the disease at which the animals were examined (between the
initial paralysis and the moribund state).

Gross Appearance of Organs.—No clearly recognized gross abnormalities could
be discerned in the brain or spinal cord, except for the occasional identification of the
inoculation tract in the intracerebrally infected animals. The spleen showed moderate enlargement in some of the animals, and the lungs were at times congested. Occasionally the liver was pale, and in one intravenously inoculated animal, it was yellowish in color.

**Histological Findings.**

**Spinal Cord.**—The spinal cord was found to be the site of histopathological changes in fifty of the fifty-six mice. The six mice whose spinal cords proved to be negative will be discussed below. Of the fifty mice with positive findings, eighteen had been inoculated intracerebrally, twelve intravenously, nine intraperitoneally, and three subcutaneously, while four each had been infected by gavage and nasal instillation. The lumbar and sacral segments were involved forty-five times, the thoracic segments and the cervical region thirty-six times. One or both anterior horns showed abnormal changes at many levels of the spinal cord in each animal listed as positive, while the posterior horns were less often involved. Even in those mice in which the lesions were most severe, there were many levels at which no abnormalities were found. In addition to being the most frequent site of lesions, the lumbar cord was also the region where they were most severe. They were classified as 4 + in four animals, as 3 + in ten, as 2 + in ten, and as + in nine, while thirteen were + - and + --. The cervical cord, although frequently involved, was less often implicated than the lumbar region. The majority of the lesions were approximately of the same severity as those at the lower level, but the most severe did not attain the intensity of the worst in the lumbar segments. Four mice showed 3 + lesions of cervical segments, ten 2 + lesions, nine +, and thirteen + - or + --. The changes in the thoracic region were relatively infrequent and also milder in degree. Only two mice showed 2 + lesions, while the other five had lesions of lesser severity.

Where the **anterior horns** were most severely affected, all of the grey matter was involved in its entire dorsoventral extent with some extension into the bases of the **posterior horns** (Fig. 1). In the majority of instances, only a part of a given anterior horn showed abnormalities and these were usually in the ventral half of the horn. Where the lesions were least developed, they were at times confined to the ventral margin of the anterior horn.

The outstanding feature of the histopathology in the anterior horns was the degeneration of the **nerve cells** (Fig. 1). On the average, one-half or less of the ganglion cells were destroyed or were undergoing necrosis while the proportion ranged roughly from an involvement of one-tenth to a total disappearance of the neurocytes. The evidence of nerve cell injury ranged from mild changes, such as diffuse or central fragmentation of Nissl substance, to total disintegration of the cell (Fig. 2). The chromatolysis was of varying degree and was accompanied by a swelling of the cell and often eccentricity or margination of the nucleus with final extrusion. Some cells had lost their Nissl substance, but had retained a centrally placed nucleus. The cytoplasm and nuclei of these cells showed varying degrees of loss of staining power, the increasing pallor being climaxed by complete fading out of the cell without fragmentation. The cytoplasm of other ganglion cells was coarsely or finely vacuolated or reticulated in addition to showing tigrolysis, and occasionally became coarsely granular. The nuclei at times showed irregular corrugation or crenation of their membranes with clumping of their chromatin. Occasionally, the oxychromatin
became prominent or the nucleoli were eccentric or were extruded. Shrinkage of the nerve cell body was often associated with a total loss of Nissl substance, homogeneous cytoplasm which was deeply stained (eosinophilic in the hematoxylin-eosin stain), and shrunken central nucleus in which the chromatin material had completely coalesced into a solid, deeply staining oval mass in which the nucleolus could no longer be discerned. Intracellular neurofibrils in such heavily damaged necrotic cells were found to be extensively fragmented and the fragments swollen and distorted, and often neurofibrils could not be stained. In other nerve cells which gave evidence of lesser degrees of injury, the neurofibrils were often surprisingly well preserved, although coalescence, swelling, and tortuosity of the fibrils were occasionally seen. Swelling and distortion of dendrites, axones, and of myelin sheaths related to the degenerating ganglion cells were observed.

The inflammatory reaction was usually mild and relatively inconspicuous (Fig. 1). There was perivascular infiltration by lymphocytes, large mononuclear cells, and polymorphonuclear leucocytes. The cells in the Virchow-Robin spaces were not ordinarily numerous and often fewer in number than those located interstitially in the parenchyma of the involved anterior horn. In addition to being present in the affected grey matter, similar perivascular infiltration was encountered on radii, extending from the affected grey matter into the adjacent anterior and lateral white columns (Fig. 1). Occasionally near the point of emergence of an anterior, or entry of a posterior, root, a tiny focal area of edema and polymorphonuclear infiltration was encountered in the white matter. The diffuse parenchymal infiltration was somewhat more marked, and most often restricted to that portion of the anterior horn showing nerve cell degeneration (Fig. 1). Here lymphocytes and polymorphonuclear leucocytes were found near the damaged ganglion cells. Where the injury was obviously great and cell death had occurred, polymorphonuclear leucocytes were at times gathered at the cell membrane indenting it or lying in deep hollows in the cytoplasm. In some instances, the nerve cell, its nucleus gone and its cytoplasm granular, swarmed with polymorphonuclear leucocytes which permeated its disintegrating body (Figs. 2 and 3). A similar mild inflammatory reaction was observed in the leptomeninges in the ventral sulcus (Fig. 1), and over the ventral and ventrolateral aspects of the spinal cord, and rarely over its dorsolateral and dorsal surfaces. At times, it was very sparse or absent, and rarely it was moderate in degree. Lymphocytes, large mononuclear cells, and lesser numbers of polymorphonuclear leucocytes were present in the subarachnoid space and pia.

A moderate microglial reaction was present in the affected areas of the anterior horns in the majority of animals (Figs. 4 and 5), and in some instances, this was marked. In general, it paralleled the ganglion cell degeneration, lagging behind it. There might, however, be some dissociation so that the microglial activation outstripped the nerve cell destruction. The microglial cells became hypertrophied and multiplied. Their bodies became elongated, their processes shortened, coarsened, and irregular, and their nuclei lengthened and slender, and often curved or irregularly sinuuous (Fig. 5). Conversion into lipoid-laden phagocytes, so called compound granule or gitter cells, was rarely observed in this group of animals. The perineuronal proliferation of these elements about a degenerating nerve cell, known as satellitosis, was not common, although regularly observed. The same was true of their presence.
in clusters within indentations and hollows in the cytoplasm of a necrotic nerve cell, participating in the process of neuronophagia.

