on the completion of twenty-five years of his professorship. The Science Reports are so well known to scientists working along many varied lines that nothing need be said to emphasize and enlarge upon their value and worth. The present volume is an outstanding one. It signalizes not only the personal efforts and accomplishments of Professor Honda, but also the great contributions of his pupils in the university and in the world-renowned Research Institute for Iron, Steel and Other Metals.

Of the 97 papers, 24 are contributions from American and European workers. A wide range of subjects is discussed, including metallurgy, magnetism, mechanical properties of materials, chemistry, spectroscopy, x-rays, mechanics, mathematics, meteorology and instrument design. However, 54 of the papers deal with metallurgy and magnetism, reflecting Professor Honda's influence in these fields. Many of the papers, especially those by American and European contributors, are in the nature of theses summarizing work which has extended over a long period. For this reason, they should prove especially valuable for reference.

The volume contains a bibliography of the 167 scientific papers and 8 books written by Professor Honda and a brief biography. Unlike our own custom in similar volumes, no photograph is included.

LYMAN J. BRIGGS

# SPECIAL ARTICLES

## A RECENTLY ISOLATED STRAIN OF POLIOMYELITIC VIRUS

IN the winter of 1934 an outbreak of poliomyelitis with a high mortality rate occurred in Sacramento, California. Fresh cord from a fatal case was obtained through the courtesy of Dr. Paul Guttman, of the Sutter Hospital, and proved to contain poliomyelitic virus upon inoculation of a monkey. The animal became completely paralyzed and was sacrificed in 6 days after injection of 2 cc of the 10 per cent. suspension intracerebrally and 8 cc intraperitoneally. The virus could be transmitted in series to other monkeys, and since then has been carried successfully through eight generations. Because of the fulminating and severe course of the outbreak, largely among high-school students in Sacramento, it was thought of interest to make a comparison of this virus with the monkey passage strain originally received from the New York City Health Department, and with several others on hand, especially one (Jackson) that had previously been recovered during the summer of 1934 from a fatal case in San Francisco.

The disease in the monkey after intracerebral inoculation was clinically similar to that usually noticed with the monkey passage strain, increased temperature, excitability, tremor, staccato voice, followed by flaccid paralysis of the extremities and complete prostration within 6 to 11 days after injection. The incubation period was usually 6 to 7 days, similar to that of the more active passage strain, but in making comparison it should be recorded that 10 per cent. instead of 5 per cent. cord was generally used as the basic suspension. The former upon titration has proven viable in a 1–200 to 1–400 dilution. The passage strain on the other hand could be titrated to a dilution of 1–3200 from a 5 per cent. suspension, so that the more recently isolated strain lacked the higher infectiousness shown by the older adapted one. The Jackson also lacked this more active virulence, although on one occasion it was potent in a 1–800 dilution.

Recently Trask and Paul[1] have reported a slight variation in a strain of poliomyelitic virus isolated from a case in southern California during the same year, 1934. Their strain showed an affinity for the peripheral nerves with greater and more constant regularity than with the other strains tested. In like manner this new Sacramento virus also seemed to have this property, since it was found unexpectedly that very small quantities of filtered suspension could produce the disease with typical paralysis when given intradermally. In attempting to immunize 2 monkeys, one was given 0.5 and 1 cc of filtered virus (Berkefeld N filtrate), respectively, one week apart, and the other 0.2 and 0.6 cc, respectively, at a 9-day interval. Both animals developed poliomyelitis within a week after the second inoculation. At the same occasion five other animals were immunized to the active passage strain by the same route, being given larger doses (1 to 5 cc) of unfiltered material over a 5-week period without any casualties.

Cross neutralization tests were performed to determine any possible serological differences with the other strains. From previous experiments made at various times, no difference in cross immunity had ever been noticed between the monkey passage strain and several recently isolated human strains (N. Y. and Fl) kindly sent by the Rockefeller Institute and by Dr. J. R. Paul, of Yale University, respectively. Any differences were those of lower virulence or of inability to produce the disease unless with large doses.

Serum was obtained from 2 monkeys, Nos. 1334 and 1499. The former (1334) was immunized to the Sacramento strain of virus and the latter had recov-

[1] J. D. Trask and J. R. Paul, *Jour. Bacteriol.*, 31: 527–530, 1936.

ered from an attack of the disease and was then hyperimmunized with the same strain. Three separate tests with serum of No. 1334 and two with serum of No. 1499 taken at different periods during immunization all failed to protect against the standard amount (1–25) of monkey passage virus, while on the other hand the serum of each animal neutralized its homologous virus. Neutralization tests were also made, using the Sacramento strain diluted either 1–10 or 1–25 against serums of animals immunized to the Jackson and to the passage strains of virus, respectively. Neutralization occurred in 4 of the 5 trials, including one using hyperimmune horse serum of high potency.[2]

Tests for cross tissue immunity were then made in which 3 animals were used that had recovered from an attack of the disease after receiving the Sacramento strain and 2 that had been immunized to this same virus. All 5 monkeys were given intracerebral injections of the passage virus, three receiving a 1–50 dilution and 2 the undiluted 5 per cent. suspension. Two animals withstood the inoculations and 3 became paralyzed. The former were both animals which had recovered from the first attack of the disease, while only one of the group was among the less resistant series.

