ACTIVITIES
OF THE NATIONAL FOUNDATION
FOR INFANTILE PARALYSIS
IN THE FIELD OF
VIRUS
RESEARCH

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Of the ills of mankind infantile paralysis is admittedly a long way from the most deadly. In any one year, or in any given epidemic it does not leave its crippling mark upon a large proportion of the children of any community. These truths are sometimes cited in deprecation of our constantly increasing intensive and extensive effort against this crippling malady. These are also the facts used by public health authority to soothe citizens at those times when the increase of cases of infantile paralysis begins to make front page headlines.

The National Foundation for Infantile Paralysis is essentially the American people's foundation and as such it is responsible to them. The most skilful propaganda has failed to remove infantile paralysis from its top rank as a terrorer of the people. The human insight of fathers and mothers looks through the reassuringly low sickness and death rates displayed to them by our public healthmen. The fact that relatively so few children are killed or lamed by the paralytic terror — that truth is no comfort to parents if their own baby is wrecked for life at life's beginning.

Even though the incidence of infantile paralysis is low compared to certain other and major ills, yet it cannot be dismissed as no serious menace to society. This is what is socially most disturbing about the paralytic plague: crippling relatively few children and young people in any given year, each epidemic adds to an ever mounting accumulation of living human wreckage. From pneumonia after a few days' ordeal one dies or gets better. From our almost yearly epidemics of infantile paralysis — each one no account statistically — there is a growing totality of tragedy often worse than death. The number of infantile paralysis cripples alive in our land to-day is not exactly known, but it runs into hundreds of thousands.
II

THERE is no greater challenge than that of infantile paralysis to medical science, again in spite of the relatively few that this disease maims and kills. Maybe, if public health authorities and men of medical science could offer citizens some hope of prevention or cure, then there would be an end of public panic notable in epidemic seasons. But this is the fact about infantile paralysis, admitted by the medical and public health experts of the Committee on Virus Research and the Committee on Epidemics of the National Foundation for Infantile Paralysis, at their first meeting, in July, 1938 —

After thirty years of research, in the laboratory and in the field, knowledge leading to the prevention, cure, or control is not yet available.

Orthopedic surgeons can somewhat mitigate the deforming and crippling effects of the disease. They can soften the cruelty of the after effects of it upon individual children.

But public healthmen have no science to guard children against epidemic infantile paralysis. No individual child can be so guarded with absolute certainty, though, if its parents are well-to-do and sufficiently frightened, that individual child can be given some protection by removing it far from the zone of epidemic influence, provided the child is not already harboring the virus when it is so sequestered from the plague's marauding.

Furthermore, in spite of claims persisting among certain men of medicine, physicians have no serum or medicine to check or cure the malady in its acute, early states — with proven power to prevent subsequent maiming or fatal outcome.

This then was the challenge faced by the scientific and public health experts of the National Foundation for Infantile Paralysis at the beginning of their activities a year and a half ago. They are faced with the responsibility of disbursing the money of American fathers and mothers in such a way as to meet that challenge as rapidly as possible. The experts must be haunted by the worry of parents when ominous figures — sometimes accompanied by public health authority's assurance that "the situation is under control" — appear on newspaper front pages. This riddle must give the foundation's experts sleepless nights because they realize that more and more parents — to whom they are responsible! — know that the infantile paralysis situation remains under control of God, not man.

So the expansion of the fight against infantile paralysis is without question justified.

III

It is interesting that our scientific ignorance as to cause and prevention of infantile paralysis became crystallized at the first meeting of the Committee on Virus Research and the Committee on Epidemics, in July, 1938. In their deliberations the members of these committees were joined by Doctor Max M. Peet and Doctor Morris Fishbein of the Committee on Education. The experts assembled had been asked by Mr. Basil O'Connor, President of the National Foundation for Infantile Paralysis, to formulate sound recommendations, which might be quickly broadcast to health officials, in event of an infantile paralysis epidemic in the Summer of 1938.

Should schools, swimming pools, playgrounds, movie theaters be closed in such an event? How long should stricken children be quarantined? Should their families be restricted in their movements? Votes were taken among all present, to see if a consensus in regard to any of these measures might be arrived at. The differences of opinion in regard to each specific question, in regard to each measure proposed, were remarkable. Not a single incontrovertible fact could be
brought forward. Not a single unanimous opinion, based upon fact, was recorded.

