Dear Dr. Sabin:

We deeply regretted your not being able to attend the first meeting of the Advisory Committee on Gamma Globulin. Your letter to Dr. Langmuir was read to the Committee, and your comments on various aspects of the proposed studies were fully discussed.

The Committee was interested in your comment on the fact that the cases with a shorter incubation period are generally more severe than those with a longer incubation period. They felt that this point was not completely applicable to the situation in the household since most of the cases subsequent to the index case are not secondary cases but co-primaries who probably were infected at varying periods of time outside the household. However, it seems to me that it will be necessary to take this point into consideration in the final analysis of the data by a further subdivision of the time intervals and some internal comparisons with regard to severity of disease.

Your second point concerning the changing age distribution of cases as the epidemic progresses will obviously have to be taken into consideration in the final analysis of any data collected from areas where community prophylaxis is used.

Since it is highly desirable that the members of the Committee be kept informed of both the plans and operations of the study, I am enclosing copies of the following documents:

(1) Minutes of the meeting including a summary of recommendations of the Committee
(2) A memorandum by Dr. Langmuir concerning his discussion with representatives of the American Physical Therapy Association regarding the procurement of physical therapists for the study
(3) A memorandum to the State Health Officers outlining the study plans.

I would greatly appreciate any comments you may have on the final recommendations of the Committee.
I sincerely hope it will be possible for you to attend future meetings of this Committee, which will be called to further consider various aspects of this study.

Sincerely yours,

Abraham M. Lilienfield, M.D.
Secretary
Advisory Committee

P. S. I am returning the charts you so kindly sent us.

cc: Dr. A. D. Langmuir
MINUTES OF THE FIRST MEETING OF ADVISORY COMMITTEE ON NATIONAL PROGRAM FOR EVALUATION OF GAMMA GLOBULIN IN THE PROPHYLAXIS OF POLIOMYELITIS, MAY 28-30, 1953.

The Advisory Committee held its first meeting in Atlanta, Georgia, at CDC headquarters on May 28 and 29, with several members of the Committee continuing to meet on May 30. Dr. Languir, Chairman, called the meeting to order and reviewed the present system for the allocation and distribution of gamma globulin, and the need for a plan to evaluate gamma globulin this year. He recommended the appointment of Dr. Lilienfeld as Secretary, which was approved, and then turned the chair over to Dr. Lilienfeld because of other meetings at which his presence was necessary.

The Committee reviewed the following basic documents that had been prepared in advance: (1) The objectives of the Evaluation Program as stated in the memorandum to State Health Officers, dated May 21, 1953, and 2) the Proposed Studies for the Evaluation of Gamma Globulin. The Committee decided it would discuss the plans in the following order:

(1) Evaluation of gamma globulin  
(2) General Epidemiological Studies  
(3) Administrative Aspects

The Committee first considered the possibility of measuring the effectiveness of gamma globulin in preventing paralytic poliomyelitis in contact prophylaxis. Three possible methods of measuring this effect were reviewed as follows: 1) comparing secondary attack rates among those receiving gamma globulin with previous experience; 2) comparing frequency distribution of secondary cases in time with previous experience; 3) comparing secondary attack rates among individuals who received gamma globulin with those who did not.

The Committee felt that the comparisons with past experience were of a dubious nature and the comparisons suggested in 3) were between non-comparable groups. It was the consensus of opinion that it would not be possible to evaluate the preventive effect of gamma globulin without a planned control study, which was not feasible at this time.

The Committee then considered that it would be possible to measure the modification effect of gamma globulin by comparing the severity of disease among groups of cases which have not received gamma globulin with those who have received it at varying intervals prior to onset. A letter from Dr. Sabin, commenting on the fact that the cases whose onsets were earlier in the incubation period may be the more severe cases, was read. The Committee did not feel that the observations made by Dr. Sabin were completely applicable to the present study. However, the possibility of this type of bias should nevertheless be looked into in the final analysis of the data.

In order to study the modification effect, it would be necessary to identify multiple case households, and determine the severity of disease among those who did and those who did not receive gamma globulin. This could be done by a physical therapist at 50 - 70 days after the onset of the case. Since
about 3% of all reported cases are subsequent cases in multiple case households, one could expect about 1,500 such households in the country. The Committee thought that each of these households should be identified and a muscle evaluation performed on as many cases in these households as possible, with a minimum objective of 750-800. The number of households to be investigated in each State was not particularly large so that the individual State Health Department would not be burdened with such investigations.

The Committee then reviewed a form, prepared in advance for use in investigating these households. Many changes were suggested which were to be incorporated into the final form. The Committee recommended that all forms used in the study be copied and the copies be forwarded to the National Evaluation Center which should be established in CDC.

