

experiments with them to determine whether *Simulium* transmits pellagra would be futile.

MR. S. J. HUNTER: I may say that the results of the experiments in the laboratory failed to prove that the monkey was susceptible.

PRESIDENT W. D. HUNTER: Is there any further discussion? If not, the next paper is by Mr. C. T. Brues on "The Transmission of Infantile Paralysis by *Stomoxys calcitrans*."

THE RELATION OF THE STABLE FLY (*STOMOXYS CALCITRANS*) TO THE TRANSMISSION OF INFANTILE PARALYSIS¹

A Résumé of Observations by Brues and Sheppard and of Experiments by Rosenau and Brues

By CHARLES T. BRUES

Infantile paralysis, more accurately designated anterior poliomyelitis or acute epidemic poliomyelitis, is a disease which has aroused much interest in the United States for a number of years on account of its serious nature and much increased prevalence. Complete ignorance as to the way in which it spreads and develops in epidemic form has also served to augment the dread of this disease. It affords me great satisfaction, therefore, to be able to present today a résumé of some observations and experiments bearing on the probable method of transmission of infantile paralysis.

These entomological investigations were conducted under the auspices of the Massachusetts State Board of Health and have extended over a period of two years. The State Board had previously conducted extensive investigations along various lines under the guidance of an advisory committee consisting of Drs. R. W. Lovett, M. W. Richardson, M. J. Rosenau, Theobald Smith, J. H. Wright and J. L. Morse, and Doctor Richardson later gave much of his time to further the success of the entomological work. During the summer of 1911 an extended series of entomological field observations was made by the writer in association with Dr. P. A. E. Sheppard who was studying the epidemiology of the disease for the State Board of Health. The more important facts then ascertained have already been published in the *JOURNAL OF ECONOMIC ENTOMOLOGY*²

¹ Contributions from the Entomological Laboratory of the Bussey Institution, Harvard University, No. 62.

² Brues, C. T. and Sheppard, P. A. E. The Possible Etiological Relation of Certain Biting Insects to the Spread of Infantile Paralysis. *Journ. Econ. Entom.* Vol. 5, No. 4, pp. 305-324 (1912), previously briefly abstracted in the *Monthly Bulletin of the Mass. State Board of Health* for December 1911, pp. 337-340.

together with the hypothesis based on these observations, that *Stomoxys calcitrans* might be responsible for the spread of poliomyelitis, aided possibly by other blood-sucking flies. During the summer of 1912 an attempt was made by Prof. M. J. Rosenau of the Harvard Medical School and the writer to transmit the disease experimentally through the agency of *Stomoxys*, using monkeys for this purpose, as these animals are susceptible to poliomyelitis. The successful outcome of this work was announced in September, 1912,¹ and was soon afterwards confirmed by Doctors Anderson and Frost of the Public Health and Marine-Hospital Service, who repeated the same experiments with similarly positive results.²

Infantile paralysis was first recognized as a distinct disease in 1840 by Heine, a German surgeon who found that the spinal cord was the site of attack. Many years later, Strümpel in 1848, suggested that the lesions in the cord were caused by an infectious agent, and in 1890 Medin published the first good clinical account of poliomyelitis. Within the last ten years, Wickman in Sweden and various others, both in Europe and America, have investigated the disease with great care, so that its clinical, epidemiological and pathological aspects are well known.

The living organism which causes the lesions in the spinal cord is not known, but it has been demonstrated to be an ultraviolet virus which passes through a Berkefeld filter only with difficulty, suggesting that it is just beyond the range of visibility.³ Its pathogenic activities are mainly restricted to the anterior portions of the spinal cord where the motor nerves take their origin, and the resulting degeneration of these motor nerves produces a more or less complete paralysis of the corresponding muscular elements. The arms and legs are most frequently affected, although paralysis of many other muscles is common in varied combinations, sometimes bilateral or unilateral, but often irregular in distribution. In fatal cases, death usually results from a paralysis of the respiratory muscles and consequent asphyxiation. The actual mortality is rather low, averaging from 12 to 17 per cent, when only typical, paralytic cases are considered. In

¹ Rosenau, M. J. and Brues, C. T. Some Experimental Observations upon Monkeys Concerning the Transmission of Poliomyelitis through the Agency of *Stomoxys calcitrans*. Bull. Mass. State Board Health, Sept. 1912, pp. 314-317.