The admission of this confusion may be said to be the first constructive step taken by those concerned with the activities of the foundation in the field of virus research. The scientific ignorance here accepted caused Doctor Thomas M. Rivers, Chairman of the Committee on Virus Research, to attempt a breakdown of this blanket ignorance into the basic unknowns existing in regard to infantile paralysis. It may be asked why such a profusion of enigmas should remain, in regard to this malady? Had not thirty years passed since bacteriologists had trapped the virus of the lambling sickness in apes and monkeys? Granted. Had there been dearth of experiments or lack of scientific interest? On the contrary. Since 1909, thousands of experiments have been made upon myriads of monkeys. Scores of investigators have built up an imposing body of facts about the monkey sickness — about infantile paralysis of monkeys. But this must be acknowledged: that this monkey science, in strange contradiction to other diseases conquered by animal experimentation, has so far disappointed the hopes of mankind.

The Committee on Virus Research therefore faced this question: is the disease in monkeys in the laboratory essentially an artificial one, having little in common with infantile paralysis as it attacks human beings in nature?

The breakdown of the basic unknowns about infantile paralysis, made by Doctor Rivers, makes it seem probable, that the monkey disease — as it has been studied in the laboratory — will not give us the answer to the infantile paralysis enigma. Here are basic questions about infantile paralysis, for which the Virus Research Committee cannot give answers —

What is infantile paralysis? Is it a clearly defined disease, like diphtheria, readily diagnosable by physicians in its acute stages? The acute disease as it shows itself in human beings cannot be defined with this degree of certainty, especially in those regions where there exist other virus diseases attacking the human nervous system.

Does one single virus cause infantile paralysis, or are there several sharply different varieties or strains of this virus? No clearly distinct varieties of the presumed virus have been clearly established, in the sense that separate types of the microbe of pneumonia are known to exist.

How does the virus of infantile paralysis get into the human body, in nature? Are all possible gateways of the virus into the human body adequately surveyed, or is one single important gateway surely established? No.

How does the virus leave the body of a person sick with infantile paralysis, or the body of a “healthy carrier” of this virus? It has been found in a limited number of instances in the nose and throat of human beings. Recently — as will be explained in detail later — it has been discovered in the intestinal discharges of sick and healthy persons during an epidemic. Yet this does not explain how the virus spreads through the community.

Are the details of the pathology, that is to say the study of the harm the virus does to human tissues, clearly established? Do we know every part and tissue of the human body attacked and damaged by the virus? While a considerable body of fact as to the effect of the disease on monkeys has been gathered, the gaps in knowledge of human pathology are deplorable.

Is it true — as has been maintained — that the virus can only propagate itself, and spread in the human body by way of the nerves and nerve cells? This is not settled.

Since infection by way of the nose can be prevented — in monkeys — by instilling certain chemical substances into their noses at varying intervals before an attempt is made to infect these animals, does this justify a field test, aiming this way to prevent the epidemic spread of infantile paralysis among human beings? The answer of the Virus Research Committee is no. Because it is not definitely known that the
virus gets into human beings by the nose route, and even if this were known, no sufficiently safe and powerful "chemical blockading agent" is available for human use.

Is the possibility of discovering a preventive vaccine against human infantile paralysis to be discarded? No. And yet, at present it must be admitted that this possibility is remote, because no method exists, at present, of getting large amounts of highly concentrated infantile paralysis virus with which to conduct the necessary preliminary animal experiments.

Why, out of a given human population, are only a relatively small number of people stricken with infantile paralysis to the point of being temporarily or permanently crippled by the disease? This is not known.

Does the susceptibility of the few, and the resistance of the many depend upon something inherent in people? Or are susceptibility and resistance acquired? Are they conditioned by human environment? No definite answer. Although, recently, Dr. Albert B. Sabin has announced discovery of a natural barrier in certain tissues, which prevents the polio virus from attacking the nervous system.

What is known about the chemical and physical nature of the virus, obtained from human beings, and capable of paralyzing monkeys in the laboratory? Very little. It is known that the virus can be preserved for a long time in glycerine. It is known that it is a particle of extremely small size compared to other disease-producing viruses. It has not — as have certain other viruses — been obtained in a highly purified condition.

Can the virus be propagated outside the monkey or the human body? Not up till now. Numerous attempts have so far resulted in failure.

Is there any present indication that the acute disease in human beings or monkeys is amenable to chemical control or cure? No. But it must be admitted that no large scale or persistent attempts have been made to solve this problem.

DOES the above gloomy portrayal of our lack of useful knowledge about infantile paralysis justify discouragement in regard to the ultimate conquest of the disease? By no means. For fifty-five years after the discovery of the deadly streptococcus — in spite of an enormous amount of research by laboratory men and physicians — there existed no cure for the ravages of this germ. Then suddenly came the discovery of sulfanilamide. Pasteur first observed the microbe of pneumonia some fifty-eight years ago. Thirty years passed before serums were discovered effective against certain types of the pneumonia microbe. Even so, the use of these serums was not sufficiently simple to enable physicians to make a dent in the pneumonia death rate. It is only this year — after fifty-eight years of effort — that the new wonderful weapon of sulfapyridine bids fair to give our physicians the chance to reduce pneumonia to one of the minor causes of dying.

