October 3, 1955

Dr. Henry W. Kumm
The National Foundation for Infantile Paralysis
120 Broadway
New York 5, New York

Dear Henry:

In accord with your request I am sending you herewith a brief progress report to supplement the semiannual progress report and the information contained in my letter of September 10 - all this for presentation to the Committee on Virus Research and Epidemiology.

1. Search for strains possessing minimal pathogenicity for monkeys by the spinal route. Since the semiannual report was written, three such strains turned up during our screening of poliomyelitis viruses recovered from the stools of healthy children which were obtained by Doctors Fox and Gelfand in the New Orleans region. This included two Type 1 strains ("P2149" and "P2226"), and one Type 2 strain ("P712").

The search for variants capable of producing a cytopathogenic effect in capucin monkey kidney cells revealed that some but not all Type 1 strains may possess a few particles out of a very large population which can produce a cytopathogenic effect in capucin monkey kidney cells. These particles have been segregated from the others and passaged in series in capucin monkey kidney sufficiently to get away from the original population of virus particles derived from the cynomolgus monkey kidney cultures. Although tests on several strains are still in progress, those that were completed on one Type 1 strain indicated that the particles which have the special capacity for producing a cytopathogenic effect in capucin cells are as pathogenic for monkeys by the spinal route as was the parent virus. Although tests on two other strains are scheduled for the near future, it would now appear that this approach is not promising and will therefore not be pursued further in 1956. Further work in progress on attempts to find variants which will propagate in chick embryo indicates that this is not a promising line of work and will not be pursued in 1956.
2. Additional observations on human volunteers. Most of the men who were fed the experimentally segregated attenuated poliomyelitis viruses in January 1955 were available for a check on the level of their antibody six months after ingestion of the virus. In all instances, the titers were either the same or higher at six months as at three months. In a number of instances the higher titers occurred in those volunteers who were fed a second type of virus three months after the initial ingestion of another type.

In my letter of September 10, I wrote you of a new series of tests which were to begin at Chillicothe on September 13. A total of 27 men were used. Six men were used for each of the three Type 1 strains that were tested (LSc, "P2149", and "P2226"), six men for the Type 3 strain, and three men who lacked both Type 1 and Type 3 antibody received a mixture of equal amounts of Type 1 ("P2149") and Type 3 ( ) viruses. Each strain was tested in a dose of 0.1 ml and 0.001 ml. The viruses this time were fed in a cherry syrup rather than in milk in the hope that this might lead to a larger number of virus particles being trapped on the throat. From the results that have been obtained, it would appear that this was achieved although one cannot be certain to what extent the strain of virus might have played a part.

At any rate, while none of the volunteers who received virus in milk in January in a dose of .001 ml had virus multiplication in their throat, 6 out of 11 of the present group presented evidence of viral multiplication of the throat after ingestion of 0.001 ml. Alimentary infection was established in all volunteers and the tests performed on serial bleedings up to two weeks after ingestion of the virus indicated that all but one developed antibody, many of them within one week after ingestion of the virus. The one who thus far has not developed antibody received 0.1 ml of the "LSc" virus and has exhibited very active viral replication in his throat and lower alimentary tract. Many of the volunteers, particularly in the group which received "P2149", developed their antibody within one week after ingestion of the virus. Of special interest is the fact that all three volunteers who were fed a mixture of about $10^6$ TCD$_{50}$ of the Type 1 "P2149" strain and the Type 3 strain developed antibodies for both Type 1 and Type 3 viruses. This lack of interference in the case of these two strains in human volunteers is to be contrasted with the complete suppression of multiplication and antibody response to the Type 3 Leon virus when it was fed to chimpanzees with a mixture of our Mahoney and YSK attenuated viruses. Preliminary tests on the current human volunteers already indicate that apparently both Type 1 and Type 3 viruses multiplied simultaneously in the pharyngeal wall. However, many additional tests still remain to be done before a complete picture will be available.

Tomorrow, on October 4, a new series of tests are scheduled to begin on another group of 20 volunteers at Chillicothe. Twelve men will be used for the Type 2 strain "P712" in doses ranging from 0.1 ml to 0.0001 ml. One man who is without antibody for all three types of polio will receive a mixture of all three types. Four men who are without antibody for Type one
and Type 2 will receive a mixture of 1 and 2, and three men without antibody for Types 2 and 3 will receive a mixture of Types 2 and 3 viruses.

The studies on both groups of these volunteers should be completed by the end of this year and at that time we may be in a position to decide which of the strains are most suitable for further progressive studies in human beings. At this time, we are testing in monkeys two additional Type 3 strains which were recovered in healthy children in the New Orleans area. Only if they should exhibit a markedly lower pathogenicity for monkeys by the spinal route than the [missing] strain now under investigation, would tests in human beings be carried out.

As matters stand now, therefore, it would appear that the major effort in 1956 would be concerned with an extension of studies in human beings of the strains that prove to be the optimum ones in the current tests. These studies would be essentially the ones that were outlined in the memorandum accompanying the 1956 application. It would be my plan to prepare at least 10 liters of each of the selected strains, carry out the most extensive safety and control tests on them, and then use aliquots of these basic lots for all the projected studies in human beings. Because of the high titers which the strains yield in monkey kidney tissue culture, it is conceivable that the cultures could be diluted at least 20 to 100 fold for use in human beings. Accordingly, each cc of culture fluid may be sufficient for 20 to 100 or more doses.

3. Present status of work and plans on chimpanzee-rhinitis and steatorrheic enteritis viruses. As I reported to you in my letter of September 10, there seems little question that a virus which is either identical or closely similar to the one recovered from the chimpanzees with rhinitis is responsible for infection in human beings - as evidenced from the serological survey data that we obtained. Further experimental studies that were carried out on chimpanzees since the last semiannual report gave new indications of resistance in convalescent chimpanzees and further indicated that tests on human beings would not be very significant except in children or adults who happen to be without antibody for this virus. Although there is a possibility of doing such tests on a small scale at Chillicothe (I have found a few of my volunteers without antibody for this virus), I did not want to jeopardize the work on poliomyelitis at Chillicothe by proposing a new type of experiment.

Dr. G. A. Andrews of the National Institute of Medical Research in London, has expressed a great interest in this virus and in accord with his request I have sent him some of the chimpanzee-rhinitis virus for tests on human volunteers in England.
As indicated in the semiannual report, the virus that was associated with steatorrheic enteritis was found to belong to the same group as the chimpanzee-rhinitis virus. Further cross immunity studies strongly suggest that these two viruses are very closely related, if not identical, antigenically.

With kindest regards,

Sincerely yours,

Albert B. Sabin, M. D.