A Proposed Provisional Definition of Poliomyelitis Virus

Committee on Nomenclature of the National Foundation for Infantile Paralysis[1]

SOME CONFUSION EXISTS AT PRESENT as to what restriction should be applied to the use of the term *poliomyelitis virus* as opposed to the allied terms *encephalomyelitis* or *encephalitis* virus. Furthermore, there are differences of opinion regarding the status of so-called murine poliomyelitis viruses and their suitability as models in poliomyelitis research. Thus, there seems to be a need for clarification regarding questions of nomenclature, and already several attempts have been made to achieve this end.[2]

The object of these proposals is to define the limits of the use of the term *poliomyelitis virus*. There is little doubt that a group or family of poliomyelitis viruses exists. The question at issue is: What neuronotropic strains should be admitted to this family group? Probably a true classification would be inadequate at this time, but until such time as proper means are available for designating individual members of this family, as Poliomyelitis Virus A, B, or C, etc., the following plan is proposed as a temporary substitute.[3]

These proposals are not presented as authoritative or official, or as a set of standards which should necessarily supersede the recommendations of any official scientific bodies which have previously been concerned with these matters. They are presented, rather, as an expression of opinion of this particular Committee at this particular time.

I. Poliomyelitis Viruses

Diagnostic criteria. The term *poliomyelitis virus* should be used to designate strains of the agent originally described as the cause of poliomyelitis in man, regardless of the source from which it may be recovered in nature. Viruses isolated from the spinal cord of fatal cases of human poliomyelitis or the throat washings or feces from typical cases occurring in characteristic seasonal outbreaks may be tentatively presumed to be poliomyelitis viruses. Their exact identification, however, must be based, first, upon *clinical and histopathological* manifestations of the disease produced in monkeys; second, upon *host range*; third, upon *immunological relationships*; and finally, upon *physicochemical properties of the virus.*

(a) *The experimental disease in monkeys.* The monkey is the preferred host for diagnostic studies of newly isolated strains, since those regions of the primate brain which characteristically are free of lesions in poliomyelitis are poorly developed or absent in lower mammals. The use of the monkey, therefore, eliminates an important difficulty which occurs in differentiating poliomyelitis from other neuronotropic diseases—in rodents, for example—on the basis of distribution of cerebral lesions.

(i) *"Clinical" signs.* Monkeys in which experimental poliomyelitis is produced usually manifest certain characteristic "clinical" signs after a variable incubation period (4–20 days in over 90% of cases). Fever, tremor, and spasticity of muscles, usually followed by paralysis within a day or two, are common signs. Other findings are similar to those observed in human poliomyelitis. The occurrence of severe generalized tremors, accompanied by definite flaccid paralysis, is almost without exception pathognomonic of poliomyelitis in the monkey. Cranial nerve paralyses occur, but are less common; paralysis of tail musculature is so rare as to lead to the suspicion of a spinal lesion due to some other cause. *All of the aforementioned signs may be absent or escape detection,* but the diagnosis can, nevertheless, be made by means of histopathological findings.

[1] Members of the Committee are: C. Armstrong, D. Bodian, T. Francis, Jr., A. B. Sabin, and J. R. Paul.

This outline was discussed at a meeting held on July 14, 1948, during the First International Conference on Poliomyelitis held in New York City. Besides the members of the above-mentioned Committee the following were present: R. Thompson, S. O. Levinson, A. J. Shaughnessy, H. A. Howe, J. H. S. Gear, G. Dalldorf, L. Aycock, P. R. Lépine, I. M. Morgan, R. Ward, C. W. Jungeblut, J. L. Melnick, S. Gard, T. M. Rivers, H. M. Weaver, and T. E. Boyd. At this meeting the four items in the *Summary and Recommendations* of the outline were submitted to vote and were all passed unanimously.

[2] This matter was considered at the Fourth International Congress for Microbiology held in July 1947 in Copenhagen, Denmark. It was further discussed at a Conference on Immunologic Types of Poliomyelitis Virus sponsored by the National Foundation for Infantile Paralysis and held in Washington, D. C., January 8, 1948, at which time the above-mentioned *ad hoc* Committee on Nomenclature was formed.