Yet it must be admitted that, during the first year of the work of the National Foundation’s Virus Research Committee, discouragement among research workers in regard to infantile paralysis was noticeable. It is to be explained that, up to the present, research on this disease has not been nationally planned or in any way co-ordinated. Investigators wishing to study infantile paralysis have been supported by funds from the institutions with which they were connected. Or, more recently, they have been aided, upon their voluntary request, by funds from the International Committee for the Study of Infantile Paralysis, from The President’s Birthday Ball Commission for Infantile Paralysis Research, and more recently by funds from the National Foundation for Infantile Paralysis. During the past year and a half during which the Virus Research Committee has functioned, there has been a notable lack of applications for grants in aid.
of research upon significant problems regarding infantile paralysis.

The reasons for this lull in the battle are not far to seek. They are to be found, it is believed, in a succession of hopes disappointed during recent years. Critical study has thus far dissipated the hope that serum was of proven value, either in cure or prevention of infantile paralysis. The test of an alleged preventive vaccine, generously financed by the President's Birthday Ball Commission, resulted in a disappointing negative. Hope then arose that chemical blockade might be the answer, in preventing epidemic spread of the disease. Recent events make it probable that this expectation, too, must go into the discard.

At this point, however, important activity of the National Foundation for Infantile Paralysis and its precursor, the President's Commission, can be recorded — even if the results of the research are negative ones. Investigators working with financial support from the President's Birthday Ball Commission, and more recently from the National Foundation for Infantile Paralysis, have established a basic fact —

Namely: that the virus of infantile paralysis acts differently when it is freshly isolated from human beings, than it acts after it has been passed in the laboratory for a long time through a succession of monkeys. This discovery has dashed hopes of chemical blockade in the following way.

The study of the “monkeyized” virus of infantile paralysis, for many years, in the laboratory, had led investigators to hope that the disease might have an Achilles heel. From this monkey science it was concluded by certain workers that there was one principal gateway by which the paralytic terror could find a way into the living human body. You can paralyze and kill monkeys by pouring suspensions of monkey infantile paralysis virus into their noses. From high up inside a monkey’s nose, it was found that the virus could find its way into the brain and spinal cord — by way of the nerves of smell.

It became the widely held belief, for a time hardly disputed, that the infantile paralysis virus, in monkey or man, could only spread and multiply inside of nerves and nerve cells. Was not this then a weakness of the paralytic death? If it was safe to reason from monkey to man, then it seemed likely that the only way — in human epidemics — that the virus could spread, was by the gateway of the tiny hairlike endings of the nerves of smell high up inside the human nose. These are the only nerves exposed to the outside world. Hopes now arose, and again, from monkey science. Might it not be possible to block this lone gateway of the infantile paralysis virus?

In monkeys, yes. By dropping solutions of alum or picric acid into monkeys’ nostrils, Doctor Charles Armstrong of the United States Public Health Service found that these animals could be protected against subsequent inoculations of infantile paralysis virus by way of the nose. Dr. E. W. Schultz of Stanford University, in researches supported by funds from The President’s Commission and later by the National Foundation, discovered that zinc sulphate was a still more powerful preventive of monkey infantile paralysis. For a month and even more after this cheap and simple drug was applied inside monkeys’ noses, it was impossible to infect them by the nasal route, even when overwhelming doses of virus were instilled.

It is true that there is something artificial about the monkey disease. When you give a monkey infantile paralysis by way of his nose, and then put him into a cage crowded with healthy simians, the paralytic plague does not spread to these healthy ones. The monkey disease is an artificial sickness. But this hoped-for method of prevention was tried out, in man, notably in the recent Toronto infantile paralysis epidemic. There was no apparent preventive effect. Yet it must be admitted that, because the doctors failed to get the zinc sulphate thoroughly up into a large proportion of the Canadian children’s noses, this human test cannot be said to be
conclusive. But again it must now be acknowledged that other objections are dashing hopes for chemical blockade against human infantile paralysis.

When the zinc sulphate solution is thoroughly applied, it not only causes a considerable amount of discomfort and pain, but it completely — if temporarily — destroys the sense of smell. This loss of sense of smell is shorter in children, lasting hardly more than two weeks. It may continue for months and even for a year in some older people. Dr. Schultz, working under a grant from The National Foundation for Infantile Paralysis, has discovered that, to block the entry of the virus, in monkeys, it is necessary to apply zinc sulphate so thoroughly as to destroy the membranes of the region of the monkey’s sense of smell. In time these membranes seem to repair themselves. But among children, what would happen to their smell sense, if the zinc sulphate had to be applied to the insides of their noses repeatedly during a long, serious epidemic?