Three monkeys immunized to the monkey passage strain over a long period of time and resistant to intracerebral inoculation of their homologous viruses were also given similar inoculations of the Sacramento strain. Two of these remained well, although one developed a high temperature, accompanied by nervousness and excitability, while the third became severely paralyzed in both legs, with partial arm paralysis. The test doses in each case were usually large, 2 cc intracerebrally and 10 or 15 cc intraperitoneally of a 10 per cent. suspension.

Neutralization tests with serums from 3 monkeys immunized against the Jackson strain showed protection against the passage virus when used in a 1–25 dilution, while 2 animals (Nos. 1354 and 1371) immune to the Jackson strain were also immune after intracerebral inoculation of the more potent heterologous virus, in a 1–25 dilution. All control animals succumbed to this same dose. In all respects except high potency the Jackson strain seemed immunologically similar to the passage virus.

On the other hand, there is apparent difficulty in the interpretation of the results with the Sacramento strain. While there is a certain degree of cross protection, it is mainly manifest in one direction. Protection was noted when serums were used from monkeys immunized to the passage virus or, with one exception, when animals had been immunized to this strain. While the serum of this latter animal protected against its homologous strain of virus and it was also immune against intracerebral inoculation, yet neither its serum neutralized the Sacramento strain nor was the animal itself resistant against a massive dose of the latter virus.

In contradistinction, tests with the Sacramento serums never protected against the passage virus, and 60 per cent. of the immune Sacramento monkeys lacked tissue immunity against this same strain.

From the evidence presented and from accumulating reports of others, it appears that not all strains of poliomyelitic virus are quantitatively or even qualitatively similar. References are either to a quantitative difference, as shown by the lower invasive power of the more recently isolated strains when compared with the far more virulent monkey passage virus, as recently reported by Kessel and his associates[3] or to comparisons of the differences in neutralizing ability of immune serums against recently isolated or passage strains.[4,5,6,7] Burnet and Macnamara,[8] however, recorded a qualitative difference between their Australian poliomyelitic virus and that of the MV strain of the Rockefeller Institute, as have Paul and Trask[9] in this country for two human strains recovered in the eastern United States. The former reported that two monkeys recovered from an attack of poliomyelitis induced by the Australian virus were not immune to the MV strain, while one animal partially paralyzed by the latter succumbed to a later inoculation of the local virus. These results are very similar to those presented here for the new California strain. Somewhat similar properties are shown, except that the latter strain also offers the affinity for the peripheral nerve trunks not so readily shown by the others, except for the one recently reported by Trask and Paul.[10] Since their virus was also recovered in California during the same year, although from a widely separated locality, one might expect a closer relationship. Erber and Pettit[11] in France have alluded to a possible lack of identity among 4 separate recently isolated strains. Their results were not sufficiently definite, however, to draw any real distinctions in differentiation.

[2] B. F. Howitt, SCIENCE, 80: 621–622, 1934.

[3] J. F. Kessel, R. VanWort, R. T. Fisk, and F. D. Stimpert, *Proc. Soc. Exp. Biol. and Med.*, 35: 326, 1936.

[4] E. R. Weyer, *Proc. Soc. Exp. Biol. and Med.*, 29: 289, 1931.

[5] S. Flexner, *Jour. Am. Med. Asn.*, 29: 1244, 1932.

[6] B. F. Howitt, *Jour. Infect. Dis.*, 53: 145, 1933.

[7] J. R. Paul and J. D. Trask, *Jour. Exp. Med.*, 61: 447–464, 1935.

[8] F. M. Burnet and J. Macnamara, *Brit. Jour. Exp. Path.*, 12: 57–61, 1933.

[9] J. R. Paul and J. D. Trask, *Jour. Exp. Med.*, 58: 513–529, 1933.

[10] *Loc. cit.*

[11] B. Erber and A. Pettit, *Compt. rend. Soc. de biol.*, Paris, 117: 1175–1178, 1934.

