

peared, which originated in the gas, indicating the presence of gamma rays.

The electrons ejected from the carbon appeared to have energies which were distributed from about 700,000 electron volts downward. It does not seem that the loss of energy of the electrons in getting out of the target can account for such a large proportion of low energy tracks. The carbon is essentially a thin target, since the depth to which it can be activated by the deuterons is very small compared to the range of the ejected electrons. If it can be established, with certainty, that the energy spectrum of positive electrons emitted from nuclei is continuous, it will be of profound theoretical importance in dealing with the problem of the continuous negative beta ray emission.

Both the decay period (14 minutes) and the maximum energy of the electrons from carbon indicate that the active isotope here concerned is the same as in the case of boron bombarded with  $\alpha$  particles, as reported by Curie and Joliot. A calculation on the basis of the length of time of bombardment and the half life indicates that one radioactive atom is produced for about  $10^{10}$  deuterons incident on the target.

We have previously shown that carbon bombarded with deuterons emits gamma rays of hardness corresponding to about  $3 \times 10^6$  volts, during the time of bombardment. This we associate with the emission of protons and the formation of  $C^{13}$ . Three gamma ray quanta are emitted in this process for about  $10^8$  deuterons at 900,000 volts. It seems, therefore, that when carbon is bombarded with deuterons, not more than 1 per cent. of the transformations give as a product the radioactive  $N^{13}$ , while the remaining 99 per cent. give  $C^{13}$ .

C. C. LAURITSEN  
H. R. CRANE  
W. W. HARPER

KELLOGG RADIATION LABORATORY,  
CALIFORNIA INSTITUTE OF TECHNOLOGY,  
FEBRUARY 27, 1934

#### THE PORTAL OF ENTRY AND TRANSMISSION OF THE VIRUS OF POLIO-MYELITIS<sup>1</sup>

BOTH human and experimental poliomyelitis evince considerable evidence toward the belief that the virus of poliomyelitis enters the nasopharynx rather than the gastro-intestinal tract.

In acute cases the virus has been demonstrated in the nasal secretions or nasopharyngeal mucosa, where it may persist for some time. The nasal secretions of abortive cases, of healthy carriers and, on one occasion, the dust of the sick room, have been shown to contain the virus. In one instance, virus was found

<sup>1</sup> From the Department of Bacteriology of New York University and Bellevue Medical School and the Department of Neuro-Surgery, McGill University, Montreal, Canada.

in the nasopharyngeal washings of a patient five days prior to the onset of symptoms. On the other hand, with the exception of one unconfirmed report, the virus has not been demonstrated in the feces of human cases. These facts and the epidemiology of the disease recently reviewed<sup>2</sup> suggest that the virus enters the upper respiratory tract and is spread by its droplets rather than by the excretions of the gastro-intestinal tract.

There is considerable experimental evidence to confirm these findings. In *Macacus rhesus* monkeys introduction of a virus-soaked tampon high up in the nares, injection of virus into the nasopharyngeal mucosa, application of the virus to the scarified mucosa or spraying the virus into the nose have all proved infective. Recently, several workers have reported consistent infection by the administration of multiple intranasal inoculations. We ourselves have a strain of "nasal" virus which gives uniform infectivity upon the administration of 0.2 cc of a 10 per cent. suspension into each of the upper nares. On the other hand, only three of the many who have fed the virus to monkeys have reported positive results. As yet the virus has not been recovered from the feces of poliomyelitis infected animals. Yet in such animals, it can easily be demonstrated in the nasal mucosa or nasal secretions, where it persists for a considerable length of time.

The propagation of the virus from its portal of entry to and through the central nervous system has not been studied extensively. There is evidence indicating that it may travel along the olfactory nerves to the brain. Virus has been demonstrated in the olfactory bulbs during the incubation period following the intranasal inoculation of virus in monkeys by Flexner and Clarke and Faber and Gebhardt. However, the latter authors were unable to follow the distribution of the virus throughout the rhinencephalon. Therefore, the transmission of the virus to the brain is in need of further study and, despite the evidence favoring the nasopharynx as the portal of entry, the small number of carriers and the low incidence of direct contact infections make additional proof desirable. From recent and careful review of the subject, the following is quoted:<sup>2</sup> "Although the pathological anatomy of poliomyelitis has received intensive study for a period extending over more than a hundred years, investigators have not reached an agreement with regard to the atrium of infection or the path of transmission of the virus within the organism. It is to be hoped that research will be continued along these lines until sufficient evidence has been obtained to permit of an authoritative statement."

In order to determine whether or not the virus

<sup>2</sup> "Poliomyelitis," International Committee. Williams and Wilkins, Baltimore, Md.

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.

MAURICE BRODIE,

National Research Council Fellow

ARTHUR R. ELVIDGE

### BOOKS RECEIVED

- Carnegie Institution of Washington Year Book No. 32, July, 1932-June, 1933. Pp. xix + 388. The Institution.  
 CHILDS, W. H. J. *Physical Constants*. Pp. viii + 77. Dutton. \$1.20.  
 OGDEN, C. K. *The System of Basic English*. Pp. ix + 320. Harcourt, Brace. \$2.50.  
 POUND, ARTHUR. *The Turning Wheel*. Pp. xvi + 517. Illustrated. Doubleday, Doran. \$3.50.  
 SOKOLNIKOFF, IVAN and ELIZABETH S. SOKOLNIKOFF. *Higher Mathematics for Engineers and Physicists*. Pp. xiii + 482. Illustrated. McGraw-Hill. \$4.00.