[3] An attempt has recently been made to classify the viruses of the "poliomyelitis groups" in the 1948 edition of Bergey's *Manual of determinative bacteriology (2).* Under one genus *(Legio),* the classification includes: human poliomyelitis virus, lymphocytic choriomeningitis virus, pseudolymphocytic choriomeningitis, Theiler's mouse encephalomyelitis virus, avian encephalomyelitis virus, and swineherd's disease virus. Under human poliomyelitis virus the experimental hosts listed include monkey, and for some isolates, cotton rat, mouse, guinea pig, and white rat. We do not believe that this classification is sufficiently critical or adequate.

(ii) *Histopathological findings.* The histopathological lesions of poliomyelitis in the brain and in the spinal cord are so highly characteristic in nature and distribution that it is important to confirm clinical findings with pathological study. The lesions essentially duplicate those of human poliomyelitis, in type and in distribution. In the spinal cord, lesions are concentrated in the gray matter, and primarily in the anterior horns. *Signs of damage to motor nerve cells must be present* in the acute stage (severe diffuse chromatolysis, neuronal necrosis, neuronophagia, and "outfall" of cells). In addition, focal and diffuse infiltration of leucocytes in areas of nerve cell damage, and perivascular "cuffing," always accompany these signs of nerve cell damage or destruction.

An important differential point is the pattern of distribution of cerebral lesions. The brain-stem contains lesions in every case, but lesions may be variable in severity. The cerebral cortex is generally spared except for the precentral gyrus. The cerebellar hemispheres are generally spared, except for the vermis, but the deep cerebellar nuclei are usually involved, especially the roof nuclei. The basis pontis and inferior olives contain lesions only infrequently and are never severely involved.

(b) *Host range.* Primates are the only known experimental hosts for most strains isolated directly from human or extrahuman sources. Any virus which produces the characteristic experimental disease in monkeys, but does not infect other mammals, may be considered as poliomyelitis virus. Certain strains (Lansing, MEF_1, Y-SK, and Ph) isolated from typical human cases have the additional capacity of producing paralytic poliomyelitis in mice, hamsters, and cotton rats but not in guinea pigs or rabbits. These strains, so far as is known, are immunologically closely related to the Lansing-1938 strain. Any new virus which is atypical with respect to host range should be classified only after complete consideration of its other properties.

(c) *Immunological diagnosis.* Any virus which is immunologically distinct from any previously established poliomyelitis virus but which possesses the above-mentioned diagnostic properties must, nevertheless, be considered as a poliomyelitis virus. Any virus that is immunologically identical to a previously established poliomyelitis strain may be tentatively considered as a poliomyelitis virus.

(d) *Physicochemical properties.* These properties are useful adjuncts in diagnosis. Too few details are known, however, for them to be considered as distinguishing qualities.

(i) *Size of virus.* An important property in identifying poliomyelitis virus is its small particle size. Results of ultrafiltration studies yield an estimated diameter in the range of 8–12 mμ. Electron microscopy studies have not yet clearly established the size and shape of the virus.

(ii) *Resistance to ether* is a striking but not specific characteristic. It may serve as an additional differential point between poliomyelitis and certain other neurotropic viruses.

Special Strains of Poliomyelitis Virus

The evidence that there are multiple types of poliomyelitis virus is strong, as determined by immunity tests. Examples of these are numerous and will not be particularized here.

One type, of which the Lansing virus is the original and classical example, perhaps deserves special mention. This virus, originally isolated (1938) from a human case (*1*), meets the criteria of a poliomyelitis virus as listed in paragraphs I (a–d) and in addition is infective for cotton rats, white mice, and hamsters. Also, from these rodents it was found capable of reinfecting monkeys—its immunological characteristics being maintained. This strain, moreover, is neutralized by human sera from many localities.

Several other strains (MEF_1, Y-SK, and Ph) generally as well as antigenically similar to the Lansing strain of virus have been isolated from various parts of the world. These strains, therefore, constitute an immunological group of viruses which is considered coordinate for classification purposes with other groups of poliomyelitis virus immunologically similar to each other and antigenically distinct from the Lansing group.