² Anderson, J. F. and Frost, W. H. Transmission of Poliomyelitis by Means of the Stable fly, *Stomoxys calcitrans*. Public Health Reports, Vol. 27, No. 43, pp. 1733-1735. (October 1912.)

³ Since this article was written, Flexner and Noguchi (Journ. Amer. Med. Assoc., February 1, 1913) have obtained in cultures, extremely minute bodies of variable size and appearance which they believe may be the causative organism. This, however, is still somewhat in doubt.

addition there are undoubtedly many mild, atypical or abortive cases which are difficult of diagnosis. Of the remaining 83-88 per cent, about 25 per cent, recover entirely, some very quickly and a few others only after a number of months, while about 60 per cent remain permanently crippled in varying degrees. Children under six years of age are most commonly affected, approximately two thirds of the cases falling into this period. Adult cases are far less frequent, but here the mortality is correspondingly higher, and there is less likelihood of regained muscular control in non-fatal cases. Poliomyelitis is difficult to recognize in its earlier stages, for the preparalytic functional disturbances are not ordinarily at all commensurate with the grave nature of the disease. Prognosis is equally difficult, owing to the subsequent very erratic course of the infection.

On account of its greater prevalence in the Scandinavian peninsula and in Germany, it has been suggested that poliomyelitis was introduced into America from one of these European countries. However this may be, during the last seven or eight years our own country has suffered more than any other, although the increased prevalence of the disease here has been paralleled in parts of Europe, and outbreaks have occurred in the West Indies, in Australia, and in other parts of the world. For several years prior to our entomological work, there had been a growing suspicion among those familiar with the disease, that poliomyelitis like several other epidemic diseases, might be insect-borne. Since no data had been collected with this possibility directly in mind, it was necessary to determine a number of points by means of the direct observation of a large series of cases, before it was possible definitely to suspect any particular insect as a probable carrier. However, from previously made studies on the epidemiology of the disease, it appeared that many facts suggested some relation between insects and poliomyelitis.

Cases usually appear sporadically and very frequently in such a way as to render it very difficult to explain their origin on the basis of infection by personal contact. They also show a seasonal distribution very different from what might be expected of a contact infection. In winter the disease almost disappears, at the time when children are in closest association both in schools and elsewhere, but rapidly increases in prevalence during the summer, in late June and July, to a maximum in August, then rapidly decreases in September and October to the very slight winter incidence. Geographically, again, poliomyelitis does not follow the lines of densest population, but is on the contrary, quite generally typical of rural, or at least semi-rural districts. Thus in Massachusetts, in 1909, of the cities and towns where the disease occurred, the twenty-five most affected

showed an incidence ranging from 5.26 to 1.12 per thousand (averaging 1.94), the average population of these places being 3,294; the twenty-five least affected showed an incidence of from .15 to .012 per thousand, (averaging .098) and had an average population of 32,217. Complete data concerning many other regions are difficult to collocate, but the greater rural incidence seems to be an established fact. The significance of this distribution becomes very great when we consider the fact that both domestic animals and the majority of insect species are most abundant over the same areas where poliomyelitis appears in its most extensive outbreaks.

With these, and other considerations of minor importance in mind, it became possible to draw some tentative conclusions which might be strengthened or disposed of by the actual examination of the environment of a series of cases.

