Poliomyelitis Vaccine

A Report on Field Trials in Southern Alameda County in 1954

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• *Southern Alameda County was the only area in California to take part in the 1954 nationwide field trials for testing poliomyelitis vaccine. Besides the contribution made in evaluating the vaccine, other benefits were:*

1. Participation contributed to the control of a serious communicable disease.

2. Inoculations of vaccine during the field trials in all probability prevented some cases of paralytic poliomyelitis among children in southern Alameda County.

3. The community became better informed about poliomyelitis and more interested in the local health department.

4. Local physicians had an opportunity to contribute to important research and to give a valuable community service.

5. The staff of the Alameda County Health Department became better informed and better prepared for any future responsibilities in poliomyelitis immunization programs.

Other conclusions reached as a result of participation in the 1954 field trials are that the initial planning of the study was hasty and not sufficiently representative of medical and administrative thinking. If the trials had been planned for 1955 instead of 1954 there would have been sufficient time for research to be completed, professional information to be assured and for sound design of study.

GREATLY ACCELERATED RESEARCH in the field of virus diseases in recent years has led to a much better understanding of epidemiologic factors, particularly with regard to poliomyelitis. Great sums of money have gone into intensive studies of that disease, many directed to the ultimate prevention of it or of its paralytic consequences. In fact for a time knowledge accumulated more rapidly than it could effectively be disseminated. Hence the pronouncements in the autumn of 1953 that a trial vaccine was ready for large-scale testing—that, in fact, plans were already well laid for such testing by the National Foundation for Infantile Paralysis —came as a surprise to many physicians.

It seems clear that the studies of Jonas Salk did certainly justify large-scale testing. Few will question, however, that nationwide field trials, as proposed for the spring of 1954, encountered many obstacles as a result of the rush to prepare for them.

It was obvious that an undertaking of this size could be carried out only by local health departments. Plans were such that only certain areas in the country could be considered. The following factors were the basis for possible selection: (1) A high incidence of poliomyelitis among children in the first, second and third grades of school; (2) a large population in these age groups selected for the study, and (3) a well-organized local health department with an interest in the study.

Although some technical information had been published in a few professional journals (a greater amount of publicity had appeared in the lay press) many questions remained to be answered. Virologists, epidemiologists, health officers and practitioners hastened to ask them. These questions had to do with the following:

1. *Safety of the vaccine.* Was the live virus altered in such a way that it could not produce disease? Was kidney tissue a safe element, or was there danger of nephrotoxic effects?

2. *Potency.* Could this particular vaccine reasonably be expected to protect against paralytic poliomyelitis?

3. *Biologic assay.* What procedures were reliable?

4. *Intervals between injections.* What schedule should be used?

5. Was aqueous vaccine likely to produce immunity as good as that produced by an adjuvant-base vaccine?

6. Follow-up and evaluation plans.

7. Administrative arrangements for carrying out the trials.

8. Was it reasonable to believe that solid immunity could result from inoculation of killed virus?

It soon became obvious that although some of these questions could be answered satisfactorily at the time, others could not. It was evident that rather detailed field trial plans had been formulated before

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some of these questions could be answered, and before all the necessary research data had been gathered. But the additional data were forthcoming, and did lend support to the plans. That these results were known at such a late stage and that they were further delayed in their circulation, however, points up an important problem encountered in the 1954 Field Trials. Much of this type of difficulty would have been avoided had the early planning been more representative of health department thinking. And many of the questions about the vaccine might well have been resolved even before plans for an extensive trial were undertaken.

It became clear that the country was in the midst of hurried plans for field trials before the great majority of practitioners and health officers could become well informed about the vaccine itself. There were more than a few physicians who were understandably confused on the subject. But the field trial plans continued, centered on nationwide testing in selected areas. Children in the second grade of school would be injected with aqueous vaccine containing killed virus of the three known types. First and third grade children would serve as uninoculated controls. The trials would involve perhaps 2,000,000 children, and the inoculations would be given according to this schedule: the first on zero day; the second on day seven; and the third, or booster injection, on day thirty-five. About 2 per cent of the children inoculated would also have blood specimens drawn for antibody studies before and after the series of injections. Inoculations were to begin early in the spring and be completed before school was over. Areas for testing were to be proposed by state health departments and approved by the National Foundation for Infantile Paralysis.