Special designation of poliomyelitis strains. Under special circumstances it might be helpful if strains of poliomyelitis were, for the present, labeled by the year and the locale where obtained. In addition, the number of passages in monkeys should be indicated. Thus, the Smith-Hartford-1942-M_5 strain indicates that the strain was isolated from material collected in 1942 from patient Smith in Hartford and had been through 5 transfers in monkeys. If the strain is derived from an extrahuman source, this should also be included as, for example, Chicago flies-1943-M_2[4]. If the above *special designation* of strains were used, the need for the qualifying adjectives of *human* or

[4] The number of passages of the virus in each host could be indicated. Thus, Y-SK-New Haven-1937-$M_{22}CR_5m_{10}$ indicates that the Y-SK strain in question was isolated from a sample collected in 1937 in New Haven and was then taken through 22 passages in monkeys; the 22nd generation of the virus in monkeys was passed to cotton rats and 5 serial passages carried out, following which it has had 10 serial passages in mice. The symbols, M, CR, and m refer to the following host species: *Macaca mulatta, Sigmodon hispidus,* and *Mus musculus,* respectively. If species other than these are used, their symbols should be described with a footnote giving the appropriate scientific name of the species.

monkey- or *murine-adapted* would be unnecessary. In fact the designation of strains as human poliomyelitis virus, monkey-adapted poliomyelitis virus and murine-adapted poliomyelitis virus is unnecessary, undesirable, and confusing.

II. Other Neurotropic Viruses

It has been suggested that there exist in nature viruses which, except for the fact that they have not been shown to produce poliomyelitis in man and have a somewhat different host range from the human poliomyelitis viruses, possess similar physical properties and produce a poliomyelitis-like disease in lower animals under natural conditions, and that in a broader genetic classification these viruses should be included with the poliomyelitis group. The virus responsible for the indigenous paralytic disease of mice (Theiler's TO) and the virus of "Teschen's" disease of swine, about which relatively little is known, have been proposed for inclusion in such a classification. Although it would appear that among the various neuronotropic viruses, all of which, including the poliomyelitis group, are in one sense encephalomyelitis viruses, the Theiler "TO" virus most closely corresponds to the poliomyelitis group as regards its affinities for various tissues and nerve centers, this Committee believes the time is not ripe for setting up a *broad* genetic group of animal poliomyelitis viruses.

(a) *Murine neuronotropic viruses.* In this group are included viruses which are known to be of murine origin, as well as others, whose natural habitat is still obscure but which were originally recovered from mice, cotton rats, or hamsters inoculated with various materials. These form a heterogeneous group as regards pathogenicity, host range, and immunologic relationship, although the size of those "measured" thus far is of the same general magnitude as that of human poliomyelitis virus. Most of the viruses in this group can produce paralysis in mice and in recent years have frequently been designated as "mouse poliomyelitis" (in the case of those whose natural habitat is regarded as the mouse, e.g. TO, FA, GD VII), "poliomyelitis-like," or simply as "poliomyelitis," particularly when the original inoculum was derived from a patient with poliomyelitis or from a known human strain of poliomyelitis virus, e.g. Columbia SK, MM. None of these viruses fulfills the criteria set forth in the preceding section for the poliomyelitis group of viruses which includes those strains that infect rodents, such as the Lansing, MEF_1, Y-SK, and Ph. These murine neurotropic viruses have often been chosen for experimental work on poliomyelitis and have been a serious source of confusion and error in work with poliomyelitis viruses in rodents. In the opinion of this Committee, the classification of these viruses as poliomyelitis viruses is not warranted.