The astrocytes within a zone of degenerating nerve cells showed a minimal reaction. They became hypertrophied, their nuclei becoming more prominent, their cytoplasm increased in amount, and their processes were more numerous. This was always slight but was more frequent at the margins of the anterior horn near its junction with the white matter. Rarely the capillaries in an affected zone showed endothelial hyperplasia. The endothelial cells increased in number, their cytoplasm became more abundant, and their nuclei plumper. Congestion was not common, and mild when present, and edema of the tissues even rarer. They were associated only with the severer lesions.

Reference has been made to six mice of the total of fifty-six in which no cord lesions were found. The observations in only three of these are considered significant, the cord examination in the other three being incomplete. In view of the absence of lesions at many levels of the spinal cord in animals found to have lesions at other levels, the possibility is given that lesions were missed in these three.

Medulla.—The medulla was involved in thirty-five of the fifty-six mice, fourteen having been inoculated intracerebrally, three intravenously, eight intraperitoneally, and five subcutaneously, while four were infected by gavage and one by nasal instillation. The lesions were of 4+ severity in one, 3+ in two, 2+ in eleven, + in thirteen, and + and ++ in eight.

These were marked chiefly by foci of moderate perivascular and diffuse infiltration by lymphocytes and polymorphonuclear leucocytes, and by moderate microglial proliferation. Ganglion cell necrosis was rare, and milder degrees of ganglion cell degeneration were common, but still relatively infrequent. Congestion, edema, and capillary changes varied, but were rarely conspicuous. Astrocytic reaction was virtually lacking, except in the few severer lesions. The lesions occurred most frequently in the dorsal grey masses in the floor of the fourth ventricle, and in the reticular formation. Leptomeningeal infiltration, like that in the spinal leptomeninges, was quite mild and occurred in the ventral midline and dorsolaterally, especially near the lateral angle of the fourth ventricle.

Pons.—This portion of the brain stem was the site of lesions in thirty-three mice, of whom, eleven were inoculated intracerebrally, seven intravenously, five intraperitoneally, and four subcutaneously, while five were infected by gavage and one by nasal instillation. The changes were for the most part moderate in degree and number. In one instance, the lesions were 4+, in five 3+, in twelve 2+, in six +, and in nine ++ and ++. Here again, as in the medulla, lesions were most frequent in the grey matter in the floor of the fourth ventricle and in general in the dorsal half of the pons. They were often conspicuous at one lateral angle of the fourth ventricle and in the reticular substance. Their general nature was similar to that in the anterior horns with the difference that in general nerve cell degeneration, although present, was not as conspicuous. In some foci, it might be intense, but usually the diffuse infiltration by lymphocytes and polymorphonuclear leucocytes, the microglial activation, and the perivascular infiltration overshadowed the ganglion cell changes. Congestion and edema varied as in the spinal cord and were usually relatively mild. Leptomeningeal infiltration by lymphocytes and
polymorphonuclear leucocytes occurred ventrally and near the lateral angles of the fourth ventricle.

**Cerebellum.**—This structure was involved in twenty-six mice. Eight were inoculated intracerebrally, seven intravenously, five intraperitoneally, and three each were infected by gavage and nasal instillation. The lesions were comparatively few in number and moderate in degree. In four mice, they were of 3 + intensity, in seven 2 +, in nine +, in six + - and + - -. They were located in the tectal nuclei and focally in the folia, involving the molecular and Purkinje cell layers (Fig. 9). The histological character of the lesions was in general similar to that described in the other grey masses. Ganglion cell necrosis was seen somewhat more often than in corresponding lesions in the brain stem.

**Midbrain.**—This portion of the brain stem contained lesions in nine mice. Five were inoculated intracerebrally, three intravenously, and one subcutaneously. The lesions were few and scattered, and were more often dorsal than ventral. The inflammatory changes, perivascular and leptomeningeal, usually predominated and the ganglion cell degeneration was rarely severe.

**Hypothalamus.**—This area of the cerebrum was affected in eighteen mice. Six were inoculated intracerebrally, one intravenously, two intraperitoneally, and one subcutaneously, while five were infected by gavage and three by nasal instillation. The intensity of the changes were 4 + in one, 3 + in three, 2 + in three, + in four, and + or + - - in seven. They were thus for the most part mild and were moderate in number. Their histological character was similar to that of the midbrain lesions.

**Thalamus.**—This locus was the site of lesions in thirty-three mice. Ten were inoculated intracerebrally, five intravenously, seven intraperitoneally, and three subcutaneously, while five were infected by gavage and three by nasal instillation. The lesions were 4 + in three mice, 3 + in five, 2 + in thirteen, + in eight, and + - and + - - in four. The majority of the lesions were, therefore, of moderate number in individual mice. These occurred more often in the dorsal than in the ventral portions of the thalamus and more frequently near the midline than laterally. The changes were predominantly diffuse and perivascular infiltration by cells like those seen elsewhere with associated microglial proliferation and relatively little, if any, ganglion cell degeneration. Such nerve cell changes were found principally in those intracerebrally inoculated animals in which the inoculation tract reached the thalamus.

**Corpus Striatum.**—This zone was involved in twenty-two mice. Six each were inoculated intracerebrally and intravenously, two intraperitoneally, and three subcutaneously, while four were infected by gavage and one by nasal instillation. In six instances, the lesions were 3 +, in six 2 +, in six +, and in four + - in intensity. The changes varied, therefore, from mild to marked but were chiefly of the inflammatory and reactive microglial type with relatively few ganglion cell changes. Although occurring in many animals, lesions were few in any single animal and often unilateral.

**Cerebral Cortex.**—The cerebrum was subdivided roughly into thirds in its rostro-caudal extent in recording the distribution of lesions. The changes in the olfactory centers, referred to below, were separately noted. Lesions of the pre- and post-
central areas, of the anterior third of the parietal area, and of the parorbital, anterior limbic, and prelimbic areas were listed under anterior third of the cerebrum; lesions of the posterior two-thirds of the parietal area, and of the superior temporal, posterior limbic, paracentral, and insular areas were listed as located in the middle third of the cerebrum; and lesions of the retrosplenial, occipital, middle and inferior temporal, and calcarine areas as occurring in the posterior third of the cerebrum.