PLANS FOR FIELD TRIAL CHALLENGED

Although many states accepted the field trial plan as originally proposed, others raised serious questions:

1. Would the study method proposed give the conclusive answers sought?
2. Were the procedures adequate to assure safety of the vaccine, and
3. Were adequate provisions being made for follow-up and evaluation?

California, in particular, insisted that a sound trial would necessarily include use of a placebo, and insisted, further, that satisfactory answers be obtained to the questions regarding safety of the vaccine before the state would agree to participate. It was only in February, after many weeks of nationwide publicity about the trials, that satisfactory information was made available to California which permitted a sound decision to be made. On the recommendation of an Ad Hoc Advisory Committee, the State Department of Public Health agreed to participate, and this decision received the approval of the State Board of Health.

There were several areas in the state considered suitable—among them, San Diego County, a portion of Los Angeles County, and southern Alameda County. Whether from lack of funds, early rise in incidence of poliomyelitis, or from lack of community interest, all areas but southern Alameda County ultimately indicated they could not take part. Southern Alameda County remained under consideration only because of a keen interest on the part of the community, and a sincere desire on the part of the local health department staff to engage in this program. The decision by the Alameda County Health Department to participate was reached only after considerable efforts had been made to get the necessary information—and only after thorough analysis of the meaning participation would have. The great public interest, and the opportunity to provide an unusual community service were factors of obvious importance. And, of course, the fact that Alameda County could make a contribution to the nationwide study was of no little consequence.

Designation of the southern part of the county by the State Department of Public Health as a trial area followed, and active local planning got under way. The county health officer called together a group made up of representatives of the medical profession, of the local chapter of the National Foundation for Infantile Paralysis, of school systems, of Parent-Teacher associations, of newspapers and the staff of the county health department. A representative of the State Department of Public Health who attended presented information about the trials in some detail. After discussion ended, the opinion of the group was asked for. It was quickly forthcoming in a motion endorsing local participation and promising full cooperation from those present. The group requested that the county health department proceed with the planning and ask for whatever help would be needed.

A small planning group was quickly formed, composed of the county health department staff, with a representative from the local chapter of the National Foundation for Infantile Paralysis, and a member of the State Department of Public Health. Meetings were held twice weekly at regularly scheduled times. Early meetings were geared to the following objectives: (1) Approval by the local medical societies, and agreement by their members to participate in the trials; (2) interest among school personnel; (3) interest among parents and a desire to take part, and; (4) a well-informed local health department staff willing to give the extra time and effort needed for a successful job.

Professional interest already abounded, and active local medical support was forthcoming as soon as adequate information was made available. Not only did local physicians approve participation, but they volunteered to give the injections in the schools. Early talks to local physicians by the health officer, and by members of the State Department of Public Health were instrumental in providing information and in gaining support. Later, printed information of a technical nature was circulated by the health department to Alameda County physicians in an attempt to answer their many questions.

This material presented a rather comprehensive idea of the preparation, testing and use of the vaccine, and local practitioners greatly appreciated it, for they had no other easily available source of such information.

Interest of school personnel was necessary, since the trials were based on their active participation. So an early meeting was arranged with the 30 school administrators in the area, and current plans were presented. Their endorsement resulted, and each agreed to request the approval of his respective school board. After many approvals had been obtained, one school board raised the question of legal liability, and asked the opinion of the district attorney. A preliminary statement from the district attorney's office made it plain that public schools lacked the authority to take part in the study, and, further, pointed out that the injections could be given in the schools only after regular school hours. It appeared, for several days, that all plans had been in vain, but in a final legal opinion a way was found. Injections could be given during school hours, but school personnel could take no part in the trials. The first big hurdle was cleared.

INFORMING THE PUBLIC

The public desire for information was satisfied largely through talks to parent groups by physicians of the county health department and by local practitioners. Newspaper and radio coverage were also extensive. In the later stages, printed information prepared by the local health department was sent to all parents of first, second and third grade children. Public health nurses, as well, contributed a great deal toward public education.