On the second day of the meeting, Miss Miriam Jacobs, Physical Therapist, reviewed an abridged system of muscle evaluation developed by Dr. Jessie Wright that could be utilized for the muscle evaluation necessary in this study. Various members of the Committee expressed the desire to have the physical therapists in their own States trained in the use of this method.

The Committee then reviewed the possibility of collecting general epidemiological information concurrently with the gamma globulin study. Committee members from health jurisdictions where epidemiological investigation of all routine cases are carried out volunteered to obtain the same information in a consistent manner and to prepare tabulations of the necessary data which would be consolidated and analyzed at the National Evaluation Center. The data collected would be concerned primarily with testing a genetic hypothesis and the influence of various provoking factors.

The Committee then briefly reviewed the types of administrative data that would be of value. (These are outlined in more detail in the attached summary).

The question of community prophylaxis was reviewed. No definite plans were formulated, although it was recommended that as much data as possible be collected in those areas where this method is used. In analyzing the changes in the age-specific attack rates before and after gamma globulin is administered, it would be necessary to take into account the changes of the age distribution of cases that occur during an epidemic, as suggested in Dr. Sabin's letter, which was read to the Committee.

During the afternoon of May 29, the Committee met jointly with the Epidemic Intelligence Service Officers, where an outline of the plans recommended by the Committee was presented and discussed.

On the morning of May 30, several members of the Committee met informally. At this time it was suggested that it would be possible to study the effect on modification in community prophylaxis by comparing the severity
of disease among cases who received gamma globulin with those who did not in areas where community prophylaxis was used. This idea was incorporated into the recommendations of the Committee.

Attached is a summary of the final recommendations of the Committee that was prepared for general distribution. This summary is to be considered part of these Minutes.

Respectfully submitted,

Abraham M. Lilienfeld, 
Secretary

Att.

June 9, 1953
SUMMARY OF RECOMMENDATIONS

ADVISORY COMMITTEE ON NATIONAL PROGRAM FOR
EVALUATION OF GAMMA GLOBULIN IN THE PROPHYLAXIS OF POLIOMYELITIS

The Advisory Committee met in Atlanta, Georgia, on May 28-30, in accordance with the Preliminary Announcement of the Gamma Globulin Program which was distributed to all State Health Officers on May 21, 1953. The recommendations of the Committee are summarized as follows:

A. General Recommendations:

1. In view of the scope and cost of the national effort to produce and distribute gamma globulin, a maximum effort should be made to obtain consistent and useful information on a national scale to evaluate the effectiveness of gamma globulin as actually used.

2. Each state should participate to the limit of its capacity in the collection of consistent and useful information.

3. The CDC should make available to the limit of its capacity epidemiological and statistical consultative services and personnel to assist the states in this joint national effort.

4. A National Evaluation Center should be established in the CDC to coordinate the services provided to the states by CDC, and to receive reports from participating states for tabulation and analysis. Consolidated reports should be distributed at regular intervals to all participants.

B. Specific Recommendations:

1. Evaluation of Contact Prophylaxis

   a. Prevention of Paralysis

       The Committee decided that a controlled study would be necessary to evaluate the effectiveness of gamma globulin in the prevention of paralysis. Since such a study is not feasible in this country this year, the Committee recommended that the primary objective of the national program should be the study of the modifying effect of gamma globulin on the severity of disease.
b. Modification of Paralysis

The study of modification can be made by comparing the severity of disease among groups of cases which have not received gamma globulin with those which have received it at varying intervals prior to onset. The most comparable groups of these types can best be obtained on a national scale by identifying multiple case households (i.e., household with two or more reported cases). The following data should be obtained on each reported case in these multiple case households:

1. Verification of diagnosis.
2. Verified date of onset.
3. Date, amount and site of gamma globulin administered, if any.
4. History of factors that may influence paralysis.
5. Severity and location of paralysis based on 50-70 day standardized muscle grading by a physical therapist.

2. Evaluation of Community Prophylaxis

The Committee recognizes that mass or community prophylaxis will be utilized in such a wide variety of ways that a simple plan for evaluation cannot be devised. It recommends, however, that in each area where community prophylaxis is employed, the following information be collected:

a. The name, age, address and date and site of administration of gamma globulin for each individual who receives it.

b. A record of each reported case of poliomyelitis occurring in the population before, during and subsequent to community prophylaxis. This record should include, in addition to routine identifying data, the verified date of onset, the date, site and amount of gamma globulin administered, if any, history of provoking factors and the severity and location of paralysis as determined by 50-70 day standardized muscle grading by a physical therapist.