**Anterior Third of Cerebrum.**—In spite of the fact that evidence of the inoculation tract, in the intracerebrally inoculated animals, was encountered more than twice as frequently in the posterior third of the cerebrum as in the middle and anterior thirds combined, the last was the most frequent site of severe lesions. The anterior third of the cerebrum was involved in thirty-one mice, of which thirteen had been inoculated intracerebrally, nine intravenously, four intraperitoneally, and one subcutaneously, while two each had been infected by gavage and nasal instillation. In twelve, the changes were of 4 + intensity, in twelve 3 +, in four 2 +, and in three + or + −, the average severity of the lesions being greater than that of those in the middle and posterior thirds of the cerebrum. The lesions were nearly always bilateral and more marked on one side. The ganglion cell changes, the diffuse, perivascular, and leptomeningeal infiltration, the microglial reaction and the other features of the pathological process were in general similar to those seen in the anterior horns of the spinal cord (Fig. 6). Here again, ganglion cell necrosis predominated, while the reactive inflammatory and glial changes were usually less intense and the leptomeningeal infiltration was secondary and focal.

**Middle Third of Cerebrum.**—This area of the cerebrum was involved in twenty-nine mice. Twelve of these animals had been inoculated intracerebrally, six intravenously, four intraperitoneally, and one subcutaneously, while three each had been infected by gavage and nasal instillation. In three mice, the lesions were of 4 + intensity, in eleven 3 +, in eleven 2 +, and in four +. Although these lesions were fairly severe, on the average they were definitely less so than those in the anterior third of the cerebrum. They were ordinarily bilateral and usually more intense on one side. Their histological characteristics were like those described in the anterior third of the cerebrum.

**Posterior Third of Cerebrum.**—This portion of the cerebrum was affected in twenty-four mice, of which eleven were inoculated intracerebrally, five intravenously, one intraperitoneally, and two subcutaneously, while three were infected by gavage and two by nasal instillation. In ten of these mice, the lesions were of 4 + intensity, in four 3 +, five 2 +, three +, and in two + and + − −. The inoculation tract as noted above was very frequent in this area in the intracerebrally inoculated animals, and was associated with the severest lesions, predominating on one side. The histological features of the lesions were essentially similar to those seen elsewhere in the cerebrum, often with the additional changes characteristic of a recent puncture wound of the brain.

**Rhinencephalon.**—Under this designation are included ganglia olfactoria, tubercula olfactoria, septal area, amygdaloid nuclei, and hippocampi. This region was involved in fifty-one mice, of which sixteen had been inoculated intracerebrally, eleven intravenously, eleven intraperitoneally, and three subcutaneously, while six were infected by gavage and four by nasal instillation. Thirty mice showed lesions
of 4 + intensity, fourteen of 3 +, three of 2 +, two of +, and two of + - - . The lesions were, therefore, very severe in the majority of the animals and this region was most regularly involved. The histological character of the changes was like that in other portions of the cerebrum with ganglion cell degeneration markedly predominating (Fig. 7).

Olfactory Bulbs.—Unfortunately, the olfactory bulbs were not examined in each mouse. They were studied in twenty-one mice of which two were inoculated intracerebrally, four intravenously, six intraperitoneally, and two subcutaneously, while three were infected by gavage and four by nasal instillation. Nineteen of these twenty-one mice had lesions in their olfactory bulbs. One of the intravenously, and one of the intraperitoneally inoculated animals were free of such changes. The lesions were of 4 + intensity in twelve animals, 3 + in three, 2 + in three, and + in one. The changes were of considerable severity, therefore, in the majority of the animals, including all of the intranasally infected, and some of each of those infected by each of the other routes. In three instances, in the two intracerebrally and one intraperitoneally inoculated mice, the lesions were isolated and unilateral. In most instances, however, the lesions were widespread and involved the glomerular, external granular, gelatinous, and mitral layers, and the external portion of the internal granular layer (Fig. 8). When the changes were less severe, they affected only the outer layers, the glomerular and external granular laminae for instance or the internal granular layer alone. The nature of the histological abnormalities was similar to that described under rhinencephalon, the ganglion cell changes predominating.

Other Organs.—The lungs were moderately congested in six of the fifty-six mice, the spleen showed congestion of its pulp and moderate numbers of polymorphonuclear leucocytes in its sinuses in ten, there were focal necroses of the liver in one mouse, and a fatty liver in another, an aspiration pneumonia in one, and acute gastric ulcers in one animal. These findings in other organs were obviously secondary or unrelated to the lesions in the central nervous system. No definite changes were detected in the lymphoid tissues that could be confidently related to the disease.

In reviewing the histopathological findings in the mice, it is clear that although a poliomyelitis of varying degree is constantly present, a poliomegalenititis definitely overshadows it. The regular involvement of the anterior horns at either the lumbar or cervical enlargement or both is striking, but the average severity of the lesions and the frequency of involvement falls below that noted for the cortex in the anterior third of the cerebrum, in the rhinencephalon, and in the olfactory bulbs. As has been noted above, there are no outstanding differences in the distribution of the lesions at the late stages of the infection that can be correlated with the varying portal of entry. This will have to be investigated further in animals examined during preparalytic stages of the infection. The histopathological changes seen in the anterior horns are dominated by ganglion cell degeneration which on the average affects approximately half of the neurones, while the inflammatory reaction, perivascular, diffuse, and leptomeningeal and microglial activation are usually mild or moderate,
and congestion and edema are mild. The progressive diminution in ganglion cell involvement as one ascends the central nervous system is reversed in the cerebral cortex and olfactory centers and the relative degree of involvement or participation of the various elements in the process reverts to that observed in the anterior horns. The significance of this observation will be discussed later.

**Observations on Guinea Pigs**

Recently Jungeblut and Sanders (1941, 1942) (6, 8) succeeded in establishing the above murine virus in guinea pigs and in maintaining the infection in series. Transmission of the infection from mouse to guinea pig succeeded by intracerebral, intraperitoneal, intravenous, and subcutaneous routes, while serial passage from guinea pig to guinea pig is as yet successful only by intracerebral inoculation. Single passages from guinea pig to guinea pig succeeded a few times by intravenous inoculation of brain and spinal cord. The effective dose of the murine virus for intracerebral inoculation of guinea pigs was $\frac{1}{10}$ cc. of a 10 per cent suspension of mouse brain, while intraperitoneally, subcutaneously, and intravenously, 1 to 2 cc. were necessary. In transmission from guinea pig to guinea pig, by the intracerebral route, $\frac{1}{10}$ cc. of a 10 per cent suspension of mixed brain and spinal cord was effective, while the few times that intravenous inoculation succeeded 1 cc. was used. The incubation period was approximately 2 to 4 days. A preparalytic fever terminated when flaccid paresis of the hind limbs supervened. This was sometimes more marked on one side. There was rapid progression to complete flaccid paralysis of the hind limbs, while the animal remained alert and apparently well otherwise. Its fur remained sleek and it often moved along briskly by the active use of its forelimbs while the hind limbs dragged behind. Weakness of one or both forelimbs at times followed, and occasionally there was slight intermittent tremor of the head. Complete flaccid paralysis of one or both forelimbs might develop, respiratory difficulty occurred, and the animal became prostrated and died in from 5 to 8 days. More recently, the course of the infection in serial guinea pig passages became more rapid so that the animals died in from 3 to 5 days. Partially paralyzed animals have recovered.