It is, furthermore, proposed that the term "mouse poliomyelitis" be discontinued and that to some of these strains (e.g. TO, FA, GD VII) so designated in the past the term originally used by their discoverer, Dr. Max Theiler, be applied, namely, *spontaneous mouse encephalomyelitis* (*10*). Some properties of this group of viruses and the ways in which they differ from the poliomyelitis viruses are as follows:

(i) *TO.* This virus has been recovered under natural conditions from the feces of most stocks of mice and from the spinal cord and brain of mice with paralysis of the extremities. Experimentally, after intracerebral inoculation, as well as in the indigenous disease of mice, it produces paralysis predominantly of the posterior extremities, which is associated with lesions in the anterior horn cells of the spinal cord and brain stem and to a lesser extent of the cerebral cortex. Its size (8–12 mμ) is the same as that of poliomyelitis virus. Only some strains are pathogenic for cotton rats. It differs from the poliomyelitis viruses in that (1) no strain has been found pathogenic for monkeys; (2) it can be propagated in chick embryos; and (3) it is not neutralized by "normal" adult human sera which neutralize the Lansing and other strains of poliomyelitis virus.

(ii) *FA* and *GD VII.* These strains have not been found in the intestinal contents of mice, but were recovered from the nervous system of mice during the course of work with other viruses. They also differ from the TO strain in (1) their ability to give rise to encephalitic signs as well as paralysis and to extensive lesions in the cerebral cortex as well as in the spinal cord and brain stem; (2) shorter incubation period, high titer achieved in the nervous tissue, greater invasiveness by peripheral routes such as the intraperitoneal; and (3) capacity to perform serological tests (both complement fixation and neutralization) with them. Except in tests in which interference might have affected the cross-immunity pattern, there is no evidence of immunological relationship between these viruses and the TO strain. Unpublished data available in several laboratories suggest that viruses, with properties similar to those of FA and GD VII but immunologically unrelated to them, have been encountered in mice. The FA–GD VII group is pathogenic for cotton rats and is easily propagated in the chick embryo. The differences from the poliomyelitis group listed for the TO virus also apply to the FA–GD VII group.

The strains of virus designated as WP, NY 65, NY Pool II, and CC which were recovered from mice by Jungeblut and Dalldorf would appear to belong to the spontaneous mouse encephalomyelitis group.

(b) *Other viruses producing paralysis in rodents which have been called poliomyelitis or poliomyelitis-like.* In this group are included viruses which are immunologically different from the TO-FA-GD VII group and have a somewhat broader host range, which may include guinea pigs, albino rats, and monkeys,

although the disease produced in the latter is encephalitic. The natural habitat of this group is still obscure, although the circumstances under which they have been recovered suggest that rats and hamsters may constitute at least one source. The properties of some of these viruses and the chief ways in which they differ from those in the human poliomyelitis group are as follows:

(i) *Columbia SK.* Jungeblut and Sanders, passaging the SK strain of poliomyelitis virus (now known as Y-SK) in cotton rats, recovered a virus which has proved to be pathogenic for cotton rats, mice, guinea pigs, albino rats, and, in the later passages, also gave rise to encephalitic disease in monkeys. In mice this strain of virus yields titers of 10^{-7} or more and is highly pathogenic by the intracerebral, intranasal, intraperitoneal, intravenous, and other peripheral routes including feeding. It has been propagated in the chick embryo. Most of the present available evidence indicates that this strain is immunologically different from the original SK virus, maintained by passage in monkeys (*5*), and, unlike the original virus, is not neutralized by pooled adult human serum possessing antibodies for poliomyelitis virus. On the other hand, the original Y-SK strain, which has also been propagated in cotton rats and mice, behaves like the Lansing strain of poliomyelitis virus, has retained its immunologic identity with the original virus as passaged in monkeys, and does not possess the properties exhibited by the "Columbia SK" virus (*6*).