Interest within the health department was at a high pitch, and early efforts were concentrated to provide a well-informed staff, each member with an adequate understanding of the trials. Special educational meetings were held for the nursing staff early in the planning, and at a later meeting the entire staff heard the plans explained by Dr. Robert Korns, a member of the Vaccine Evaluation Center Staff. Minutes of planning meetings were circulated so the whole staff could keep abreast of developments.

VOLUNTEER HELP

Agreements were reached with the local chapter of the National Foundation for Infantile Paralysis regarding financial support, and the chapter also agreed to be responsible for recruiting the volunteer help needed.

Because of the public enthusiasm for the study, volunteer recruitment was no great problem. The forms that parents were required to fill out giving permission for vaccination were prepared, and sent to parents, and were returned. Clinics were scheduled, and time for the injections approached. But there were serious doubts that the vaccine could arrive in time. Final safety testing had to be completed and the lots officially approved before they would be released for shipment. Again, plans had to proceed without assurance they could be carried out. Physicians were assigned to clinics and notified of the work schedule. Recorders were trained, volunteer nurses recruited and clinic teams formed. But the vaccine was further delayed. It was not until April 25 that any vaccine was released, and only the afternoon before injections were to begin that shipment to California started. At the very last moment the National Foundation had decided against California participation, for reasons still not clear. It was only after urgent assurances from the state health officer and from local National Foundation for Infantile Paralysis chapter officials that the vaccine was put on its way.

It did arrive, and, quite dramatically, just two and a half hours before injections were to begin. But the clinics operated as scheduled, the injections were completed, and the first easy breaths drawn.

By June 10, 1954, 7,166 children had received three injections each—half of them with vaccine, half with placebo—all identified simply by a code, the key to which was known only at the Evaluation Center in Michigan. A hundred local physicians and some six hundred other volunteers had taken part. The entire staff of the county health department, including all sanitarians and clerical personnel, had been directly involved. Clinics were held May 5 and 6, May 12 and 13, and June 9 and 10, in 90 different schools.

The first part of the study was over, but important responsibilities remained. To give any meaning to the trials, careful follow-up and good evaluation had to be assured. Blood studies for antibody titrations were to be made on all family members in any family in which there was a case of poliomyelitis and a child of the study age group. And stool specimens were to be collected for virus isolations in similar circumstances. Uniform diagnostic criteria were to be applied, and prompt reporting was a necessity. Muscle grading examinations were to be arranged for children in the study ages who con-

tracted poliomyelitis. Promptness was necessary in reporting cases to the Evaluation Center, as well as completion of attendant epidemiological histories. Responsibility for the follow-up was shared with the State Department of Public Health. The period of follow-up extended from May 10 through December 31 of 1954.

Results of the follow-up now reveal that a total of ten cases confirmed as poliomyelitis occurred during this time among children in the study age group in southern Alameda County. Seven of these ten cases were among children who did not receive any injections. The remaining three cases all occurred in children who had received the placebo.

The final results of the nationwide trials became known April 12, 1955, and need no repeating.

A review of the participation of southern Alameda County in the study brings out the following conclusions:

1. Initial planning of the study was hasty and not sufficiently representative. If the trials had been planned for 1955, instead of 1954, there would have been sufficient time for research to be completed, professional information to be assured, and for sound study design.

2. Public health authorities in many areas were willing to accept without argument a trial originally designed on an unsound basis. Save for the insistence from some states, no placebo trials would have been conducted, and the results could not have been so conclusive.

3. Participation in the study contributed to the control of a serious communicable disease.

4. Inoculations during the field trials in all probability prevented some cases of paralytic poliomyelitis among children in southern Alameda County.

5. The community became better informed about poliomyelitis and more interested in the local health department. Increased public respect for the health department resulted.

6. The 1954 Field Trials provided the first real opportunity to work with the local chapter of the National Foundation for Infantile Paralysis, and proved in still other ways that teamwork was possible.

7. Local physicians had an opportunity to contribute to important research, and to give a valuable community service.

8. Members of the staff of the Alameda County Health Department are better informed, more interested, and have greater self-assurance for future undertakings.

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