The rapid demonstration of this possible danger was made possible by the courage of Dr. Schultz in establishing a serious objection to the human use of the zinc sulphate method he himself had developed as a brilliant protective for monkeys.

But now another objection to possible chemical blockade has arisen, and this may be a still more serious and fundamental one. Drs. J. D. Trask and J. R. Paul, of the Yale University Medical School, supported by funds from the President’s Birthday Ball Commission and later by the National Foundation, have discovered that certain strains of infantile paralysis virus act differently when they are studied fresh from human beings, than they act after they have been passed through monkeys for a long time, in the laboratory. The old laboratory, monkeyized strains of virus are hard to pass from monkey to monkey when one inoculates them under or into a monkey’s skin. But when certain samples of infantile paralysis virus — fresh from fatal human cases —

are tested, it is found that they are highly infectious by simple skin inoculation! May this not then also be their property in nature — for humans?

Is the gateway by the nerves of the sense of smell then the only human gateway of entry of the disease? Does some mysterious change occur in the virus passed for a while through the bodies of monkeys in the laboratory, making it deeply different from the virus as it goes from man to man — in nature? It begins to seem so.

And yet for thirty years most of the experimental work on infantile paralysis has been done with old monkeyized strains of virus — infectious for monkeys by way of their noses but not by way of their skins. It is possible that the importance of the nose route in laboratory infantile paralysis is an artificial condition, in the words of Doctor Lester S. King, brought about by some degree of change in the virus and without necessary relation to the natural disease in human beings.

Further, recent scientific news makes it seem still more doubtful that, in nature, the virus of infantile paralysis gets into human beings by the nose route. Autopsies have been made on children and adults dead of infantile paralysis. If the entry of the death was by way of the nerves of smell, then — according to animal experiments — definite traces of the trail of the virus should be found in the smell nerve cells. Such a tell-tale trail of invasion by the natural virus has not been found in human beings.
If it remains enigmatic how the virus of infantile paralysis invades human beings, how it gets into them, is there any knowledge regarding the way the virus may leave the human body? Of either sick or healthy people? For it has long been suspected, though not proved, that, in a human epidemic, though few become paralyzed or are obviously sick with infantile paralysis, yet many people may harbor the virus. These may well be dangerous carriers of the sickness. And if it should be possible to establish how the virus gets out of the human body, might the public health point of attack be concentrated here, as it is concentrated effectively in diseases like typhoid fever?

Such a possibility — it can by no means yet be called a probability — now appears, thanks to the recent work of Drs. J. R. Paul and J. D. Trask, of Yale University Medical School, and of Dr. S. D. Kramer, of the Michigan State Health Department Laboratories. Both these groups are supported in their work by funds from The National Foundation for Infantile Paralysis. Both are striking out on a new trail, in that they are sticking as close as possible to the human disease, and to the local environment in which the disease seems to flourish. Their recent discoveries may at last bring information that health officers may find valuable. At least the new facts will have to be taken into consideration by these officials during coming infantile paralysis epidemics.

For many years it has been suspected that the virus not only entered but left the human body by way of the nose and the upper part of the throat. Some three hundred tests have been reported by searchers attempting to find traces of the virus in the nose and upper part of the throat. Only ten percent of these have revealed virus. On the other hand, many years ago it was reported from Sweden that the virus of infantile paralysis can be found in the intestinal discharges of patients sick with the disease. This fact was then lost sight of. But, during the past few years a powerful new method of getting the virus over from human beings into monkeys has been evolved. Drs. Paul and Trask notably — as well as other workers — have recently reported that the paralytic terror can easily be recovered from intestinal discharges. And not only from paralytic human cases but also from what are called the “abortive,” non-paralytic types of the disease. And not only during the active stages of the disease, but also while patients are convalescing. And, while the virus could only be recovered from ten percent of cases when it was looked for in the nose and throat, it was found twice that frequently in the intestinal discharges.

This question now confronts health officers: will these stool examinations tell them more about the existence and spread of the virus in families and communities? This new question now faces our scientists: to what extent must infantile paralysis be considered an intestinal disease? And is the existence of the virus in the intestine important in efforts at prevention?

It is only fair to say that these questions cannot yet be answered. It is conceivable that the fact of the virus leaving the human body by way of the intestine is a purely incidental one, and that contamination of food, of hands, et cetera, by intestinal discharges may not be the first link in the chain of the spread of the disease from one human being to another.

Yet the recent observations of Drs. Trask and Paul demand attention of health officers. For, during the Charleston epidemic in the summer of 1939, these investigators found the virus of infantile paralysis in the sewage of that city. Their tests indicate that large amounts of the virus may exist in sewage during epidemics.

