Progress in Research on Poliomyelitis

The "journey into the unknown" of poliomyelitis is traced from before 1938 to the present—and projected into the future—by one who has been along much of the journey.

By HARRY M. WEAVER

RESEARCH is primarily and essentially a journey into the unknown, for the principal purpose of solving problems that disturb us, and for which we have no satisfactory solution. Prerequisite to the solving of any problem is the exploration, study, and understanding of all those areas of knowledge that are related directly or indirectly to the problem which has been posed. Without the benefit of the perspective that comes with such knowledge, one encounters the grave risk of deciding, prematurely, that a problem has been solved, only to learn to his sorrow, at some future date, that all of the relevant facts were not at hand.

Although great forward strides have been made in the general field of the medical sciences, far more remains to be learned than is known today. I am inclined, therefore, to be somewhat hesitant in drawing sweeping conclusions relating to poliomyelitis, because, it seems to me, the many voids in our knowledge of the medical sciences leave us without the depth of perspective we should have.

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This informal review of research, here somewhat condensed, was presented at a special meeting of the Board of Trustees of the Foundation in New York City on January 26, 1953. In his talk, Dr. Weaver pointed to limitations of time and space, remarking his "regret that it has been necessary to omit many very interesting and several potentially important observations."

Limitations and Scope

It is impossible for any one individual totally to comprehend the program of research against poliomyelitis. Seldom has there been assembled such an array of talent, representing so many diverse fields of scientific specialization, all working toward a single common objective. The intensity with which the individual members of this coordinated team carry out their work results in an ever growing and ever changing body of knowledge about poliomyelitis. No sooner does one investigator tentatively suggest a concept to explain some unresolved problem, than we find one or more other workers subjecting that concept to the acid test of quantitative experimentation. This constantly changing body of knowledge causes no little confusion in the minds of those persons who attempt to keep abreast of this progress. But, because this program of research is dynamic, our knowledge about poliomyelitis is approaching with unusual directness and rapidity the objective for which we all strive, i. e., the absolute and total truth.

Because of the fact that we are conducting research on so many different aspects of poliomyelitis—the virus, its host, the acute disease, its after-effects, methods of prevention and of treatment—it is difficult for any one individual to stay abreast of even the basic principles, and it is impossible for him to comprehend totally

256490—53——3

the inferences and subtleties of this rapidly changing body of knowledge.

Finally, because poliomyelitis so frequently results in crippling, because this disease selectively affects most commonly the healthy child in the very bloom of his youth, because poliomyelitis is prone to strike with such dramatic suddenness, we are understandably anxious to rid ourselves of the dread that this affliction will strike down one of those dear to our own hearts. It is only natural, therefore, that into any report on research we try to read a new cure, a new preventive, or, at least, a new means of ameliorating the crippling after-effects of this affliction.

A Review of Progress

My intention is not to state or imply that the means are now at hand whereby we can protect ourselves from the paralytic consequences of an infection with the virus of poliomyelitis, but rather to review, within the limitations to which I have already referred, the very considerable progress that has been and is being made in an effort to provide some practical means to control this disease. We may examine the results of research in the field of poliomyelitis in relation to four different periods of time: (*a*) prior to 1938, (*b*) from 1938 through 1947, (*c*) from 1948 through 1952, and (*d*) the years that lie ahead.

As we discuss the research of prior years, we should not lose sight of the fact that in all fields of human activities—and the medical sciences are no exception—hindsight, as compared with foresight, is very much more penetrating, illuminating, and satisfying. In assessing the work of prior years, we have available a vast body of scientific knowledge that simply did not exist when that research was being conducted. And may I be the first to point out that the body of scientific knowledge, to which I have just referred, is not by any stretch of the imagination of the making of the National Foundation for Infantile Paralysis and its grantees alone. We have unhesitatingly applied to our work in poliomyelitis, where applicable, knowledge that has emerged through no effort of ours, but because some individual or group supported an investigation on some problem which seemed totally unrelated to poliomyelitis. We are fortunate that a sharing of knowledge is the accepted way of research. Indeed, it is not unlikely that when the work of the National Foundation has been completed, history may record the fact that its greatest contribution was not the bringing forth of some practical means to control poliomyelitis, but that it stimulated and supported a cooperative effort of many scientists, from which effort emerged the knowledge requisite to fashioning the answer to one of man's even more distressing problems.