**Methods.**—The guinea pigs were killed by chloroform and their brains, spinal cords, and other organs were removed at once and fixed in 10 per cent formalin. The subsequent handling of the tissues was similar to that employed for the mice. In the study of the neural lesions, their approximate position and severity was noted and the intensity graded in the same manner as described for the mice.

**Material.**—A group of sixteen guinea pigs were studied histologically. Of these, 1

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1 On occasions, dilutions of 1:500 have been effective.
eight were inoculated intracerebrally with \( \frac{1}{10} \) cc. of a 10 per cent mouse brain suspension of the 72nd or a subsequent serial passage of murine poliomyelitis virus, one was inoculated intraperitoneally with 2 cc. of a similar 10 per cent mouse brain suspension, one was inoculated subcutaneously with 2 cc. of a 10 per cent mouse brain suspension, four were inoculated intracerebrally with \( \frac{1}{10} \) cc. of a 10 per cent suspension of mixed guinea pig brain and spinal cord, and two were inoculated intravenously with 1 cc. of a similar suspension. The animals were sacrificed between the time of development of a complete flaccid paralysis of the hind limbs and the occurrence of prostration.

In this late stage of the disease, the pathological findings were in general similar, except for the supervention of a separate, clearly distinguishable additional toxoplastic infection in the two guinea pigs which had been inoculated intravenously with a cavian strain. Their spinal cord and some of their brain stem lesions were in all respects similar to those to be described below in the remaining fourteen guinea pigs and clearly due to the transmitted virus. These two animals will be reported upon separately elsewhere.

GROSS FINDINGS.—Except for evidence of the inoculation tract, no gross abnormalities were noted in the brain or in the spinal cord. The spleen was slightly enlarged in three animals. The lungs were mildly congested in three guinea pigs and considerably so in three. In the last group of animals, there were small, slightly raised, lighter colored areas on the cut surfaces of the lower lobes.

HISTOLOGICAL FINDINGS.—

Spinal Cord.—The spinal cord was the site of lesions in all fourteen guinea pigs. The lumbar and sacral segments were involved in each, the anterior horns always being affected, while the posterior horns showed abnormal changes in all but one. The intensity of the lesions in the anterior horns in this region was 4 + in ten animals, 3 + in three, and 2 + in one, while in the posterior horns, they were considerably less marked, being 4 + in one, 3 + in two, 2 + in five, + in two, and + — and + — in three.

The thoracic segments were involved in nine guinea pigs, the anterior horns being affected in each, and the posterior horns in five. The intensity of the lesions in the anterior horns was 4 + in four, 3 + in two, and 2 + in two, while in the posterior horns, it was 4 + in two, 3 + in one, and + in two. Thus, although the abnormal changes were less frequent in the thoracic region, they were of the same order of severity as in the lumbar-sacral segments. The posterior horns were relatively less frequently involved in this region and again the lesions were less intense on the average than in the anterior horns.

The cervical segments were involved in all fourteen guinea pigs, the anterior horns being affected in each and the posterior horns in twelve. The severity of the changes in the anterior horns was 4 + in ten animals, 3 + in three, and + — in one, while in the posterior horns it was 4 + in three animals, 2 + in five, + in two, and + — in two. The lesions were, therefore, similar in frequency, distribution and intensity in this region to those in the lumbar-sacral portion of the spinal cord.

The anterior horns showed abnormal changes throughout their entire dorsoventral extent where the lesions were most severe (Figs. 10, 11, and 13) and at corresponding levels the posterior horns might exhibit equally intense changes throughout or in their
ventral two-thirds. It was more often the case that the ventral half or less of the given posterior horn was affected, and that the lesions were much less intense. Where the anterior horns were only partially affected, only the ventral extremities of the posterior horns might be involved or they might be free of lesions. At some levels only one anterior horn was involved (Fig. 10).

The most conspicuous feature of the process in the anterior horns was the degeneration of the nerve cells (Figs. 10, 13, 14, and 17), and where this was most severe, they might completely disappear (Fig. 13). More often from one-half to two-thirds of the neural elements were found in varying stages of degeneration, while the remainder might be remarkably well preserved. The details of the ganglion cell changes were essentially like those observed in the anterior horns of the spinal cord in the mice, and, therefore, will not be described further. Necrosis of ganglion cells occurred as well in the posterior horns, chiefly in their ventral portions, but was much less frequent there. In one guinea pig of those inoculated intracerebrally, single or multiple, round, eosinophilic intranuclear bodies, somewhat smaller than the nucleolus, were found in some of the ganglion cells (Fig. 18). There was no margination of the chromatin.

Although the inflammatory reaction was moderate, it was definitely more advanced than in the mice. Both the perivascular and diffuse infiltration were more florid (Fig. 13), the latter more so than the former. Lymphocytes, large mononuclear cells, and polymorphonuclear leucocytes were present in the perivascular spaces (Fig. 21) in variable numbers in the anterior horns, and in the affected portions of the posterior horns, and in the latter they might overshadow the ganglion cell changes. Similar perivascular infiltration was found irregularly and to a minor degree in the white columns near the involved portions of the grey. The diffuse infiltration consisted of lymphocytes and polymorphonuclear leucocytes (Figs. 14, 16, and 17), and more closely paralleled but always lagged behind the nerve cell changes. Polymorphonuclear phagocytosis of nerve cells similar to that described in the mice was frequent (Figs. 15 and 16). Leptomeningeal infiltration was quite mild and was usually ventral, including the ventral sulcus (Fig. 12). In places, it was also seen in the dorsal and dorsolateral portions of the leptomeninges as well. It was chiefly lymphocytic in type (Fig. 20) with variable numbers of polymorphonuclear leucocytes and large mononuclear cells.

