

ters which are rarely or never affected in the early stages (that is, centers with high immunity) are reached by the virus and succumb to it. Thus, the final pathological picture in all cases is similar, as apparently the susceptibility to virus of various parts of the CNS is independent of the portal of entry (see also Pette, Demme, and Környey<sup>11</sup>). However, even terminally it is possible to observe in certain cases differences in the distribution of lesions, depending on the portal of entry. For example, if the virus is inoculated by some other portal than the intranasal one, signs of virus invasion in the late paralytic stages may occasionally be observed as far forward in the olfactory system as the tuberculum olfactorium, but, in contrast with intranasal cases, apparently never in the olfactory bulbs.<sup>12</sup>

### 10739 P

#### The Pia-Arachnoid as a Barrier in Experimental Poliomyelitis.\*

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The occasional demonstration of poliomyelitis virus in the cerebrospinal fluid of experimental animals has given rise to a series of experiments and speculations regarding the rôle of this body liquid in the dissemination of the disease through the central nervous system. Such investigations as those of Clark and Amoss<sup>1</sup> and Hurst<sup>2</sup> who produced experimental poliomyelitis regularly by intracisternal and intrathecal inoculation have led to the assumption recently made articulate by Schaeffer and Muckenfuss<sup>3</sup> that intracerebral inocula may be effective at sites far distant from the point of introduction. In previous observations the permeability of the ependyma and the possibility of injury to the pia-arachnoid are factors which have not been properly controlled. The following experiments indicate that under ordinary conditions the leptomeninges

<sup>11</sup> Pette, H., Demme, H., and Környey, St., *Deutsche Z. f. Nervenhe.*, 1932, **128**, 125-252,

<sup>12</sup> Sabin, A. B., and Olitsky, P. K., *J. Am. Med. Assn.*, 1937, **108**, 21.

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<sup>1</sup> Clark, P. F., and Amoss, H. L., *J. Exp. Med.*, 1914, **19**, 217.

<sup>2</sup> Hurst, E. W., *J. Path. and Bact.*, 1932, **35**, 41.

<sup>3</sup> Schaeffer, M., and Muckenfuss, R. S., *Am. J. Path.*, 1938, **14**, 227.

constitute an effective barrier—so effective that large amounts of active virus may be present in the cerebrospinal fluid without any clinical indication of poliomyelitis.

These experiments fall into 3 groups: (a) virus dripped over an exposed cortical surface with intact pia; (b) virus introduced into the lumbar cistern with intact pia; (c) virus introduced at either of the above sites after deliberate pial injury.

Fifteen animals were used in the first group. The cerebral cortex was exposed by opening an oval dural flap 3 cm by 2 cm which was centered over the paracentral lobule with the long axis in a rostro-caudal direction. Great care was taken to avoid injury to the pia, although the arachnoid was undoubtedly torn in places. One-quarter to three-quarters cc of 20% MV virus in salt solution was then dripped over the exposed cortical surface, the edges of the dural flap being elevated to insure as wide dissemination as possible. The dura was then carefully sutured and the incision closed. Eight controls were prepared by the direct intracerebral inoculation of 0.25 cc and 2 by intranasal inoculation of the same virus suspensions. All but 2 of the controls became paralysed within 4-9 days while the operated animals remained well over a period varying from 11 days to 4 months. In 9 instances fever was recorded but there was no suggestion of paralysis.

The second group comprised 7 animals in which virus was introduced into direct pial contact in the lumbar subarachnoid space. Three of these animals received 0.5 cc of active virus dripped over the exposed lumbar enlargement. This type of procedure had the disadvantage that most of the virus escaped into the surrounding muscles although an infective dose undoubtedly came in contact with the cord. In this group 2 direct cord inoculations resulted in paralysis while the animals receiving virus drips remained free of either fever or paralysis. In order to introduce larger quantities of virus intrathecally, 4 animals were prepared with an exposure of the dura of the lumbar cistern. This was then carefully nicked and cerebrospinal fluid was allowed to escape freely. A blunt curved needle was then inserted through this small opening and 0.5 cc of active 20% MV virus in salt solution was dispersed among the roots of the cauda equina. In this way complete retention of the inoculum was obtained. A control was prepared by direct piqure of 0.4 cc of the same virus into the sacral cord. As in the previous series, the control succumbed within 4 days and the experimental animals showed neither fever nor paralysis.

Of the 22 animals which resisted the introduction of virus into

the cerebrospinal fluid 11 were sacrificed for histological study: 11 were subsequently given intracerebral or intranasal inoculations. Two of these were resistant to infection while the remaining 9 contracted typical poliomyelitis.

The last group is concerned with animals in which pial injury was produced either accidentally or deliberately. In the cortical drip experiments the dura was not sutured in 5 cases. Although the inoculum was reduced to 0.05 cc of 20% virus in 3 of these animals, paralysis resulted in each instance. At autopsy the chief finding was a cortical herniation which was either very hyperaemic or frankly necrotic. In 2 instances a suture needle injury to the cortex was followed by paralysis.

The idea that infection was made possible by a change in pial permeability is confirmed by the following experiment. In 3 animals 0.5 cc of a distilled water suspension of 20% MV virus was carefully introduced into the lumbar cistern by the technique already described. In each instance paralysis resulted although autopsy revealed no visible damage to the cord or nerve roots.

The protective barrier of the pia is thus conceived to be largely a mechanical one, and under the influence of factors which bring about changes in its permeability. Under normal conditions it is probably effective enough to render the cerebrospinal fluid of the subarachnoid space negligible as a virus-disseminating medium. These findings may be interpreted as contributing further evidence for the neurotropism of poliomyelitis virus. The resistance of the ventricular ependyma will be similarly considered in succeeding experiments.

## 10740

### Penetration of Sesame Oil Painted on the Capon Comb

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Androgenic substances, extracted from human urine by a method previously reported,<sup>1</sup> were dissolved in sesame oil and applied to the surface of the combs of white leghorn capons. Since percutaneous

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<sup>1</sup> McCahey, J. F., Hansen, L. P., and Soloway, D., *J. Urol.*, 1937, **38**, 397.