

travels along the olfactory nerves, a bilateral section and partial removal of the bulb and tract was carried out on a series of *Macacus rhesus* monkeys through a transfrontal approach. In five experiments, these monkeys and controls with intact olfactory nerves were given nasal instillations of cord containing virus. In each case the control animals came down promptly, whereas the experimental animals remained well. In one experiment, whereas the three experimental animals withstood three inoculations given on successive days, two controls were paralyzed within short incubation periods after a single inoculation of virus. After this, the serums of the monkeys with cut olfactory bulbs were tested for antiviral substance, two of them against one infective dose of virus and the other against two infective doses. In no case did the serums neutralize; showing that the animals were in no way resistant to the virus. In a final experiment, two experimental animals resisted twelve intranasal instillations, whereas the control became paralyzed after a single injection.

The nasal mucosa is innervated not only by the olfactory nerves, but also by branches of the V and VII cranial nerves. In addition, virus can percolate from the nasopharynx to the tonsils with its intact nerve supply. Yet upon cutting the olfactory tract no infection occurred, indicating clearly that the first cranial nerve is the only one of the nasopharynx that can transmit the virus of poliomyelitis from the nasopharynx to the central nervous system. Over a period of three weeks, animals received twelve intranasal inoculations, of which considerable must have dribbled to the gastro-intestinal tract. This observation, together with the clinical and experimental data of others, discounts the gastro-intestinal tract as the portal of entry.

Whether the olfactory nerve affords the virus a passageway because it is non-medullated, or because its neurones lie in the nasal mucosa and are thus exposed to the virus, has yet to be determined. The fact that infection *via* the sciatic nerve succeeds only if it is injured, and inasmuch as injury to the nerve is followed by myelin degeneration, suggests that the lack of myelin may render the olfactory nerve vulnerable to the virus.

The next problem to consider is whether the virus spreads along the nerve fiber proper or its perineural lymph space. Inasmuch as the separation of the olfactory nerve fibers and their surrounding lymph spaces would involve considerable technical difficulty and since the lymph spaces drain into the subarachnoid space and the nerve fibers are continuous with those of the rhinencephalon, it was decided to determine whether the virus spread through the central nervous system by the spinal fluid or by the nerve

tracts. Therefore, the spinal cords of monkeys were severed in the dorsal region and separated, the dura carefully closed and an intact flow of spinal fluid demonstrated over the gap. In one animal, virus inoculated into the brain failed to infect the lower segment of the cord, while virus inoculated into the lower segment did not penetrate above the point of separation. Infectivity or non-infectivity of the segments was determinable by presence or absence of microscopical lesion and demonstrable virus. These results, which are in keeping with the findings of Jungeblut and Spring, show that the spread of the virus through the central nervous system is along nerve tracts rather than by means of the cerebrospinal fluid and inasmuch as the perineural lymph spaces of the olfactory nerve continue as the subarachnoid spaces and the nerve fibers continue in the central nervous system, the virus must travel along the fibers of the nerve.

Besides demonstrating that the virus travels along nerve fibers as Hurst and Fairbrother, Jungeblut and Spring, Faber and Gebhardt have suggested, the above experiment indicates that there is not hematogenous spread of the virus, for the blood supply was intact for each segment. It appears, therefore, that experimental poliomyelitis is a disease of the central nervous system exclusively, as the pathology and the difficulty of demonstrating virus outside of the central nervous system indicate; whether the human disease is as entirely neurotropic as the experimental disease or whether the latter has acquired this property through continued passage is being investigated.

It has been shown that experimental poliomyelitis is entirely neurotropic and that the virus travels along the olfactory nerve fibers to the central nervous system, where it is propagated along the nerve tracts. Since only the olfactory nerve of the nasal cavity can carry the virus and because no infection was obtained when large amounts of virus reached the gastro-intestinal tract, the portal of entry then must be the nasal cavities.

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