(ii) *MM virus.* This was recovered by Jungeblut and Dalldorf (*4*) from the brain of a hamster which died 19 days after inoculation with material from the medulla and cord of a patient with poliomyelitis. Although the original human material was not pathogenic for cotton rats, mice, or guinea pigs, the virus recovered from the brain of the dead hamster was found to be highly pathogenic for hamsters and for mice, cotton rats, and guinea pigs, *but not for monkeys* or rabbits. In mice this virus reaches intracerebral titers of 1×10^{-11} (for the 0.03-cc dose) and intraperitoneal titers of 1×10^{-9}. It is also highly invasive by other routes, including feeding, in mice and other rodents, particularly in younger animals. Both intracerebral and peripheral inoculations produce paralysis which is associated with lesions in the anterior horn cells of the spinal cord, but lesions are also widespread in the remainder of the central nervous system. The size of this virus appears to be in the same range of magnitude as that of poliomyelitis virus. Although many contradictory and irregular results have been published on the immunological relationships of both the Columbia SK and MM viruses, Dalldorf's unpublished studies have recently been quoted by Schatz and Plager (*9*) as indicating that the MM virus is serologically similar to the Columbia SK virus, but different from both the Lansing-type poliomyelitis viruses and the spontaneous mouse encephalomyelitis viruses of Theiler. Although the original human material from patient MM contained a virus which produced poliomyelitis in the rhesus monkey, the MM virus derived from the hamster brain is not pathogenic for monkeys, and apparently no work has been done to determine whether or not any immunological relationship existed between the monkey-pathogenic virus in the original human material and the virus derived from the hamster brain. Jungeblut and Dalldorf, in their original report (*4*), stated that the data, "while suggesting that a direct transfer of poliomyelitis virus was obtained from man to hamster—with further transfer from hamster to cotton rats and white mice—are admittedly insufficient actually to prove such transmission. The possibility that accidental contamination may have occurred with a latent virus, or with a virus carried in the laboratory, cannot be ignored." The recent report of F. K. Sanders (*8*) of a "poliomyelitis-like" virus, unrelated to Lansing virus, picked up during the course of passaging Lansing virus in hamsters, suggests that hamsters, like mice, may perhaps be a source of spontaneous encephalomyelitis viruses or that accidental contamination with a hamster-pathogenic virus present in the laboratory might have occurred.

(iii) *The so-called "encephalomyocarditis" or EMC virus.* This was recovered by Helwig and Schmidt (*3*) by mouse inoculation from the pleural fluid and spleen of a chimpanzee in Florida, which died exhibiting bilateral hydrothorax, pulmonary edema, pericardial effusion, and myocarditis. This virus, which originally was described as producing paralysis in mice, associated with myelitis and myocarditis, was further studied by Warren and Smadel (*11*), who, after failing to identify it with "some 20-odd viruses" including the Lansing and Y-SK poliomyelitis viruses, found that serologically (as well as on the basis of its physical and pathogenic properties) it belonged with the MM and Columbia SK viruses.

The Columbia SK, MM, and EMC viruses are highly viscerotropic as well as neuronotropic. None of them gives rise to an experimental disease in monkeys like that produced by the various strains of human poliomyelitis virus, regardless of whether they had been passaged in monkeys, cotton rats, mice, or hamsters. The 1941 preliminary report of Theiler (*10*) that in his hands the Lansing virus, after prolonged passage in mice, had lost much of its pathogenicity for monkeys (an observation occasionally repeated by others) is often quoted to indicate that monkey pathogenicity may be lost as a result of adaptation of a poliomyelitis virus to other hosts; it should be recalled, however, that the Lansing strain mentioned by Theiler retained its immunological identity as well as its original pathogenic characteristics in mice. The capacity of the Columbia SK, MM, and EMC viruses to produce paralysis in rodents, associated with lesions in the anterior horn cells of the spinal cord, is also exhibited by such viruses as yellow fever, dengue, vesicular stomatitis (the Indiana strain regularly producing primary paralysis of the posterior extremities in intracerebrally inoculated guinea pigs) (*7*), and, depending on the dose, route of inoculation, age of the animal, also the various members of the encephalitic group, e.g. Japanese B, St. Louis, Russian Spring-Summer, WEE, EEE, etc. Except

in so far as these latter could be classified along with the poliomyelitis viruses as neuronotropic they are not considered as belonging to the group of poliomyelitis viruses. Therefore, it is the opinion of this Committee that there is insufficient justification for the use of the terms "poliomyelitis" or "poliomyelitis-like" in connection with the Columbia SK, MM, EMC, and related viruses.

III. Summary and Recommendations

(1) The term *poliomyelitis virus* should be used to designate strains of the agent originally described as the cause of poliomyelitis in man and only these. It is identified by the characteristic experimental disease in the monkey, by the character and distribution of histological lesions in the spinal cord and brain of infected primates, by its host range, and by its immunological properties.