The microglial reaction was similar in type to that observed in the mice but was in general much more marked in degree (Fig. 17). It always paralleled the ganglion cell degeneration and at times passed beyond it in intensity. In such instances, the cellularity of the involved anterior horns was greatly increased, the welter of lymphocytes, polymorphonuclear leucocytes, and hypertrophied microglial cells being dominated by the latter. Where the changes were severest, there occurred a moderate conversion of microglia into lipoid-laden phagocytes, or compound granule cells. This was more frequent and more conspicuous than in the mice, but never massive. These phagocytes were encountered in the perivascular spaces in varying numbers in such zones. Glial satellitosis and neuronophagia was often observed (Fig. 17).

Astrocytes exhibited the same minimal reaction described in the mice. Where the lesions were severest, moderate congestion and considerable edema might be observed.
(Fig. 13) and these were on the average greater than was usually seen in the mice. Occasional small recent hemorrhages were encountered in some of the more intensely involved anterior and posterior horns. Mild endothelial hyperplasia of the capillaries was seen with a fair degree of regularity in the affected grey matter.

**Medulla.**—The medulla was the site of lesions in two of the fourteen guinea pigs. These were small, scattered and few in number. They were marked chiefly by perivascular and, at times, associated focal leptomeningeal infiltration by lymphocytes, and less frequently, fewer large mononuclear cells and polymorphonuclear leukocytes. Rarely similar cells were seen in the nearby parenchyma. Ganglion cell degeneration and microglial activation were lacking. In two additional guinea pigs, there were mild focal areas of leptomeningeal infiltration ventrally and laterally without the presence of parenchymal lesions.

**Pons.**—In two guinea pigs, moderate to marked focal lesions were encountered, chiefly in the dorsal portion of the tegmentum. Their essential histological features were similar to those of the changes observed in the anterior horns with the difference that ganglion cell degeneration was not nearly as prominent. There was mild ventral and dorsal ventrolateral infiltration of the leptomeninges of the same character seen about the medulla.

**Cerebellum.**—None of this group of fourteen guinea pigs showed any changes in the cerebellum.

**Midbrain.**—Three guinea pigs exhibited lesions in this portion of the brain stem. These were few in number, mild in degree, bilateral, chiefly dorsal, and of the same character as in the medulla. Perivascular infiltration by lymphocytes was their chief characteristic and when they were near the surface there was an associated focal leptomeningeal area of infiltration. In four additional guinea pigs, mild or marked leptomeningeal infiltration by lymphocytes and occasional large mononuclear cells and polymorphonuclear leukocytes were seen on the ventral surface of the midbrain.

**Thalamus.**—Four guinea pigs showed scattered and limited lesions in the anterior and posterior portions of the dorsal aspect of the thalamus near the midline. These were unilateral in three animals, and associated with the inoculation tract in one. Three were of + + + intensity and one was 2 +. Ganglion cell degeneration, except as associated with the inoculation tract, was absent. Mild perivascular and diffuse infiltration by lymphocytes and occasionally polymorphonuclear leucocytes and a somewhat more marked microglial proliferation were their essential features.

**Hypothalamus.**—No strictly hypothalamic lesions were encountered in this group of guinea pigs.

**Corpus Striatum.**—This portion of the cerebrum showed limited involvement in three animals. In two, the lesions were associated with a portion of the inoculation tract, were unilateral, and were of 4 + and + + severity respectively, while in the third they were of + intensity. Their character was similar to that of the lesions described in the thalamus.

**Cerebral Cortex.**—The same rough subdivision into thirds in recording the distribution of lesions described for the mice was employed for the guinea pigs.

**Anterior Third of Cerebrum.**—The cortical areas in this portion of the cerebrum contained lesions (Fig. 19) in five guinea pigs. These were of 4 + intensity in two,
3 + in one. They were associated with an inoculation tract in three animals and were relatively few in number. In two, the lesions were bilateral. Ganglion cell degeneration was present in these lesions, but was usually mild. In a few, it was severe. The accompanying inflammatory reaction consisted of moderate and sometimes marked perivascular and diffuse infiltration by lymphocytes and, at times, polymorphonuclear leucocytes. The microglia hypertrophied and multiplied, and this change was at times quite marked.

Middle Third of Cerebrum.—The cortical areas in this zone were affected in seven guinea pigs. Three showed lesions of 3 + intensity, one of 2 +, one of +, and two of + −. In three the lesions were bilateral and in four they were associated with the inoculation tract. In general, they were even fewer in number and of lesser severity than those in the anterior third of the cerebral cortex, but had similar histological features.

Posterior Third of Cerebrum.—This zone of the cortex was involved in six animals which showed lesions of 4 + intensity in three, and + − − severity in the three others. The lesions were all unilateral and associated with an inoculation tract in three guinea pigs. They were limited in number and extent, and in the three instances in which they were very mild, consisted essentially of slight leptomeningeal and nearby cortical perivascular infiltration by lymphocytes. The severer lesions in the remaining three animals resembled the more intense, but limited changes described in the anterior third of the cerebrum.

Rhinencephalon.—Lesions were present in seven animals, all intracerebrally inoculated. In two, these were confined to the hippocampi. Four had only unilateral lesions. Three of these showed lesions of 4 + intensity and were associated with the inoculation tract. Of the remainder, one had lesions of + severity, one of + −, and three of + − −. Except in the severest lesions, ganglion cell degeneration was absent or minimal and the changes were inflammatory and glial.

Olfactory Bulbs.—The olfactory bulbs were examined in nine guinea pigs. They contained no lesions in seven animals, unilateral isolated 4 + lesions in one animal, and a few unilateral 2 + lesions in another. In each of the affected animals, the lesions were near the posterior extremity of the bulb and the gelatinous, mitral, and internal granular layers were involved, particularly the last. Perivascular and diffuse infiltration by lymphocytes and microglial reaction were associated with little or no ganglion cell degeneration.

Other Organs.—The spleen showed congestion of the pulp and moderate numbers of polymorphonuclear leucocytes in the sinuses in three guinea pigs. In three animals, there was mild pulmonary congestion and in three others, this was severe and associated with a lobular pneumonia. No lesions were found in the kidneys.