As a matter of fact, members of nearly all groups of insects which by their life-history seem suited to play a part in the dissemination of disease, have been implicated either as specific or contaminative carriers of disease in man or the higher mammals. The seasonal distribution of poliomyelitis makes it evident at once that insects like fleas, which are known to carry plague; lice which transmit typhus fever; or bedbugs, which are suspected of distributing kala-azar fever, could hardly account for the high summer incidence and practical winter disappearance of poliomyelitis. They vary somewhat in abundance with the progression of the seasons, but are nevertheless quite prevalent all through the winter. Mosquito-borne diseases of course, show a very decided æstival periodicity, but at least in the case of yellow fever, malarial fever and dengue, spread very rapidly in epidemic form, involving a much greater percentage of the population of a community. This is quite to be expected, on account of the general abundance of mosquitoes and their great persistence in search for human blood. For this reason they enjoy great opportunities of infection in the presence of a case of one of these diseases, and exhibit a corresponding activity in distributing the organisms later among other persons. Thus, while poliomyelitis appears in truly epidemic form, it has never developed into extensive outbreaks, comparable with those of mosquito-borne diseases. There appeared, however, no very decided reason why some relatively rare mosquito might not be concerned, except that the summer abundance of poliomyelitis does not show any regular relation to rainfall or to general mosquito prevalence. Ticks are known to act as vectors for a number of diseases, but on account of their method of attachment to the skin of the host for considerable periods, are very noticeable, and in none of the cases visited could we demonstrate the occurrence of a tick bite, either by

examination or by questions relative to the history of the case before the onset of symptoms. Certain Reduviid bugs are known to carry a trypanosome disease of man known as barbiero fever in the American tropics, but as all of our native species of this family appear to inflict very painful bites, the failure to obtain histories of such bites, seemed to eliminate these bugs from any connection with poliomyelitis.

There remain various Diptera with blood-sucking habits, and some of these seemed to offer the most promising field for investigation. Many, however, for one reason or another fail to meet all necessary requirements. Gadflies, of the genus *Tabanus* have been sometimes especially noticeable in localities where epidemics of poliomyelitis have occurred, notably in maritime towns, but they are not so abundant in the inland rural communities. Their place is there taken by the related *Chrysops*, but these do not occur in the later part of summer, when the disease shows its greatest incidence. On account of their great thirst for blood, the small black flies of the genus *Simulium* have been suspected as carriers of a human disease known as pellagra. They are most abundant in the spring, at least in our region, and may thus be ruled out as possible vectors for the virus of poliomyelitis. The horn-fly, *Hæmatobia*, appears in abundance occasionally upon animals on farms, but was seen in the vicinity of only a small proportion of the cases visited.

In addition to the insects already mentioned, which might be expected to act as specific carriers, there are others, like the common house fly which may act as contaminative carriers for certain bacterial diseases. Such a method of spread is always supplementary to infection by contact, ingestion, etc., and as such channels of infection had not been demonstrated otherwise, it seemed very unlikely that the house fly should bear any relation to the transmission of poliomyelitis.

After thus considering the various possibilities, it appeared probable that the common blood-sucking stable fly, *Stomoxys calcitrans*, might be implicated. In fact, this seemed to be the only insect which could not be disregarded for one or more of the reasons set forth above. Briefly, the reasons for suspecting a relation between *Stomoxys* and poliomyelitis were the following:

1. The blood-sucking habits of the adult fly suit it for the transfer of virus present in the blood.
2. The seasonal abundance of the fly is very closely correlated with the incidence of the disease, rising rapidly during the summer, and reaching a maximum in July and August; then slowly declining in September and October.
3. The geographical distribution of the fly is, so far as can be ascertained, wider, or at least co-extensive with that of poliomyelitis.

4. *Stomoxys* is distinctly more abundant under rural conditions, than in cities and thickly populated areas.

5. While the disease spreads over districts quickly and in a rather erratic way, it often appears to follow along lines of travel, and it is known that *Stomoxys* flies will often follow horses for long distances along highways.

6. In a surprisingly large number of cases, it appeared probable that the children affected had been in the habit of frequenting places where *Stomoxys* is particularly abundant, *i.e.*, about stables, barn-yards, etc.

