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Production of Immunity to Poliomyelitis Virus in Motor Cells of the Monkey's Spinal Cord.*

HOWARD A. HOWE AND DAVID BODIAN. (Introduced by Carl G. Hartman.)

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The following experiments constitute a demonstration that, as in the case of the olfactory bulbs already reported,[1] certain motor cells in the spinal cord of the rhesus monkey may be rendered resistant to the effects of invasion by poliomyelitis virus by means of procedures which produce alterations in their normal metabolism. Eighteen animals were subjected to section of the sciatic nerve in the sciatic notch at intervals varying between 3 and 57 days previous to the induction of complete leg paralysis by intranasal inoculation of poliomyelitis virus. A series of 6 uninoculated controls were operated upon in a similar fashion and sacrificed at intervals between 6 and 30 days.

These animals may be grouped under two headings. The first includes those monkeys in which the nerve section either produced no effect upon the susceptibility of the cells involved, or may have slightly enhanced it. This situation was found in 3 cases where nerve section had preceded leg paralysis by 3-4 days. In this group the cells of the operated and control sides were completely destroyed and it appeared that the destruction of the former had preceded that of the control cells.

Exactly the opposite effects were observed in the second group of 15 animals in which nerve section had been carried out 6-57 days previous to leg paralysis. In these cases the entire anterior horn of the control side was destroyed while on the operated side the vast majority of the cells giving rise to the sciatic nerve were spared. In the cases of longest duration of nerve section (13-57 days) the differences between the two sides were most striking (Figs. 1 and 2). As might be expected from the analysis of the cases in the first group, showing the opposite effect, the sparing was less extensive in those animals where nerve section was of shorter duration (6-8 days). Here sparing was confined to those levels in which the majority of the cells were concerned with the formation of the sciatic nerve.

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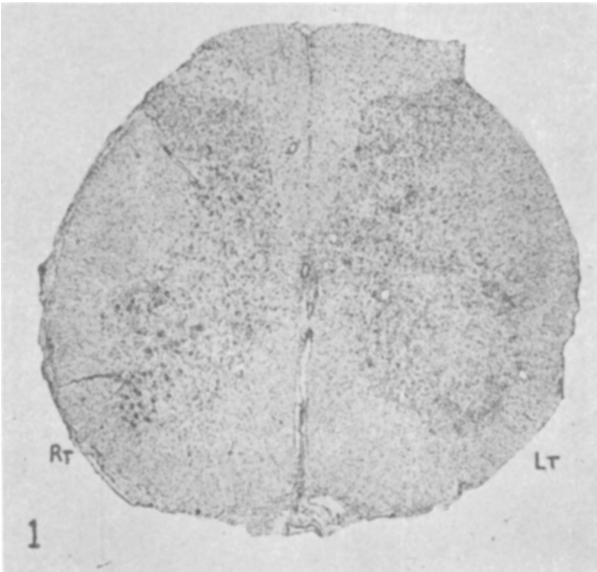
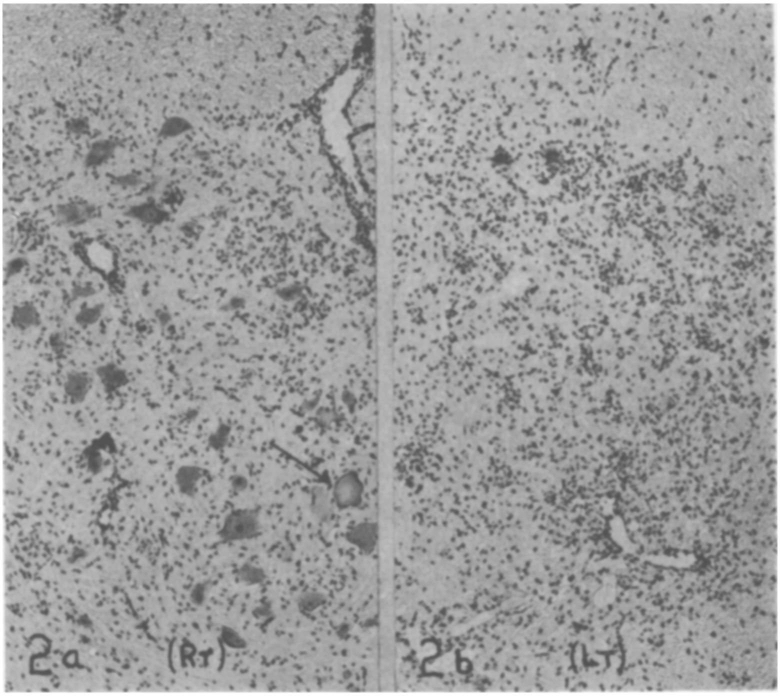