A review of the histopathological findings in the central nervous system in the guinea pigs leads to the conclusion that one is dealing with an intense poliomyelitis with which is associated a minor degree of meningoencephalitis. The lumbar and cervical enlargements of the spinal cord are markedly involved in every animal, the anterior horns being the site of the severest lesions, while the posterior horns are frequently but moderately affected. Ganglion cell degeneration is the chief feature of the
process, often involving one-half to two-thirds of the neurones, and not infrequently all of them. The inflammatory reaction, perivascular and diffuse, is mild or moderate in degree and the associated leptomeningeal infiltration is similar in type and limited in extent and location. Congestion and edema are usually mild or moderate, but they may become quite intense, particularly in the latter, and may be associated with small, fresh hemorrhages. Microglial activation is usually marked and at times very extensive. In general, there is a progressive diminution in the severity and number of the lesions as one ascends the central nervous system. Ganglion cell degeneration becomes progressively less prominent as one passes cephalad and the changes are essentially inflammatory and glial. The increase in the frequency and severity of the lesions in the cerebrum as compared to the brain stem is associated with, and principally confined to, the area of inoculation. The olfactory bulbs show only isolated lesions in two of the nine animals in which they were examined. In contrast to the mice, the cerebellum is not involved.

**DISCUSSION**

Whether the virus of human poliomyelitis has been transmitted from the monkey to rodents cannot be decided solely from a study of the pathologic changes in the central nervous system of the latter. One difficulty is the possibility that different species may react in different ways to the same virus. Another is that the types of reaction of the neural, neuroglial, and their associated mesodermal structures are rather limited and hardly specific for more than a very few conditions. Only through the biological evidence can a final conclusion be reached. However, with these reservations, the histology and localization of the lesions can offer corroborative evidence for the identity of the rodent disease with human poliomyelitis.

**Comparison of Lesions Induced in Mice by the J-S, Armstrong, and Theiler Viruses**

In the *mouse*, infected under the conditions herein described, one is dealing with a meningoencephalomyelitis. The encephalitis, particularly in the anterior third of the cerebrum, including the olfactory centers, definitely outweighs the myelitis in extent and gravity. The latter, however, is distinctly marked by being a poliomyelitis with preferential localization in the anterior horns. A comparison of the findings in these mice with those in the mice reported as infected with the Lansing strain of poliomyelitis by Armstrong (1, 2), and with those having Theiler's disease as reported by Thieier (11) and by Olitsky and Schlesinger (12) reveals certain similarities and a number of differences. Common to all is a meningoencephalomyelitis in which lesions of the anterior horns are a fairly constant feature, though often mild or moderate in degree. The details of the histopathological process in the anterior horns are essentially similar in each. Ganglion cell degeneration is the outstanding feature. Differences in the degree of inflammatory reaction, microglial
activation, and capillary proliferation probably depend upon the differences in rapidity of development of the process. The J-S virus is quite virulent and infection with it leads to death in 2 to 4 days; the Armstrong virus is less virulent, and mice often live longer than a week; while most strains of the Theiler virus do not produce paralysis till 4 days or more after inoculation. The absence of lesions in many segments of the spinal cord is noted both in the Armstrong and the present Jungeblut-Sanders group of animals. The spinal cord lesions are more frequent at the cervical level in the Armstrong group, and at the lumbar level in the J-S mice. Polymorphonuclear leucocytes are, perhaps, more frequent in the anterior horn lesions in the J-S animals than in those of either of the other two groups, and neuronophagia possibly somewhat more common in this group and the Armstrong group than in the Theiler mice.

The brain stem shows lesions in approximately three-fifths of the Jungeblut-Sanders mice, but the degree of ganglion cell degeneration is much less than that in the anterior horns of the spinal cord. The medulla and pons are about equally involved, the dorsal areas and reticular formation most commonly. The midbrain is relatively infrequently affected. In the Armstrong mice, the brain stem is involved in nearly all the animals and the lesions show a similar distribution. This difference in frequency may again be dependent upon the more rapid course of the infection with the J-S virus. In general, the brain stem distribution of the lesions in the Theiler mice, as described by Olitsky and Schlesinger (12), follows the same pattern given for the other two, and the histological changes are of similar type in all three, with neuronal degeneration being present but not prominent.

In the J-S mice, the cerebellum is involved in approximately half the animals, both the tectal nuclei and cerebellar cortex being affected. The lesions are moderate in degree and include somewhat more ganglion cell degeneration than do those of the brain stem. This is in contrast to the Armstrong and Theiler mice in which the cerebellar lesions are almost wholly of the tectal nuclei and milder in degree, chiefly inflammatory and reactive glial.

The hypothalamus is the site of lesions in over one-third of the J-S mice. Perivascular infiltration and microglial activation predominates in them. This area is not separately referred to in the other two series of mice.

The thalamus is affected in approximately three-fifths, and the corpus striatum in approximately two-fifths of the J-S mice. The lesions are essentially like those in the hypothalamus, and less frequent in the corpus striatum than in the thalamus where they are most often dorsal and near the midline. Ganglion cell degeneration is usually absent or mild except where the inoculation tract enters the area involved. Thalamic and striatal lesions are of the same type in the Armstrong and Theiler mice (Olitsky and Schlesinger), but much less frequent.

The cerebral neocortex is severely and extensively involved in three-fifths of the J-S mice, and the anterior third of the cerebrum is most often hit. Ganglion cell degeneration again becomes quite prominent in this portion of the central nervous system in contrast to the findings in the central and basal nuclei of the cerebrum, and in the brain stem. In the Theiler mice (Olitsky and Schlesinger), such cortical lesions are present in almost all the animals, but neuronal degeneration is apparently much less prominent and the lesions are very much fewer. The cortex is affected in
less than half of the Armstrong mice, and the lesions are again described as infrequent and the nerve cell degeneration as minimal.

The rhinencephalon, including the hippocampi, is affected in almost all of the J-S mice, and to a marked degree. The severity of the changes resembles that in the neocortex and often exceeds it. The hippocampi are described as being the structures in the cerebrum most frequently involved in the Armstrong mice.

The olfactory bulbs are regularly and often severely involved in the majority of the J-S animals inoculated by all the routes listed. No such lesions are encountered in the Theiler mice studied by Olitsky and Schlesinger, even in those infected by intranasal instillation and responding by paralysis. No data on this point are available in the Armstrong series.

In summary, the pathological changes in the central nervous system of the J-S, Armstrong, and Theiler mice are alike in that lesions of the anterior horns are fairly constant and similar in type in each, that each is marked by a meningoencephalomyelitis and that as one passes cephalad in the central nervous system, the frequency of ganglion cell degeneration progressively diminished in all (at least up to the cerebral cortex and excepting the cerebellum). They differ in that the J-S mice show much more severe and extensive involvement of the neocortex, rhinencephalon, and to a lesser degree of the cerebellum, while marked lesions are present in the olfactory bulbs as compared to a total lack of them in the Theiler mice. The greater virulence of the J-S virus may be in part responsible for these differences so that with a breakdown of local tissue immunity, the given area is overwhelmed. This is, however, not in consonance with the finding of approximately equal lesions in the anterior horns of the spinal cord in all three series of mice. The question of any similarity between the meningoencephalomyelitis in these mice and the meningoencephalomyelitis of monkey and man which goes by the name of poliomyelitis will be discussed later when the same problem arises in relation to the pathological changes in the central nervous system of the guinea pig.