The Years Before 1938

The National Foundation for Infantile Paralysis was created in 1938 for the purpose of initiating and supporting a comprehensive effort by scientists to develop some practical means whereby man could protect himself from the paralytic consequences of an infection with the virus of poliomyelitis. That was, and continues to be, the principal objective of this organization.

It is very difficult to describe accurately our knowledge of poliomyelitis as it existed in 1938. Research on any subject progresses in an orderly fashion through several sequential stages, of which the principal ones are: (*a*) the construction, on purely theoretical grounds, of a concept to explain one or more aspects of the problem; (*b*) the modification of the concept in accordance with what are believed to be all of the facts relating to the problem; and (*c*) the evaluation of the concept by controlled and critical experimentation.

Facts and Misconceptions

The scientific literature, prior to 1938, contains many statements about poliomyelitis that have subsequently been proven to be true. This literature also contains a vast array of misconceptions. It is not too unfair to say that, for the most part, knowledge about poliomyelitis in 1938 was so limited in extent, and so lacking in experimental proof, that it was difficult for the investigator of that day to distinguish between fiction, wishful thinking, and fact.

In 1938, the science of virology was in its swaddling clothes. Only a handful of workers were qualified by training and experience to conduct critical investigations in this field. The tools required to carry out scientific research on poliomyelitis were, for the most part, crude prototypes of those available today; and even they were in such short supply, and so expensive, that it was a fortunate worker indeed who had an opportunity to work with them. Furthermore, most work on poliomyelitis required use of monkeys, with the result that research was even further limited to those very few individuals who could obtain financial support in large amounts. In an attempt to continue work without adequate means of support, it appeared necessary to carry out with one or two monkeys experiments that should never have been attempted without utilizing scores of these animals. The result was a long period of confusion with respect to the immunology and other aspects of poliomyelitis.

Foundation Stones

However, the work on this disease prior to 1938 was by no means all bad, as may have unintentionally been implied. It is a matter of record that there were laid the foundation stones of the program of research that exists today. The significant contributions of that period include: (*a*) a reasonably comprehensive description of the clinical disease; (*b*) proof that this disease is caused by a virus; (*c*) finding of an animal host, the monkey, suitable for experimental studies with the virus; (*d*) the demonstration that the crippling after-effects of poliomyelitis occur only as an aftermath of damage or destruction of nerve cells by the virus; and (*e*) suggestive evidence that the virus may be transmitted from person to person without the assistance of an extrahuman vector.

The more serious of the misconceptions that we inherited, and with which we subsequently had to deal, included the belief that (*a*) the disease is caused by only one type of virus; (*b*) the virus is capable of reproducing itself only within nerve cells; and (*c*) the virus enters the body through the nose, and subsequently travels through the body exclusively within nerve fibers. These particular misconceptions are referred to because they tended to fix the direction of research.

The Period 1938–47

The results of research from 1938 through 1947 are difficult to describe. One of the more important accomplishments of the period was the training of additional workers and the organization of properly equipped laboratories so that a truly comprehensive and effective program of research against poliomyelitis could be instituted.

In that era we began to find out exactly what happened in the body following an infection with the virus of poliomyelitis. We learned that when disease did occur following exposure to the virus, the manifestations of disease might extend from a slight and transient fever on the one hand, to paralysis and death on the other. We learned, also, that an individual could become infected without exhibiting the slightest evidence of disease. We learned, in fact, that a "silent infection" with the virus is the rule, and that paralysis is the rare exception.