It is a curious fact observed by the Yale investigators that it is actually easier to isolate infantile paralysis virus from mild human cases — non-paralytic — than from human beings who become paralyzed. During eight years in eleven
epidemics the virus was found fourteen times in all, from people who were diagnosed to have infantile paralysis — but only in two cases were the victims paralyzed. So now, when they wish to find virus during an epidemic, these searchers look for it in the families of patients. They say they’re more likely to find it in stools collected from members of the paralyzed patient’s family — particularly those who have been ill with a brief spell of fever or vomiting.

The question now arises: just how widely is the virus of infantile paralysis distributed among human beings during an epidemic of the disease? We know now that it is not confined to those who become sick to the extent of paralysis. It is found, too, in the intestinal discharges of those who are only slightly sick. But what about healthy children and grownups who live in close contact with those stricken with the disease.

The paralytic virus has, this past year, been found in such healthy people too. Dr. Kramer, working with Dr. A. G. Gilliam of the United States Public Health Service, and with J. G. Molner, made this unexpected discovery while investigating an outbreak of infantile paralysis occurring in the Jewish Children’s Home, during the 1939 summer epidemic in Detroit, Michigan. Five children in this institution suffered frank attacks of infantile paralysis. The intestinal discharges of nineteen persons — intimate contacts of these sick children — were examined. From six of these nineteen — nearly one out of three — infantile paralysis virus was recovered. Two of these contacts had been mildly sick with minor disease not diagnosed as infantile paralysis.

But the four other contacts had not been sick at all.

Is the presence of the infantile paralysis virus in the intestines of these healthy people a transient thing? Not necessarily. In one healthy child it persisted for nineteen days. In another it was demonstrated thirty-eight days after its first detection.

So far as prevention of infantile paralysis goes, what does this startling observation mean? It is impossible to say. It cannot be certain that the healthy “contacts” got the virus from the children frankly sick with infantile paralysis. Though this is possible. It cannot be maintained that healthy infected people — harboring the virus — gave it to the children who later became paralyzed. Though this is also possible. It cannot even be maintained that infantile paralysis virus is to be found in the discharges of healthy people only in those regions where frank cases of the disease exist.

For no investigators have yet searched for the virus in the intestinal contents of large groups of people in communities or institutions where no frank infantile paralysis at all exists.

All that can now be said is that, where there are existing cases of infantile paralysis, the virus of the disease may also be frequently found in the intestines of people who have been slightly sick with non-paralytic illness, or not sick with any disease at all.

It is now at last known — something before merely suspected! — that during an epidemic large numbers of healthy people are actually discharging virus into the outside world. This is a notable advance in the fight against the sickness.

It must be recalled that, to detect the virus in sick or healthy persons, inoculation of the suspected material into monkeys is the only means as yet at the disposal of the scientists investigating this question. The shrewd observation of very slight signs of the disease in the first monkeys inoculated with human material and passing diseased material from these to new monkeys — promises a new and delicate method of finding the dangerous virus where before it was not suspected to exist. The first monkeys inoculated from humans are frequently very slightly stricken with infantile paralysis.

Will these discoveries give rise to new public health regulations designed to guard children during epidemics in the future? This is not yet known. But health officials are now confronted with new questions about infantile paralysis. How important is it to sterilize the stools of people with in-
fantile paralysis, or people in contact with patients? Does modern sewage disposal destroy the infantile paralysis virus? Is food contaminated with sewage possibly infectious? Might hands contaminated with intestinal discharges be a source of infection? These questions can now begin to be answered by our sanitarians.

Here is the enigma remaining: that nobody knows whether a child stricken with frank infantile paralysis gets its disease from another sick, or a healthy person. Nobody knows — as yet — how widely the virus is spread through a community before and during an epidemic. This is now known: that it is more widely spread than heretofore suspected. And it will be of interest to see if sanitary measures — which will now undoubtedly be intensified — will cut short epidemics in the future.

Very recent news from Australia indicates that our searchers may have been working with the wrong kind of monkey for thirty years! While it has been easy to infect the Macacus rhesus, the most commonly experimentally used monkey, with infantile paralysis, by instilling material into its nose, inoculation of the virus has been necessary to secure infection by way of the throat and tonsils. But Australian workers have made use of another monkey, the Macacus irus. This animal succumbs to infantile paralysis when infected material is merely rubbed into its pharynx and over its tonsils. Who knows whether human beings can contract the disease by mere swallowing of infected material? Is the child more like the Macacus rhesus or more like the Macacus irus in this regard?

These questions remain for workers to determine. And when you think of the difficulty of obtaining many different kinds of monkeys, such are the pitfalls that our searchers have had to contend with!