In spite of the histopathological similarities between the disease in the J-S mice and those having Theiler's disease, it is unlikely that the latter spontaneous disease of mice has been induced in the Jungeblut-Sanders animals. The differences in virulence of the two viruses, when tested in young mice by peripheral routes, or in old mice by intracerebral injection, together with the fact that normal adult mouse serum neutralizes Theiler's virus but not the J-S virus, bar such a conclusion.

Comparison of Lesions Induced in Guinea Pigs by the J-S Virus with Those in So Called Spontaneous Guinea Pig Poliomyelitis

Roemer and Joseph (13) (1910) described a presumably spontaneous flaccid paralysis in 5 per cent of their guinea pig stock, and later Roemer (14) (1911) was able to
isolate a virus from these animals, but this was lost after a few passages. The latter pointed out what he considered to be the similarity of the clinical features of this disease to those of human poliomyelitis. He summed up the pathological changes as "meningo-myelo-encephalitis of predominantly lymphocytic type." The dominating change was the meningitis which his illustration of the spinal cord shows to have been of considerable intensity. The exudate was composed of lymphocytes with some polymorphonuclear leucocytes. Perivascular infiltration of the same sort was seen in the white matter, while the grey matter also showed diffuse infiltration which was particularly marked about the central canal. The anterior horns were less involved. The ganglion cells were well preserved at first, but with the onset of paralysis, some disappeared and others stained poorly. Neuronophagia was rare. The lumbar cord was always more intensely involved than the thoracic or cervical regions. The medulla was described as being only slightly affected. The cerebral leptomeninges, both dorsal and ventral, were heavily infiltrated, chiefly by lymphocytes; the ventricles contained a similar exudate, and there was marked perivascular lymphocytic infiltration in the underlying cortex. The author concluded that there was a similarity between the pathologic changes in these guinea pigs and those of human poliomyelitis. This does not appear to be borne out by the facts he has recorded.

Neustaedter (15) (1913) and Picard (16) (1925) reported the occurrence of what they interpreted as spontaneous poliomyelitis in guinea pigs which had been in close proximity to poliomyelitis-infected monkeys. These animals again showed predominantly flaccid paralysis of the hind limbs. The virus obtained from each group of animals was lost after a few passages. An emulsion of spinal cord and spinal fluid was used for intranasal instillation in guinea pigs by Neustaedter who also claimed to have successfully transmitted the infection from a monkey to a guinea pig and back to a second monkey by nasal instillation of filtered cord material from the first monkey to the guinea pig, and inoculation of an emulsion of the brain and cord of this guinea pig into the second monkey. Picard inoculated an emulsion of spinal cord of one of his guinea pigs showing spontaneous flaccid paralysis of the hind limbs intraperitoneally into other guinea pigs with the production of a similar picture. Neustaedter briefly described the pathologic changes in his guinea pigs as consisting of mononuclear infiltration of the leptomeninges in the ventral sulcus, pericellular infiltration by similar cells in the anterior horns, advanced degeneration of anterior horn ganglion cells, neuronophagia, and hemorrhages. Pial infiltration by lymphocytes was noted about the olfactory bulbs in one of the four guinea pigs examined and in one other, the brain was examined and reported free of lesions. Picard recorded the pathologic findings in one of his guinea pigs in the following abbreviated form: "only mild infiltration of the blood vessels, scattered hemorrhages in the anterior horns, and no definite edema. Severe degeneration of the nerve cells, vacuolization, pallor, and swelling, particularly in the motor elements of the anterior horns. Neuronophagia by glial cells is relatively slight, although occasionally seen." No mention was made of the rest of the central nervous system.

In the guinea pigs inoculated with the J-S murine virus or subinoculated with the cavian-passage virus, the histopathological changes in the central nervous system...
are marked by a predominant involvement of the spinal cord. The anterior horns are primarily affected and in them the degeneration of nerve cells is the outstanding phenomenon. One-half to two-thirds or more of the neurones are affected and this involvement is definitely more marked than in the mice. The associated inflammatory and microglial reactions, particularly the latter, are more prominent than in the mouse, and congestion and edema are more conspicuous. There is a striking decrease in the intensity and frequency of lesions in ascending levels of the central nervous system and ganglion cell degeneration diminishes in the same order. A detailed comparison with the distribution of lesions in the brain in human and simian poliomyelitis, as recorded by Bodian and Howe (17) and others, cannot be made until a study of preparalytic stages of the infection in guinea pigs has been carried out.

The pathologic changes in the Roemer animals are difficult to evaluate and compare. In spite of the paucity of recorded findings, the changes in the spinal cords of the Neustaedter and Picard guinea pigs show broad resemblances to those in the J-S animals.

Pathologic Evidence Bearing upon the Identity of the J-S Virus

The investigations of Jungeblut and Sanders lead them to believe that they have transmitted the SK New Haven strain of poliomyelitis virus from monkey to cotton rat to mouse and then to guinea pigs. The histopathologic changes in their mice do not in themselves substantiate this conclusion inasmuch as the rather constant but mild anterior poliomyelitis is accompanied by a severe encephalitis. The anterior poliomyelitis, however, is striking. In spite of the fact that a severe poliomyelitis, in the sense of a marked degeneration of neurones with associated inflammation and glial reaction in the grey matter of the spinal cord, may occur in mice in certain other experimental virus infections, such as louping ill, vesicular stomatitis, equine encephalomyelitis, and St. Louis encephalitis, there are features which distinguish these from the J-S infection.

While the anterior horns of the spinal cord are regularly involved in mice infected by the J-S virus no matter what the portal of entry, they are affected in vesicular stomatitis only if the portal be a peripheral one, such as muscle. In louping ill, the constancy of the involvement of the Purkinje cells, which are only secondarily and focally affected in the J-S animals, is one of a number of differential points. In equine encephalomyelitis in mice, the rhinencephalic cortex and hippocampi are severely affected as they are in the J-S mice, but the occurrence of intranuclear inclusions in the nerve cells in the former serves to distinguish between them. The greater degree of leptomeningal infiltration and often of perivascular infiltration as well, and the frequency of the perivascular localization of lesions in the mice with St. Louis encephalitis are differential points.