We discovered also that the digestive tract of man constitutes both the portal of entry and the portal of exit of the virus. Moreover, human beings constitute the principal reservoir of the virus in nature. We learned also that the order of frequency with which individuals may be found to be excreting the virus may be listed as: (*a*) the individual with acute poliomyelitis, (*b*) household associates of the case, and (*c*) close, personal, extrahousehold associates of the family. We determined also, as one would logically expect, that the virus could be recovered in nature from those species of flies that feed and breed on human excreta. Admittedly, we were disappointed to learn that fly abatement programs did not modify epidemics of this disease.

During that same period of time, we learned that in relatively unsanitary parts of the world where it is rather easy to isolate regularly the virus in close proximity to human beings, paralytic poliomyelitis occurs much less frequently, usually in children under 5 years, and almost never in epidemic form. Comparing such regions with other parts of the world where modern sanitation is the rule, and where one seldom isolates the virus in nature except during the time of an epidemic, we find that the paralytic disease is more common, the disease is more likely to afflict older persons, and epidemics are the rule rather than the exception. Thus, we have the paradox of more paralytic disease in those parts of the world where there is less virus, and a lesser incidence where virus is more regularly found.

A closer scrutiny of this seeming paradox revealed the interesting fact that individuals living in those unsanitary—but nevertheless relatively poliomyelitis-free—parts of the world almost invariably had poliomyelitis antibodies in their blood. Furthermore, they acquired these antibodies at a far earlier age than in other parts of the world. The finding that a mixture of antibody and virus was incapable of causing disease suggested that antibodies might play a useful role in the body's defense against paralytic poliomyelitis. However, an attempt to utilize this observation to fashion a useful agent against paralytic poliomyelitis had to await the next era of research.

Advances in Treatment

The period 1938 through 1947 was also one in which great strides were made in developing more effective treatments for individuals afflicted with the disease. While it is true that no existing form of treatment has been shown to be capable of limiting the spread of the paralytic process, methods have been devised which, if correctly employed and instituted early enough, are most effective in preventing contractures of muscles. In prior years, it was the progressive contracture of muscles that brought about the horribly misshapen bodies so frequently encountered as a result of poliomyelitis.

This same era witnessed the rapid development of methods of treatment which, although incapable of curing paralysis, enabled the afflicted individual to utilize to the fullest extent possible the motor nerve cells which had escaped destruction by the virus. During that same period we began to develop more effective methods of treatment for those unfortunate individuals suffering from respiratory paralysis.

Influences on Severity

It was during this era that we learned for the first time that certain factors influence the severity of the paralytic consequences of poliomyelitis. For example, it was discovered that paralysis is more extensive and severe in those afflicted individuals who continued exhaustive physical activity during the febrile state of the disease, and that an individual is especially prone to develop the bulbar form of the disease if he contracts poliomyelitis within 30 days after removal of his tonsils and adenoids. Unquestionably a few individuals escaped the more serious consequences of poliomyelitis by taking cognizance of these observations; but the number of individuals spared must have been pitifully small. It was also observed that the incidence of paralysis is increased during pregnancy.

Paradoxical as it may seem, we also learned much when it seemed that we were learning little. We tried to circumvent many of the difficulties inherent in poliomyelitis research by attempting to unlock the secrets of poliomyelitis through work with other viruses for which simple laboratory methods were available. Although we learned a great deal about subjects other than poliomyelitis, it soon developed that the indirect approach left much to be desired. As we view that period in retrospect, it becomes painfully evident that we compounded, all too frequently, the most glaring error of the previous era—that of conducting research with inadequate numbers of animals. Again it had to be learned that conclusions drawn from improperly conceived and inadequately controlled experiments, far from contributing to progress, are apt to so confuse the issue that a practical solution to the primary problem may become buried under a mound of misinformation.