UP till now, as has been mentioned above, no attempt has been made by the Virus Research Committee of the National Foundation to define broad lines of research that might be sponsored by the foundation, or to solicit research in the field of infantile paralysis among workers not now engaged in it. The Committee has, however, at the request of Mr. Basil O’Connor, set down what its members deem to be fundamental research problems. It is felt by certain members of the Committee, though not by all of them, that the Foundation might stimulate campaigns of investigation down roads that might lead to answers to these various fundamental problems, and that the Foundation might attempt to find competent workers willing to lead these enquiries, supported by the Foundation’s funds.

The questions that now confront the Virus Research Committee are the following serious ones: Since thirty years of work at the laboratory bench have not solved the riddle of infantile paralysis, is it not time to initiate a broad study of the disease as it occurs among human beings in the field? Is it not time to expand the human epidemic study so brilliantly begun by Drs. Trask and Paul, and Dr. Kramer? Is it not necessary to reverse the old order of affairs, and let the field suggest new courses of enquiry to the workers at the laboratory bench?

It is hoped that, in the near future, the National Foundation will be in a position to aid in sponsoring and organizing a field study of infantile paralysis in which bacteriologists, chemists, public health workers, epidemiologists, nurses, and physicians can co-operate. Such a field study might well proceed on the basis that all the public health problems regarding infantile paralysis are open questions.

Nothing illustrates this more clearly than the fact that our physicians cannot even answer the simple question of what
is or is not infantile paralysis. In the West, for example, it is becoming increasingly difficult for practicing physicians to distinguish acute cases of early infantile paralysis from other virus diseases, such as St. Louis encephalitis and horse encephalitis, which also attack the human nervous system. Doctor Karl F. Meyer and Miss B. Howitt, whose work has been supported by the National Foundation, have in California — by serum studies — discovered that many persons who were diagnosed to have suffered infantile paralysis, actually suffered one of the other virus diseases of the nervous system. Now the diagnosis of infantile paralysis is made only when definite paralysis is noted.

There is as yet no test for the pre-paralytic phase of the sickness.

It is also of interest that infantile paralysis, as well as St. Louis and Japanese encephalitis and horse encephalitis, are summer diseases, and that the viruses of the latter two diseases can live in mosquitos, and that the Japanese and horse encephalitis viruses can be experimentally carried from animal to animal by mosquitos and ticks. Since it is now known that infantile paralysis virus — not old by passage in monkeys in the laboratory but fresh in the monkey from the human being — can easily infect monkeys through the skin, the possibility is re-opened that some biting insect might carry the disease from man to man from some still unknown animal reservoir to man.

This fascinating possibility can only be answered, yes or no, by a combination of field observations and laboratory studies.

Is it, after all certain, that the mysterious sub-visible author of infantile paralysis passes by contact from sick persons to healthy or from carriers to healthy, or from insects to healthy people? May not the virus be almost universally distributed among mankind in a dormant, a latent state? As the virus of cold sores (herpes) is latent in people? Then to be activated to paralytic power in some people by some still unknown conditions of the environment? Kramer and his associates have just found the virus in the stools of a high proportion of healthy children — in an epidemic. What about its presence when there is no epidemic? And what about the possible presence of infantile paralysis virus in the bodies of children and grownups who have died from some disease other than infantile paralysis?

Field workers, physicians, and laboratorians could solve this as yet never attempted problem.

Workers in the field of infantile paralysis generally admit that advance of knowledge has been frustrated by the fact that study of the disease has for thirty years been carried out with a very few strains of the virus, highly adapted to monkeys. Do these old laboratory strains of viruses really represent the nature of the virus causing the disease as it occurs in man today? To throw light upon this important point, it is planned to collect hundreds of new strains of infantile paralysis virus, obtained during epidemics by workers in the field, and studied and preserved by workers in laboratories. Such a study has already been begun by the Foundation's grantee, Dr. John F. Kessel, of the University of Southern California. Dr. Kessel has isolated at least twenty new strains of the virus from recent epidemics in that region. Some of these produce, in monkeys, a notably more mild disease than that brought on by the old "M V" virus that has been the chief source of experiment in our country during the past thirty years. From the same epidemics, however, highly fatal strains have also been recovered. And these qualities of mildness on the one hand and virulence on the other, seem to be preserved as the virus in question is passed from monkey to monkey. Also, animals recovering from attacks by the mild virus are in high proportion resistant to attack by the old, fatal, "M V" virus.
At the laboratories of many universities, from coast to coast, workers supported by grants from the National Foundation are now trying to answer one or another of the fundamental unknowns about infantile paralysis, enumerated by Doctor Rivers and the Virus Research Committee.

At Washington University, St. Louis, Missouri, Dr. Edwin H. Lennette has been studying the significance of the curious "barrier" that exists between the blood and the nervous systems — brain and spinal cord — of animals and man. Is the existence of this barrier the reason why sera, injected into the blood of children, have notably failed to check the course of infantile paralysis? Dr. Lennette has found that, when monkeys are acutely sick with infantile paralysis, this barrier is partly broken down, and sera can penetrate the nervous tissues. But most highly powerful sera even so were unable to check the course of the disease in monkeys. Another discouraging observation of Dr. Lennette is that monkeys which have recovered from an attack with the old "M V" laboratory strain of the virus, are still susceptible to a fresh strain recently passed to monkeys from human beings.