During the summer of 1911, 88 cases of poliomyelitis were visited and studied both with regard to the individual histories of the patients and to the insect fauna of their environment. *Stomoxys* was found in every case, and often in exceptional abundance, while nothing appeared which would cast doubt upon a possible association of this insect with the disease.

The suspicion attaching to *Stomoxys* seemed to be strong enough to warrant direct experimentation, and during the past summer Prof. M. J. Rosenau of the Harvard Medical School and the present writer attempted to ascertain by experiments with monkeys whether the virus of poliomyelitis could actually be transferred by *Stomoxys* under controlled laboratory conditions. For this purpose a large cage was constructed of light wood, with a flat wooden base about four by five feet in size, with sides three feet in height. The sides and a part of the top were covered with ordinary screen wire, a strip one foot wide being left along one side of the top. The inner walls were further lined with surgeon's gauze to afford a resting place for the flies, and the open part of the top provided with a large black cloth which could be lifted to give access to the interior of the cage. Specimens of *Stomoxys* were collected daily in amounts of from 300 to 500 and admitted to the cage, so that in spite of the high mortality among the flies thus caged, a thousand or more were continually present. A healthy monkey was now infected with poliomyelitis by inoculation in the brain with a lethal dose of active virus of the disease. The virus in this case was obtained by making an emulsion of bits of spinal cord from monkeys which had died of the disease after being similarly infected; it had come originally from a human case of the disease, but had been later passed through a number of monkeys, as can be done without impairing its virulence. This monkey was then exposed to the captive flies daily, by stretching it at full length and rolling it in a piece of chicken wire, then placing it on the floor of the cage. Such treatment was necessary as the agile monkey would otherwise soon have demolished the frail cage. The *Stomoxys* fed on it freely during

this period, as well as later, after paralysis had set in. This usually appears on the fourth or fifth day, and death ensues several days later. Alternating with the inoculated monkey, healthy monkeys were similarly introduced into the cage at intervals. In this way new monkeys were inoculated to keep a supply of such infected animals and additional healthy ones were exposed to the flies, which fed willingly and in considerable numbers on each occasion. Thus the flies were given every opportunity to obtain infection from the monkeys, since the animals were bitten during practically every stage of the disease from the time of the inoculation of the virus till their death following the appearance of paralysis. By the same arrangement the healthy monkeys were likely to be bitten by flies that had previously fed during the various stages of the disease on the infected monkeys. The flies had meanwhile enjoyed the opportunity of incubating the virus for periods varying from the day or two which usually elapses between consecutive feedings; to the two- or three-week period for which at least some (although a very small percentage) of the flies lived in the cage.

At this point it should be mentioned that no fear was to be entertained that the healthy monkeys might become infected on account of their being introduced into the cage in which the poliomyelitic animals had been placed. Attempts to transfer the disease under conditions of far more intimate nature have been made, but have always given negative results.

In all, twelve apparently healthy monkeys of a small Javan species were exposed to the flies in the manner described for the infected monkeys. Some were placed in the cage only once or twice, and others a number of times after varying intervals. These exposures usually lasted for about half an hour, but were sometimes more protracted. No results were apparent until two or three weeks after the experiment was well under way, and then in rather rapid succession six of the animals developed symptoms of poliomyelitis. In three, the disease appeared in a virulent form, resulting in death, while the other three experienced transient tremblings, diarrhoea, partial paralysis and recovery. It is interesting to note that several of the monkeys had diarrhoea, wherein their affection resembled the human disease more closely than the type developed in monkeys after inoculation with virus in the brain, for gastro-intestinal upsets in children are frequently associated with infantile paralysis.

In support of the clinical appearance of the disease in the fly-bitten monkeys, microscopic examination of the spinal cord revealed the characteristic lesions of poliomyelitis, but we were unable to induce the disease in further monkeys by intracerebral inoculations with

emulsions from the cords of the dead monkeys. This is at present the most accurate method of diagnosing the disease.