(2) Strains of poliomyelitis virus have been distinguished by immunological methods. With the exception of the Lansing group, they are as yet poorly defined. Some strains in this group have special properties of infecting cotton rats, mice, and hamsters, as well as primates. Human sera may contain antibodies to these strains. Because they also satisfy all other identifying criteria, their inclusion as examples of true poliomyelitis virus is justified.

(3) Certain encephalomyelitis viruses of mice, such as Theiler's TO, FA, and GD VII strains, have been termed "mouse poliomyelitis" by some. This term should be discontinued and Theiler's original designation of *spontaneous mouse encephalomyelitis* used to describe these viruses.

(4) Other viruses which produce paralysis and neuronal lesions in the anterior horns of the spinal cord in experimental animals, but which do not otherwise satisfy the criteria set down for poliomyelitis virus, should not be called "poliomyelitis virus," "mouse poliomyelitis virus," or "poliomyelitis-like virus."

References

1. Armstrong, C. *Publ. Hlth Rep.*, 1939, **54**, 1719.
2. Breed, R. S., Murray, E. G. D., and Hitchens, A. P. *Bergey's Manual of determinative bacteriology.* (6th ed.) Baltimore: Williams & Wilkins, 1948. P. 1257.
3. Helwig, F. C., and Schmidt, E. C. H. *Science*, 1945, **102**, 31; Schmidt, E. C. H. *Amer. J. Path.*, 1948, **24**, 97.
4. Jungeblut, C. W., and Dalldorf, G. *Amer. J. publ. Hlth*, 1943, **33**, 169.
5. Jungeblut, C. W., Sanders, M., and Feiner, R. R. *J. exp. Med.*, 1942, **75**, 611.
6. Melnick, J. L., and Ward, R. *Fed. Proc.*, 1948, **7**, 308.
7. Sabin, A. B., and Olitsky, P. K. *J. exp. Med.*, 1938, **67**, 229.
8. Sanders, F. K. *Fed. Proc.* (Pt. I), 1948, **7**, 309.
9. Schatz, A., and Plager, H. *Proc. Soc. exp. Biol. Med.*, 1948, **67**, 452.
10. Theiler, M. *J. exp. Med.*, 1937, **65**, 705; Theiler, M., and Gard, S. *J. exp. Med.*, 1940, **72**, 49; Theiler, M. *Medicine*, 1941, **20**, 443.
11. Warren, J., and Smadel, J. E. *J. Bact.*, 1946, **51**, 615; *J. clin. Invest.*, 1947, **26**, 1197; *Fed. Proc.* (Pt. I), 1948, **7**, 311.

Some Considerations of Bird Migration

Continental Drift and Bird Migration

The theory of continental drift postulates an original northern land mass, Laurasia, and a southern one, Gondwana. Each eventually broke into several drifting segments which became the present continents. Laurasia and Gondwana were "separated by a vast sea known as the Tethys." To explain some facts of animal distribution it is assumed that Laurasia and Gondwana occasionally drifted near one another or were at times in contact.

Wolfson (*Science,* July 9, pp. 23–30) has sought to explain the long migrations of some species of birds from hemisphere to hemisphere in terms of this theory. He assumes that at those times when the two hypothetical land masses were adjacent, certain birds happened to acquire a short migration that took them from one to the other. As the land masses drifted apart, he believes that such birds continued to migrate from one to the other until their migration may now extend nearly or quite from the Arctic to the Antarctic.

The theory of continental drift was seized upon by zoogeographers seeking to explain certain supposed anomalies of plant and animal distribution, particularly among fossil forms. Because of the relative scarcity of avian fossils and the unusual powers of dispersal conferred by flight, ornithologists are unable to determine the validity of this theory. Mammals, which are less able to cross water gaps and are represented by numerous fossils, are better material for such investigation.

G. G. Simpson (*Amer. J. Sci.*, 1943, **241**, 1–31), in connection with his extensive studies of fossil and living mammals and their distribution, summarized his conclusions with respect to the theory as follows:

> The fact that almost all paleontologists say that paleontological data oppose the various theories of continental drift should, perhaps, obviate further discussion of this