Such information will permit a comparison of age-specific attack rates, and severity of disease in relationship to the time of administration of gamma globulin.
3. Administrative Aspects

The Committee recommends that the administrative aspects of the distribution and utilization of gamma globulin be studied and documented in all states in order to provide the basis for more effective utilization of gamma globulin in the future. A number of specific questions can be answered and problems resolved only by practical experience. Among these are:

a. The extent to which the availability of gamma globulin will stimulate over-reporting of poliomyelitis. This can be measured by observing the ratio of paralytic to non-paralytic cases and the ratio of reported cases to deaths.

b. The extent of delay between the date of onset of the first case in a household and the date that gamma globulin is administered to contacts. This can be measured by tabulating data from the requests for gamma globulin submitted by physicians.

c. The degree to which communities utilize the available resources in the program. What proportion of household contacts actually received gamma globulin through private physicians' offices, health department clinics, hospital out-patient departments or specially organized programs? How are the costs of these activities met locally? Such information should be collected and documented in many communities for each of the methods of distribution, including household contacts of clinically diagnosed cases, other intimate contacts, contacts of suspected cases and community prophylaxis.

4. General Epidemiological Information

The Committee recognized a continuing need for detailed descriptive information regarding the epidemiology of poliomyelitis in order to provide the soundest possible basis for effective planning of future programs. It, therefore, recommends that a number of special studies be undertaken in areas where routine epidemiological investigations of all reported cases are feasible. Several members of the Committee are now planning such studies. They have volunteered to collect information in a consistent manner and have agreed to consolidate their findings through the National Evaluation Center.
Members of Committee:

Alexander D. Langmuir, Chairman
Abraham M. Lilienfeld, Secretary
John Chapman
*Roy F. Feemster
Thomas Francis, Jr.
*D. G. Gill
*Archie L. Gray
Morris Greenberg
William McD. Hammon

*Denotes members of Subcommittee on Epidemic Intelligence of the Committee on Infectious Diseases, Assn. of State and Territorial Health Officers.

1 Not present at meeting.
2 Represented by Dr. John E. McCroan
3 Represented by Miss Miriam Jacobs

Dr. Henry Kumm, Assistant Director of Research, NFIP and Dr. Ralph Paffenbarger, Office of Civilian Health Requirements, PHS, attended as observers.
MEMORANDUM

For the Record

June 5, 1953

Dr. Alexander D. Langmuir


On Wednesday, June 3, I visited in the office of the American Physical Therapy Association, 1790 Broadway, New York. The introduction was arranged by Dr. Harry Weaver, Director of Research of the National Foundation for Infantile Paralysis.

A conference was held with Miss Mildred Elson, Executive Director; Miss Lucy Blair, Chief Consultant and Miss Ruth Whitemore, Consultant of Professional Services (formerly Folio Services).

The general plans for the National Program for the Evaluation of Gamma Globulin in the Prophylaxis of Poliomyelitis were discussed at length. The crucial need for competent and consistent evaluation of cases by physical therapists was immediately recognized. Genuine interest in active participation in the study was expressed.

It was understood that no commitments would be made until a full and detailed plan of the study was submitted and approved, but on a large number of points, general agreement was reached in principle, as follows:

1. From 12 to 18 physical therapists will be needed in the program. These should become available by mid-July or early August and will be needed through December.

2. These Physical Therapists would be assigned to teams organized in collaboration with State Health Departments when programs are organized that are supported by CDC and that meet the minimum criteria established by the Advisory Committee.

3. The main function of the PT's will be to provide a 50 to 70 day grading of severity of the reported cases of poliomyelitis included in the studies.

4. The streamlined system for grading severity, prepared by Dr. Jessie Wright and Miss Miriam Jacobs was believed to be entirely acceptable although it had not yet been studied by APTA.

5. It would be most desirable for the PT's who are to join in the program to meet together for a short period to become familiar with the details of the program and the muscle grading system. The most appropriate time for this would be during or at the end of the one-week course now being planned by Dr. Jessie Wright in Pittsburgh, July 13 to 17.
6. For purposes of planning costs it is estimated that the services of one physical therapist including living and traveling expenses would be approximately $750.00 per month. The extent of travel for the PT's would vary widely depending upon the location of the study.

7. Administratively, the most satisfactory and workable arrangement would be for the APTA to retain full responsibility for paying salaries and expenses and working out arrangements for providing PT services to each study area. Request for the services would be made directly to APTA by the State Health Officer or the State Epidemiologist who assumes local responsibility for the study. The request would be cleared by APTA with GSC before action was taken. In each instance the physical therapist would be assigned to and be responsible locally to the epidemiologist who is directing the study in the area.

8. Under certain circumstances it is visualized that mobile field teams may be organized by GSC to cover more than one state. In these instances, request for PT services will be made directly by GSC to APTA, and GSC will assume responsibility for clearing local arrangements.