At the University of Wisconsin, Dr. Paul F. Clark is working at the delicate and subtle physical and chemical job of purifying the infantile paralysis virus — that is to say, he is trying to free it from the nervous tissues of the brain and spinal cord, trying to track down the "pure quill" so to speak, that causes infantile paralysis. In this task Dr. Clark is making progress. In the course of his experiments Dr. Clark has made an observation that may bear upon why some children, in an epidemic, come down with paralytic sickness, while others are only slightly sick and escape paralysis entirely. If he slightly inflames or damages the brains and spinal cords of monkeys by injecting horse serum into their spines or starch into their brains — small injections of infantile paralysis virus into the blood of such otherwise healthy monkeys cause them to come down with infantile paralysis. Injections which would have no effect on a normal animal.

Is it possible that some still unknown infection or some other kind of injury must be suffered by children to make them susceptible to a truly paralytic attack of the disease? In the recent epidemic in Detroit, Doctor Henry F. Vaughan and his epidemiologists — who made an exhaustive house-to-house study of all families where infantile paralysis struck in the 1939 summer — observed that a notably high proportion of children actually paralyzed, had suffered one or another kind of injury just prior to their sickness.

Dr. R. D. Lilly, of the U. S. Public Health Service, is making an intensive study of exactly what parts of the human brain are hit by the infantile paralysis virus — and how badly. Up till now there has been inadequate information on this subject. Dr. Lilly believes, from his studies, that there must be an early phase of the acute sickness, during which the virus is in the blood, before it attacks the nervous tissues. And this would, again, argue against the possibility that the disease penetrates into human beings only through their nerves of smell.

Dr. Alfred E. Fischer, of New York City, is making an analysis of the effect of tonsil and adenoid operations upon children, when these are performed during the occurrence of an infantile paralysis epidemic. He has confirmed the ominous, previously observed fact that children, so operated upon, during epidemic season, suffer the highly fatal "bulbar type" of infantile paralysis in a strikingly high proportion. It seems as if the disturbance caused by these operations gives a portal of entry for the virus direct to the brain. This observation has an important bearing on recommendations to the public and to physicians, by health officers, during epidemics.

At Ohio State University Dr. N. Paul Hudson is seeking
to infect embryos, and newly born mice, guinea-pigs, and rabbits with the virus of infantile paralysis — in an attempt to pass the disease, for experiments, to animals cheaper and more conveniently handled than are monkeys. He has demonstrated some survival of the virus in the nervous tissues of guinea-pigs — for as long as five days — but has not been able to pass the infection from animal to animal.

Dr. Karl F. Meyer, at the George Williams Hooper Foundation in San Francisco, is now embarking on a large scale field and laboratory study of the important question — above mentioned and still unanswered — of “what is infantile paralysis?” His associates have observed that it is becoming increasingly difficult for physicians, at the bedside, to separate acute infantile paralysis from other nerve-attacking virus infections — such as horse encephalitis and St. Louis encephalitis. The symptoms of the beginning disease in all three of these, in the human being, are difficult to tell apart. Many mistaken diagnoses have been discovered. Serum tests to determine which of these virus diseases are responsible for epidemics and isolated cases are being made, in the field and in Doctor Meyer’s laboratory, from every part of the eleven Western states. Doctor Meyer, his epidemiologists and laboratory workers are tracing the migrations of these nervous virus diseases in western regions.

At the City Hospital in Cleveland, Dr. John A. Toomey has been studying the possible susceptibility of small laboratory animals to infantile paralysis — though these rabbits, rats, guinea-pigs, and mice — have long been believed to be entirely resistant to the disease. He has brought forward evidence, so far, to change this discouraging belief, or fact — which has, more than anything else, frustrated progress against the disease — because monkeys are so expensive and difficult to handle. If our workers only had at their disposal a cheap, easily handled laboratory animal —

VIII

This most important of all aids to the final triumph of experimenters over the paralytic terror has now at last — so it seems — been made. The Foundation can have some small share of its glory, since the distinguished discoverer is a member of the Virus Research Committee.

In September, 1939, Doctor Charles Armstrong, of the U. S. Public Health Service, announced that he has been able to infect the Eastern cotton rat, *Sigmodon hispidus hispidus*, with the virus of infantile paralysis.

The rat is a docile one and easy to handle by experimenters. It is abundant and can be obtained in large numbers from the Southeastern States. It is said to be easily bred and reared in the laboratory. The type of infantile paralysis produced in this animal is in every way typical, and can be readily passed back to the monkey.