Inasmuch as decided immunological differences have been distinguished between separate strains of other viruses such as those of equine encephalomyelitis[12] and of human encephalitis[13,14] wherein the same clinical manifestations are given by the respective strains within each group of viruses, it may well be worth considering such a possibility for the virus of poliomyelitis. Regional differences in strains, not only in respect to invasive power or potency but in respect to qualitative dissimilarity of the antigenic structure, might help to account for the mildness of an outbreak in a certain section as compared to the severity in another. While undoubtedly the high immunity rate of the community as a whole, regardless of how accomplished, largely accounts for the comparatively low morbidity in poliomyelitis, yet sudden outbreaks with an unexpectedly high mortality rate do occur and might well be ascribed to a virus of slightly different immunological makeup combined with high infectiousness. In judging the results of serum therapy, therefore, account should be taken of possible differences in virulence of the virus in different regions combined with a possible difference in antigenic structure. A population ordinarily exposed to a milder strain of virus might not be resistant to one of greater potency and consequently would not respond as well to treatment with serum from those immune to the former strain.

In conclusion, a recently isolated strain of poliomyelitis virus has been found to possess certain immunological properties combined with a slight difference in tissue reactions that suggest the possibility of finding both a qualitative as well as a quantitative difference in the strains of virus causing poliomyelitis.[15]

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## RELATION OF CERTAIN VIRUSES TO THE ACTIVE AGENT OF THE ROUS CHICKEN SARCOMA[1]

THE belief held by some investigators that mammalian tumors are caused by viruses is due largely to the demonstration by Rous[2] that the tumor-producing agents of some chicken sarcomas do not lose their activity when passed through a Berkefeld filter. The evidence in support of this hypothesis has been set forth in detail recently by Andrewes[3] and Rous,[4] and will not be discussed here. Instead, we wish to report some observations distinguishing the active agent of the Rous chicken sarcoma No. 1 from two well-recognized virus diseases: vaccinia, an animal infection, and tobacco mosaic, a disease of plants.

The lipid fraction of the Rous chicken sarcoma is capable of reproducing the tumor in a high percentage of inoculated animals.[5] Allard[6] tested the effect of various lipid solvents on the dried virus of tobacco mosaic. Very few of them affected its activity, and the lipid extracts were always inactive. We have been unable to find reports of similar experiments with the virus of vaccinia, though many attempts to use these solvents as disinfecting agents have been made.[7]

The work of Stanley,[8] with the virus of tobacco mosaic disease, and of Northrup,[9] with bacteriophage, indicates that the infective agents in these diseases are protein in nature, and therefore we should not expect to recover them in the lipid extracts by the technique we are using. The experiments to be described were conducted with two possibilities in mind. It is conceivable that the active agent of the tobacco mosaic disease might be merely adsorbed by the protein crystals, though this would seem improbable in view of Stanley's repeated recrystallization of the proteins. In addition, they will serve as a check on the work done in this department with the Rous chicken sarcoma, as it is possible that a protein, representing the active principle, has been carried along in the lipid extract. The solvents used would seem to obviate this possibility, and chemical and biological tests have failed to reveal its presence.

The material used in the vaccine virus experiments consisted of three lots:[10] first, calf skin pulp, frozen promptly and kept in this condition until the time of the experiments; second, calf pulp dried immediately

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[12] B. F. Howitt, *Jour. Immunol.*, 29: 319–341, 1935.

[13] L. T. Webster and G. L. Fite, *Jour. Exp. Med.*, 61: 411–422, 1935.

[14] R. Kawamura, M. Kodama, T. Ito, T. Yasaki and R. Kobayakawa, *Arch. Pathol.*, 22: 510–523.

[15] Aided by grants from the anonymous Poliomyelitis Donation of the Hooper Foundation and from the President's Birthday Ball Commission for Infantile Paralysis Research.

[1] From the Department of Pathology, College of Physicians and Surgeons, Columbia University, New York City.

[2] Peyton Rous, *Jour. Exp. Med.*, 13: 397, 1911.

[3] C. H. Andrewes, *Lancet*, 2: 64 and 117, 1934.

[4] Peyton Rous, *Jour. Cancer Res.*, 28: 233, 1936.

[5] James W. Jobling and E. E. Sproul, SCIENCE, 84: 229, 1936.

[6] H. A. Allard, *Jour. Agric. Res.*, 6: 649, 1916.

[7] W. Palmer Dearing, *Am. Jour. Hygiene*, 20: 432, 1934.

[8] William M. Stanley, *Phytopathology*, 26: 305, 1936.

[9] John D. Northrup, SCIENCE, 84: 90, 1936.

[10] We wish to express our appreciation to Dr. Clowes, of Mulford and Company, to Dr. Reichel, of Sharpe and Dohme, and to Dr. Beard, of Lederle and Company, for the large amounts of vaccine virus which we found necessary in these experiments.