FIG. 1.
Lumbar cord of an animal in which the right sciatic nerve was sectioned 25 days prior to leg paralysis. Almost complete sparing of cells on the operated side.

The period of refractivity in the motor cells corresponds quite closely to the appearance of a morphological change known as "chromatolysis" or the "axone reaction". This reaction, which ensues upon section of the axone, is demonstrable principally as a reduction in the amount of Nissl substance in the cell cytoplasm. The exact nature of the physiological change which is mirrored in chromatolysis is obscure, but there are numerous reasons for believing that it involves an increase in the metabolic activity of the nerve cell itself. The reaction is apparent a few days after nerve section, but reaches a maximum in 10-20 days depending upon the amount of trauma inflicted upon the nerve and the distance from the cell body at which section takes place. For example, in 3 animals section of the upper lumbar roots at their emergence from the intervertebral foramina only 4 days previous to complete leg paralysis resulted in the production of a refractory state in the majority of the nerve cells chromatolyzed. This is several days earlier than the time at which a similar result could have been obtained by section of the sciatic nerve as far distal as the sciatic notch. This suggests that the state of refractivity to virus is indeed the result of the axone reaction, since its appearance varies in time with the latter. After the passage of several months the nerve cell may eventually regain its



FIGS. 2a AND 2b.

Figs. 2a and 2b are the right and left anterior horns of the lumbar cord of another monkey in which the right sciatic nerve was sectioned 18 days prior to complete leg paralysis. Fig. 2b shows the normal control side on which every cell appearing in the section was destroyed. Fig. 2a is taken from the same section and shows the operated side. Although practically every cell is spared, the presence of typical perivascular and interstitial lesions indicates the presence of virus on this side. Most of the cells are showing beginning recovery from chromatolysis but the cell indicated by the arrow is at the height of the reaction.

normal appearance. The correlation of the virus-refractory state with these late stages is yet to be made.

At this time one can do little more than indicate the significance of the above findings without attempting a discussion of their nature. There has been induced a reversible change in the metabolism of the nerve cell which renders it relatively refractory to the destructive effect of virus invasion. Nevertheless, such refractivity is probably only relative. This is suggested by the observation that compact chromatolytic groups are more resistant than scattered individual chromatolytic cells. In such compact groups even non-chromatolytic cells are sometimes spared. Two tentative conclusions appear to follow from the above findings: (1) that the increase in concentration of the virus occurs within the nerve cell itself and is possibly dependent upon some substrate which is reduced in chromatolytic cells, (2) that there is a threshold concentration, not achieved in the central portion of compact chromatolytic cell groups, which must be reached before the virus can become destructive. Heretofore an immunity of the cells of the CNS has been achieved only in the presence of active poliomyelitis virus. The real importance of these experiments lies in their demonstration of the fact that resistance to destruction by virus may be evoked in the normal cell without antecedent exposure to the infective agent.

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Surgical Production of Collateral Intracranial Circulation. An Experimental Study.

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Beck[1, 2, 3] and O'Shaughnessy[4, 5, 6] have demonstrated that an effective collateral blood supply to the heart can be established by the use of pedicled muscle and omental grafts. Others[7, 8, 9] have similarly employed the omentum to augment the circulation to the kidneys. The present experiments[10] were performed to determine whether an accessory arterial blood supply from an extracranial source could be provided for the brain by applying to its cortical surface a pedicled graft of temporal or suboccipital muscles.

Monkeys *(Macaca mulatta)* weighing 2 to 3 kilos were used as experimental animals. The operative approach and technic, as well as the sequence of the procedures, varied slightly during the course of

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