The first successful transmission of infantile paralysis to this cheap and convenient rodent was made with a strain of infantile paralysis virus obtained for Doctor Armstrong by Doctor Max M. Peet — also a member of the Virus Research Committee — from the brain of a boy who died from acute infantile paralysis in a small Michigan epidemic in 1937. Peet’s work was done under a grant from the President’s Birthday Ball Commission for Infantile Paralysis Research.

This discovery now opens a road for an entirely new attack on infantile paralysis — on a sector up till now closed to experimenters.

In the light of this new possibility our searchers — those who will have the courage to pioneer the new unknown where failure may again await them! — can forget all the old failures and present enigmas about the sickness —

They can forget that vaccines do not prevent it; that serums have failed to cure it; that we do not know all the ways by which the paralytic virus passes out into the world
from sick or healthy people; that we are ignorant of the roads or gateways by which the virus sneaks in to wreak its paralytic or fatal havoc; that we are in the dark about why a few children and grownups are a prey to the ravages of the sickness while the majority of all human beings are immune to these ravages; that we have no information as to whether the virus is passed to susceptible human beings from other human beings or from some still unknown carrier such as an insect.

By those bold enough to attempt the novel means of possible conquest now opened up by the passage of infantile paralysis to the cotton rat—all the above gloomy facts and still insoluble enigmas can be forgotten.

With infantile paralysis now trapped in a cheap docile animal, a new bold stab at conquest can now be made. In short, we can now attempt to find a chemical cure for infantile paralysis.

This project is already under way, under a grant from the National Foundation for Infantile Paralysis, at the Michigan State Health Department Laboratories, at Lansing, Michigan. Encouraged by a substantial grant for this purpose, Dr. C. C. Young, the Director of these laboratories, has prevailed upon the State authorities to have a special virus laboratory built—the first of its kind in the United States. In a remarkably short time this building has been erected and equipped. In it Doctor S. D. Kramer is now beginning this new adventure, which is essentially an attempt to find a ‘sulfanilamide’ for infantile paralysis.

By this it is not meant that sulfanilamide or any of its innumerable derivative chemical compounds will be the answer. Sulfanilamide is here used to indicate the goal toward which Doctor Kramer and his co-workers are now preparing to struggle. Such a short time as four years ago, bacteriologists and physicians despaired of finding a chemical cure for deadly streptococcus infections. They would have laughed at visionaries predicting a chemical treatment that would bring pneumonia—our third ranking cause of death—under control. Yet within the last four years both of these presumed impossibilities have become an accomplished fact.

And it is fundamental that this new development of chemical science has accomplished more, against highly fatal and disabling diseases in three short years, than have the serum and vaccine studies of fifty years.

It does not matter if sulfanilamide, powerful against streptococcus, and sulfapyridine, cure for pneumonia, will fail to affect the virus of infantile paralysis. This is of no moment, because the number of organic chemical compounds that it is possible to prepare is essentially unlimited.

In this young branch of medical science there has been, so far, no royal road, no simple theory that will furnish a short cut to triumph. Chemists and bacteriologists have been unable to predict what kind of chemical will draw death’s sting from the diseases caused by microbes and viruses. Nor have they gained any knowledge from the effect a chemical may have—when it is tried out against a microbe or a virus in a test tube—upon that microbe or virus when it is infecting an animal or a human being.

The new science of chemical cure of hitherto incurable disease is a long grim illogical toil of cut-and-try. Giving the disease to hundreds, to thousands of animals. Then trying, by hundreds and thousands of different new chemicals, to cure it.

It will be objected that the preparation of myriads of different chemicals for this long-shot effort to find a cure will be a terribly expensive business. That is true. But, thanks to the public spirit of the executives of the Cyanamid Research Laboratories, this objection has been overcome. The research chemists of these laboratories have agreed to cooperate with Dr. S. D. Kramer, furnishing him with a large number of different organic chemical compounds. At the Michigan Health Department Laboratories he will then infect cotton rats, and proceed to the stern business of trying
to cure them of infantile paralysis.

The work has already begun. It may well require the combined efforts of a generation of chemists and virus experts. It may fail in the long run. When one remembers the baffling craftiness of the infantile paralysis virus which has tricked the shrewd and devoted efforts of microbe hunters and public healthmen for thirty years, it might seem too much to hope that finally some harmless chemical will be found to conquer the paralytic terror. Yet, in the case of every man-murdering microbe already conquered, the same was thought—up to the moment of final victory . . .

The project of finding a chemical cure for infantile paralysis is the first long-range research effort initiated by the National Foundation for Infantile Paralysis. The scientific world will watch its progress—slow and difficult as it is sure to be — with interest. And the public will not fail to support it.

Paul de Kruif