Lessons of a Decade

Thus ended another era, comprising 10 years of work. More investigators had been trained, laboratories had been organized and equipped, many experiments had been performed—experiments which had yielded a very considerable body of knowledge; but, we had failed to enunciate, on even the most tentative basis, any method for control of paralytic poliomyelitis that was worthy of critical trial.

As that period drew to a close, it became evident that, if real progress were to be made, more exact methods of research would have to be instituted, objectives would have to be clearly defined, procedures and techniques would have to be developed to permit attaining these objectives, and individual groups of workers would have to concentrate their energies on one, or at most a very few, of the objectives.

The 1948–52 Era

During the period 1948 through 1952, the National Foundation for Infantile Paralysis instituted a policy of holding frequent informal conferences with small groups of its grantees. These "off the record" conferences provided an opportunity to critically evaluate, on a continuing basis, the status of the various research problems relating to poliomyelitis. It was in these meetings that the deficiencies in our program of research became obvious. It was here that objectives were defined, experiments designed, and workers found who were eager to devote their undivided attention, if need be, to carry out the experiments required to attain the objectives set by the group.

Reliance on group thinking to guide research can be, from an administrative point of view, a disappointing experience. However, if those concerned are principally motivated to achieve success in the total program; if the individual contributors are allowed the right to range without penalty along lines that may be ahead or even contrary to the thinking of the group; and if the conferences can be conducted in a spirit totally divorced from any employer-employee relationship—under these conditions, the effectiveness of group thinking is a stimulating experience to behold.

Credit for much of the progress in this period should be given to the many individuals who, without personal recognition, so generously contributed their thinking and suggestions to other investigators. The ingenuity, the quality, and the decisiveness of many of the recent reports on poliomyelitis reflect the effectiveness of this coordinated thinking and planning.

One of the first recommendations to come out of these conferences was that exact methods of research must be the rule. This meant fewer experiments per year, though at a vastly increased cost per experiment.

So that adequate numbers of monkeys would be available for such experimentation, and to assure delivery of uniform animals to each of the various laboratories so that the work of one could be compared with that of any other, the National Foundation established a monkey conditioning center. This center provided housing for 3,000 animals, and the supply and distribution system allowed for delivery to grantees of more than 20,000 fully conditioned monkeys annually. Without this operation many of the studies that have brought us to the point we have reached today could not have been carried out.

Determination of Virus Types

At the beginning of this era of research, we had good reason to suspect that human poliomyelitis might be caused by more than one type of this virus. Of all the problems we have undertaken to solve, none has been of greater fundamental importance than the establishment of this fact. Any hope of controlling poliomyelitis with preventive or curative drugs, preventive serums, or with vaccines; any hope of learning how the disease is transmitted from individual to individual through population groups; any hope of developing a satisfactory explanation for the fact that this disease does not affect all persons to the same extent and degree—a solution for these, and for other important problems as well—demanded that we first determine exactly how many different viruses are capable of causing human poliomyelitis. And, should more than one type of the virus be found to exist, we knew that we would then have to determine the distribution of each in nature, the capabilities of each to induce disease in the human being, and the capacities of each to induce immunity to whatever number of other types might be found.

The solution of this problem necessitated the monotonous repetition of exactly the same technical procedures on virus after virus, 7 days a week, 52 weeks a year, for 3 solid years. The number of monkeys utilized in this effort is legion. The physical effort expended by the investigators to cope with the struggles, the dodges, and the antics of this horde of primates, is almost beyond comprehension.

But, in spite of these and other difficulties, this problem has been solved. At a cost of more than $1,370,000, we have learned that there are three different types of the virus circulating throughout all parts of the world, each capable of causing paralytic poliomyelitis in the human being. We learned also that development of immunity to any one of the virus types did not convey similar immunity to either of the two remaining types. It was also observed that within each of these types, individual strains of the virus were encountered which appeared to be less virulent than other members of the same type.