An appointment was made for Dr. Abraham Lilienfeld to meet Miss Elson, Miss Blair and Miss Whittacore in New York on Wednesday morning, June 10, at 10:00 o'clock. At that time more detailed plans will have been worked out. This appointment comes just before the Conference of APTA which will be held in Dallas, Texas, June 11 to 22.

Alexander B. Langmuir, M.D.
Chief, Epidemiology Branch

cc/ Dr. Lilienfeld
Miss Elson, APTA
Dr. H. Weaver, NFIP
Dr. David Price, GSC
Executive Office, GSC
Chief, D.S.S.
To: All State Health Officers, Regional Medical Directors and Others Concerned

From: Dr. Alexander D. Langmuir, Chief, Epidemiology Branch, CDC

Subject: Plans for the National Program for the Evaluation of Gamma Globulin in Poliomyelitis

In the Preliminary Announcement of May 21, 1953 your attention was called to the National Program for the Evaluation of Gamma Globulin in Poliomyelitis that is being sponsored by the Communicable Disease Center in collaboration with the Association of State and Territorial Health Officers. The Advisory Committee, mentioned in the announcement, met in Atlanta on May 28th to 30th. A summary of recommendations for this nationally coordinated program is attached.

You will note that General Recommendations 2 and 3 urge that each State participate, to the limit of its capacity, in the collection of consistent and useful information and that CDC contribute to the limit of its capacity, epidemiological and statistical consultation services and personnel to the program.

CDC is proceeding to implement these recommendations. The National Evaluation Center has been established in the Epidemiology Branch of CDC. Dr. Abraham M. Lilienfeld has been appointed Director. Epidemic Intelligence Service officers, Nurse Epidemiologists and statistical personnel are being alerted and trained for duty in this program. We hope that each State will actively participate in this program.

You will note that the primary objective recommended by the Committee is to collect data regarding the modification of severity of paralysis by gamma globulin, which will require:

1. Identifying multiple case households (estimated to involve from 3 to 5 percent of total reported cases).

2. Providing for a field visit to determine in each reported case in these households –
   a. Verification of the diagnosis
   b. Exact date of onset
   c. History of factors that may influence paralysis
   d. Confirmed dates, sites, and amounts of gamma globulin administered.
3. Arranging for a standardized muscle grading of each of these cases by a physical therapist 50 to 70 days following onset.

4. Reporting the above information to the National Evaluation Center on copies of standard forms to be provided.

The identification of multiple case households can be performed most readily by matching the names and addresses of all reported cases in a State or local health jurisdiction. Data regarding administration of gamma globulin can be obtained from the file of the requests for gamma globulin submitted by physicians. A system of clerical procedures for this aspect of the program is being prepared at the National Evaluation Center and will be forwarded upon request.

Two field visits to hospital, clinic, or home, will be necessary. The first should be made as soon as possible after the recognition of a multiple case household and can be made by health officers, epidemiologists, public health nurses and trained investigators. These individuals should be oriented in the procedures and use of the standard form. An outline of the procedures and instructions in the use of the form are being prepared at the National Evaluation Center and will be forwarded upon request. A supply of the forms will be available for distribution to participating States.

The second visit should be made 50-70 days later by a physical therapist, or if this is impossible, by a physician or nurse trained in the use of the standardized abridged system of muscle grading now being developed.

These field visits can best be performed by evaluation teams consisting of an epidemiologist and a physical therapist working out of centrally located points and serving under the direction of the State Epidemiologist.

Within the limits of its capacity, CDC is preparing to provide:

1. Statistical consultation services on an intermittent short-term basis to all States requesting assistance in establishing procedures to identify multiple case households.

2. Epidemiological consultation services on a short-term basis to assist States in establishing programs.

3. Epidemic Intelligence Service officers and Nurse Epidemiologists to serve on evaluation teams, under the direction of State Epidemiologists. Since many more requests for the assignment of epidemiologists are anticipated than can be met with available personnel, the following factors will be taken into consideration in attempting to meet these requests:

   a. CDC epidemiological personnel now assigned to States will remain in those States undertaking programs with the understanding that they will be utilized in these studies.

   b. Assignments of other available epidemiological personnel will be made principally to areas having the largest populations or experiencing the heaviest epidemic incidence of poliomyelitis in order to obtain the maximum number of investigations of multiple case households.
c. A certain number of mobile evaluation teams may be organized to serve on an area or regional basis involving several States not included in "b" above, and will be on call for unusual epidemic situations.

Arrangements are now being negotiated for an intensive one-week course in muscle gradings for CDC epidemiological personnel assigned to this program. Negotiations are also under way with the view of obtaining an adequate number of physical therapists for assignment to evaluation teams when such services cannot be provided locally. Further information regarding these plans will be forthcoming at an early date.

Alexander D. Langmuir, M. D.
Chief, Epidemiology Branch

Attachment