It is interesting that the anterior third of the cerebrum, in which the motor area resides, is most frequently hit by the J-S virus, although in the intracere-
brally inoculated animals, the middle and posterior thirds were most often injected. This reminds one of the frequency of involvement of the motor area in poliomyelitis of monkey and man. On the other hand, the constancy of involvement of the olfactory bulbs in the J-S mice, no matter what the portal of entry be, is quite unlike the lack of lesions in these structures in human and simian poliomyelitis. In brief, there is no compelling evidence in the pathological picture in these mice which would lead one to conclude that they were suffering from infection with the virus of human poliomyelitis.

This is not true, however, of the lesions which result from transfer of the murine virus to guinea pigs. In the guinea pig, the changes in the central nervous system are remarkably like those of poliomyelitis of monkey and man. This similarity persists through repeated transmissions from mouse to guinea pig, and in the cavian series of subinoculations. It is most interesting that this species change in the character of the lesions in guinea pigs is attended by a marked fall in virulence of the virus and occasional transmissibility to monkeys. While dilutions of virus of a million or more are effective when inoculated intracerebrally in mice, dilutions approximating those necessary for the infection of monkeys by the virus of poliomyelitis are necessary in guinea pigs. The distribution and histological details of the lesions in the guinea pig approach those of the simian and human disease, poliomyelitis, very nearly. This is in accord with evidence submitted by Jungeblut and Sanders indicating that the SK strain of human poliomyelitis has actually been transferred to rodents.

**SUMMARY**

A description has been given of the lesions produced in mice and guinea pigs by inoculation of the Jungeblut-Sanders virus. The histopathological findings, although in themselves not conclusive, would tend to support the opinion that Jungeblut and Sanders have transmitted the SK poliomyelitis virus to mouse and guinea pig. In mice the virus apparently retains its affinity for the anterior horns of the spinal cord, but in a moderate degree. Associated with a marked increase in virulence of the virus, a strong affinity for the cerebral tissues, more particularly the olfactory centers, develops. On transmitting this murine variant of the virus to guinea pigs, however, the original character of the virus is again revealed. There is a reversion to a predominant affinity for the nerve cells of the anterior horns of the spinal cord.

**BIBLIOGRAPHY**

EXPLANATION OF PLATES

PLATE 1

Fig. 1. Mouse 9. Spinal cord. Almost total disappearance of ganglion cells in anterior horn of lumbar enlargement. Diffuse infiltration of grey matter by lymphocytes and polymorphonuclear leucocytes and mild perivascular infiltration. Considerable microglial proliferation. Moderate leptomeningeal infiltration, ventrolaterally and in ventral sulcus. Hematoxylin-eosin stain. × 110.

Figs. 2 and 3. Fig. 2, mouse 27; Fig. 3, mouse 33. Spinal cord. Necrotic nerve cells in anterior horns of lumbar enlargement undergoing polymorphonuclear phagocytosis. Note pericapillary polymorphonuclear leucocytes and lymphocytes in Fig. 3 and similar mild diffuse infiltration in both Figs. 2 and 3. Hematoxylin-eosin stain. × 460.

Fig. 4. Mouse 3. Spinal cord. Early microglial proliferation in area of neuronal degeneration in anterior horn of lumbar segment. Hortega’s silver carbonate stain. × 460.

Fig. 5. Mouse 3. Spinal cord. Advanced reactive hypertrophy of microglia in zone of nerve cell necrosis in anterior horn of lumbar segment. Hortega’s silver carbonate stain. × 460.
(Wolf: Rodent poliomyelitis. IV)
PLATE 2

Fig. 6. Mouse 17. Cerebrum—anterior third. Focus of necrosis of cortical ganglion cells with neuronophagia. Mild diffuse and leptomeningeal, and mild perivascular lymphocytic and polymorphonuclear infiltration. Hematoxylin-eosin stain.

Fig. 7. Mouse 37. Cerebrum. Similar lesion to that in Fig. 6 with less inflammatory reaction in the hippocampus. Hematoxylin-eosin stain.

Fig. 8. Mouse 59. Olfactory bulb. Perivascular and diffuse infiltration by lymphocytes in internal granular, mitral, gelatinous, external granular, and glomerular layers and capsule. Loss of nerve cells in all the affected layers. Hematoxylin-eosin stain.

Fig. 9. Mouse 8. Cerebellum. Folium showing focal loss of Purkinje cells, diffuse and leptomeningeal lymphocytic infiltration, and a considerable microglial proliferation. Hematoxylin-eosin stain.
PLATE 3

Fig. 10. Guinea pig 5. Spinal cord. Cervical segment. Total loss of ganglion cells in one anterior horn. Intense polymorphonuclear and lymphocytic infiltration and microglial proliferation. Moderate extension of inflammatory and reactive glial process into posterior horns. Hematoxylin-eosin stain.


Fig. 12. Guinea pig 9. Spinal cord—Cervical segment. Changes in anterior horn like those in Fig. 11. Note mild infiltration of ventral leptomeninges and those in ventral sulcus by round cells. Hematoxylin-eosin stain.

Fig. 13. Guinea pig 9. Spinal cord. Lumbar segment. Extensive nerve cell degeneration in both anterior horns. Inflammatory and microglial reactions, intense and more marked on one side. Considerable edema. Mild infiltration of leptomeninges in ventral sulcus.
PLATE 4


Fig. 15. Guinea pig 5. Spinal cord. Anterior horn of lumbar segment. Degenerated nerve cells undergoing early polymorphonuclear phagocytosis. Note well preserved nearby neurone. Mild diffuse polymorphonuclear and lymphocytic infiltration and slight perivascular round cell infiltration. Hematoxylin-eosin stain. × 460.

Fig. 16. Guinea pig 9. Spinal cord. Anterior horn of cervical segment. Detail of Fig. 14. Note advanced polymorphonuclear phagocytosis of necrotic nerve cell and partially preserved nearby ganglion cell. Polymorphonuclear leucocytes and lymphocytes in surrounding tissues. Hematoxylin-eosin stain. × 460.

Fig. 17. Guinea pig 5. Spinal cord. Anterior horn of lumbar segment. Degenerating nerve cell showing satellitosis. Diffuse lymphocytic and polymorphonuclear infiltration and advanced microglial proliferation and early neurophagia. Hematoxylin-eosin stain. × 460.
(Wolf: Rodent poliomyelitis. IV)
PLATE 5