These findings stand as one of the most important milestones in research against poliomyelitis.

The Role of Antibodies

Once we knew how many different viruses one had to protect against, it was possible to return to an observation that had been made prior to the era we are now discussing: The discovery that poliomyelitis antibodies are present at an early age in the blood of individuals who live in those parts of the world where paralytic poliomyelitis is seldom encountered. Such antibodies are found also in the blood of most adults, irrespective of where they might reside. These antibodies appear also in the blood of monkeys following recovery from an attack of poliomyelitis or subsequent to vaccination against the disease. There are, of course, three different poliomyelitis antibodies—one for each of the three different types of the virus.

Since these antibodies are found only in the blood of animals or human beings who seldom if ever become afflicted with the disease, and since such antibodies are capable of inactivating virus, it seemed to be of paramount importance to determine whether these antibodies are an essential link in the mechanism for protection against paralysis, or whether they represent some nonuseful byproduct of the process of infection.

There followed a number of animal experiments from which one could safely draw the conclusion that, if poliomyelitis antibodies are present in the blood in sufficient amount prior to an infection with the virus, the incidence of paralysis is materially reduced, and, under certain circumstances, may be entirely prevented. But this was the result in the laboratory, where it is possible to select the route of inoculation of the virus, and the amount and kind of both antibody and virus that are injected. Furthermore it is possible in the laboratory to administer these substances separately in accordance with a time schedule most favorable for the result desired. The next and obvious question was: Are these antibodies capable of protecting against the paralytic consequences of a natural infection with the virus in human beings?

Immune Serum Globulin

Fortunately, other workers had already succeeded in their efforts to develop methods to permit extracting, in concentrated form, these antibodies which are present in the blood of most adults. This product was already in commercial production, under the name of "immune serum globulin," ordinarily referred to as gamma globulin, and had already been shown to be effective against two other viral diseases, measles and infectious hepatitis. Through the courtesy of the American National Red Cross, a very considerable quantity of this valuable material was made available.

As soon as this material could be made ready for use in the field, a Foundation grantee undertook to determine the capacity of this substance to prevent paralytic poliomyelitis in human beings. The plan for this investigation exemplifies what can be accomplished through group thinking, and its execution is a fitting tribute to those who worked so hard and skillfully toward so important an objective.

Results of Field Trials

This experiment yielded two important results: (*a*) An agent which, if it could be made available in sufficient quantity, man could employ to protect himself against the paralytic consequences of a natural infection with the virus; and (*b*) a vastly more important result—the knowledge that this protection could be attributed to poliomyelitis antibodies circulating in the blood in relatively small amounts.

The field trials demonstrated quite conclusively that an injection of a sufficient quantity of this substance will confer some protection against the paralytic disease. However, the duration of effectiveness, in the dosages employed, was limited to about 6 weeks; and during the first week of this period, paralysis would appear to be lessened in severity, rather than prevented, although the number of cases developing paralytic poliomyelitis within 1 week of an injection of gamma globulin was too small to determine for certain whether or not paralysis was ameliorated.

To further complicate this situation, immune serum globulin is obtained from the blood of human beings, and has heretofore been manufactured in rather small amounts. Because of limited manufacturing facilities and supplies of human blood, we cannot hope for the production of more than a very small fraction of the amount of this material that will be sought by the American public. A central allocation authority has been established to provide for the distribution of all of this material. This will provide a mechanism to insure, insofar as it is possible to do so, the most efficient use of this scarce product.

We are fully cognizant of the fact that immune serum globulin is not a practical answer for poliomyelitis. We knew, before the field trials were ever conducted, that when poliomyelitis antibodies are injected into the body, they disappear within a relatively short period of time. If, on the other hand, the body is induced to manufacture its own antibodies, as it does following an infection with the virus, such antibodies remain in the blood for long periods of time, perhaps for many years. The principal reasons for doing the field trials were: (*a*) to determine whether or not naturally occurring paralytic poliomyelitis is preventable by poliomyelitis antibodies; and (*b*) if so, what are the minimal amounts of these antibodies that must be circulating in the blood at the time of an infection with the virus. The results of the field trials support the concept that paralytic poliomyelitis could be prevented by vaccination, if the vaccine could induce the body to produce each of the three different poliomyelitis antibodies in sufficient amounts.

Significance of Tissue Culture

But, in spite of the progress so far described, I would be very skeptical of our achieving any practical method for control of poliomyelitis within the foreseeable future were it not for yet another important discovery. This was the development of methods whereby all three types of the virus of poliomyelitis may be grown on small bits of human or animal tissues which are themselves growing in test tubes.

We have only just begun to realize the real significance of this remarkable discovery—a discovery equally applicable to a host of problems quite remote from poliomyelitis. In previous years, an investigator had no other alternative than to use large numbers of monkeys when he sought to determine whether a given material did or did not contain virus, and, if it did, in what amount and of what kind. Similarly, monkeys had to be employed to determine the amount and kind of antibody that might be present in a given sample of blood. Today, all of these experiments can be done in test tubes, and the results can be ascertained in less than one-fourth as many days as when monkeys were required.

In prior years, we could not undertake, with any reasonable hope of success, studies designed to determine the chemical and physical configuration of the virus particle. We were unable to do this because the virus could neither be obtained in sufficient quantity, nor in a simple enough menstruum, when the only source of virus was from the central nervous system tissues of monkeys. Today there is no practical limit to the amount of virus that can be produced.

Prior to the discovery of methods for growing virus in test tubes, we were without any cheap and effective laboratory procedure to sort out, from among the hundreds of thousands of chemical compounds that exist, those relatively few that might be worthy of critical trial against poliomyelitis in animals. Today, such tests are being performed in test tubes. In years past, we had far less chance than today of developing an effective vaccine. Why? Because we did not have a method that was sufficiently uniform for producing large quantities of virus; and also because viruses obtained from the nerve tissues of monkeys are contaminated with small amounts of other substances which, when injected into the body under certain conditions, are liable to precipitate destruction of the recipients' own brain tissues. It is relatively easy to standardize the growth of viruses in test tubes; and when such viruses are grown on other than nerve tissues, they are apparently free of these harmful substances.

These are not all of the practical applications that have stemmed from the development of methods for growing viruses in test tubes. But this may be enough to show why this discovery alone has, in my opinion, earned the right to be designated the keystone of modern research on poliomyelitis.

We have come to the end of the present era with a sufficient body of knowledge to know with certainty that there can be fashioned, in at least one of two ways, a practical method for control of human paralytic poliomyelitis. The first of these two methods is through use of drugs; the second is by vaccination.

Drug Potentialities

There are several reasons why the first of these objectives might be a less desirable method of control. For example, drugs are usually not effective for long periods of time and, except in the face of an epidemic, it would be difficult to insure widespread use of preventive drugs on a continuing basis. Further, if there is developed a method for control of poliomyelitis with drugs capable of arresting the spread of the disease process, one would then have to recognize that in most cases the virus would have already wrought some damage before it could be brought under the influence of the drug.

Until this past year, our attempts to find an effective drug were somewhat discouraging, because we had not developed adequate experimental methods to select chemical compounds worthy of clinical trial. Now, however, the technical difficulties have in part, at least, been overcome, with the result that we are in a much more favorable position to detect reasonably effective compounds, if such compounds exist, or if they can be made.

Vaccination Outlook

However, it would appear that the most likely way to develop an effective and practical method for control of human paralytic poliomyelitis would be through vaccination. With this method of control we would not have to await an outbreak of the disease, as we would if electing to control poliomyelitis through preventive or curative drugs. On the contrary, vaccination could be carried out prior to the expected appearance of the disease, with a much greater chance, therefore, of providing protection for all.

There are many different methods by which an effective vaccine might be prepared. The scientific literature shows that with serial passage of the virus through an unnatural host, the virus tends gradually to lose its capacity to invade nerve tissues and destroy nerve cells, without losing its capacity to stimulate production of protective antibodies. It now appears that one of the best procedures for producing this effect is that of growing the virus in test tube cultures of living tissues. From the theoretical point of view, vaccines prepared in this way should be the most effective of all. However, it is impossible to predict from animal experiments whether or not such preparations would be safe to use in human beings. Much laboratory work remains to be done before such vaccines can safely be administered to man. In a similar stage of development is another possible method of vaccination, in which living virus of all three types is administered following an injection of immune serum globulin. While these and other possible methods of vaccination are far from being ready for field trial, we may be assured that research will reflect increasing attention to these possibilities.

Finally, studies in both experimental animals and human beings have demonstrated that prior treatment of the virus with certain chemicals may so change the virus particle that it is incapable of damaging nerve cells but still able to induce formation of antibodies. Admittedly, a vaccine prepared in this way would have lost some of the capacity of untreated virus to elicit antibody formation. Fortunately, there is good reason to believe that the disadvantages resulting from chemical treatment of the virus can be largely overcome by administering the vaccine in conjunction with certain potentiating oils.

Maturation of Research

As we examine the research that was conducted from 1948 through 1952, it becomes evident, that during this era, research on poliomyelitis attained sufficient stature to stand on its own two feet. Only a few short years ago, much of our work was done with other viruses in the rather desperate hope that in this way we would learn something about poliomyelitis for which we did not have techniques to permit of effective study. Following full documentation of the work that has already taken place, it would not be to surprising to find other workers in the years to come using the virus of poliomyelitis in the hope that they may learn something about other pathogenic agents.

Research of the Future

In light of recent progress, some may hope for a positive statement as to whether or not a practical method for control of human paralytic poliomyelitis is "just around the corner." Inasmuch as research is truly an exploration into the unknown in an attempt to solve a problem for which there is no presently available solution—one must reply that if we knew exactly when and by what means we could provide the solution for a particular problem, there would be no need to conduct research. As we understand the problem of poliomyelitis today, it would be unrealistic to think that a practical method for control awaits the discovery and application of some undiscovered fundamental principle or even a new technique. It would seem that we are now in possession of the scientific principles and tools required. But, although hope in the hearts of men will undoubtedly continue to spring eternal, and such hope with respect to poliomyelitis is not without some very considerable basis in fact, no one can safely predict when that longed-for day will come. The only truthful answer is this: A practical method for control of paralytic poliomyelitis will never be forthcoming unless research is continued.

It is in this present era that we have reason to expect many important forward steps will be taken. In some instances this may mean moving from work on animals to studies with human beings. Such transitions necessarily entail some calculated risk. Often it is quite impossible to determine, in advance of doing such studies, the degree of risk involved. Those who propose such steps should not be surprised if more voices are raised in opposition than in support. The investigator will be hard-pressed to distinguish between risks of reasonable probability on the one hand and risks of unlikely possibility on the other; and he must recognize that among the outcries may be those motivated by fear or due to an incomplete understanding of the problem or to an incomplete appreciation of the social responsibility of science. Perhaps the scientist contemplating such steps can gain some comfort from the provocative observation of Raymond Fosdick that "what is wrong with the world of today is not the dreams of the idealists, but the cynicism of those who call themselves realists."

Summary

It is apparent that there has been tremendous progress in the fight against poliomyelitis, and that we are now in possession of many of the tools and basic facts with which will ultimately be fashioned a practical method for control of this affliction. It is impossible to say when this objective can be achieved, since much hard and exacting work still remains to be done. But with greater knowledge for more intelligent planning and with sharper tools for more precise experimentation, the attainment of our goal seems to be moving ever closer.

256490—53——4