Soon after these results were announced, however, Drs. J. F. Anderson and W. H. Frost of the Public Health Service repeated these experiments in the federal hygienic laboratory at Washington. They obtained the disease in healthy monkeys that had been bitten by *Stomoxys* which had previously fed on intracerebrally inoculated monkeys, and further succeeded in inducing the disease in another monkey by inoculation with emulsion of the spinal cord from one of those which had been infected by the flies.

It thus appears to have been satisfactorily demonstrated that *Stomoxys* can transmit infantile paralysis from one monkey to another. Whether this is the ordinary method of spread, remains yet to be definitely shown. It has already been stated, however, how well the seasonal occurrence, distribution and other facts connected with *Stomoxys* agree with the epidemiology of the disease.

Although many facts are well in accord with such a method of spread, the results of some investigators appear at first sight to be at variance with such a view, and these should be given careful consideration. It has been shown by a number of workers that the virus exists in the nasal mucosa. By most extensive observations, moreover, Kling, Pettersson and Wernstedt in Sweden have succeeded in many instances in producing poliomyelitis in monkeys by inoculating into the nervous system material washed from the mucous membranes of persons who had died of the disease, of those suffering from it, and of healthy persons in close contact with patients. This has led them to believe that the infection is ordinarily acquired through the mucous membranes, the virus being derived from this same site in those suffering from the disease. One important link is missing in this chain of evidence, however: it has never been shown that virus derived from the mucosa can produce poliomyelitis by implantation on the mucosa of healthy monkeys. We must, therefore, assume a fundamental difference in susceptibility between man and monkey, if these results are believed to have any significance in relation to the ordinary method of spread of poliomyelitis. Such a difference in susceptibility is improbable in view of the ease with which monkeys may be infected by other methods. A second objection lies in the fact that virus direct from the spinal cord can sometimes produce infection by implantation on the nasal mucosa, but as the virus from the mucosa cannot, so far as we know, and since, outside of the laboratory, virus from the cord never reaches the mucosa of a healthy individual, the bearing of these experiments on the possibility of natural transmission in this way must be regarded as not yet proven.

Flexner, Howard and Clark in this country, and others abroad have worked to some extent with insects of certain kinds to see whether these could retain the virus of poliomyelitis in a virulent condition in their bodies for any length of time. This has been done either by allowing the insects to feed on bits of infected spinal cord, or by allowing them to suck the blood of infected monkeys. After varying periods the insects were then ground up in a mortar and injected intracerebrally into monkeys. Positive results have been obtained in the case of house flies, bedbugs, and possibly with fleas, but only negative ones with several species of mosquitoes and lice. In all these cases, it must be remembered that the pulverized insects were injected into the brains of the monkeys, so that these results do not have a very direct bearing on the epidemiology of the disease.

The fact that *Stomoxys* does not bite children so very frequently suggests that perhaps poliomyelitis may possibly be regularly spread from some domestic animal which acts as a reservoir for the virus, and it has long been suspected that this disease in man may bear a relation to some paralytic disease of animals. On the other hand, the numerous mild cases which are usually regarded as abortive poliomyelitis may serve as reservoirs as well as the paralytic cases, and then the frequency with which *Stomoxys* bites might account for the incidence of the disease without any connections with animals. These are matters which will require much further study.

PRESIDENT W. D. HUNTER: This paper is open for discussion.

MR. C. L. MARLATT: I would like to ask a question, and that is, do I understand, from the diagram exhibited showing occurrence of the disease in the winter months (December, January, February, etc.), that the disease originated in these months, or are these cases carried over from the summer?

MR. C. T. BRUES: We have no evidence except that the winter development of the disease is rather more than might be expected from the rarity of the fly in the winter.

MR. C. F. HODGE: We have been working on the habits of this insect and are surprised to find them in the winter in the stable biting animals.

MR. BRAIN: I think Prof. Brues and his colleagues have made a very important advance in the subject of medical entomology by the discovery of the connection between *Stomoxys calcitrans* and Poliomyelitis, but I feel that a further step is necessary, and that is to ascertain how many bites of this fly are necessary for the transmission. In these experiments some 300 flies were used, but it is not known how many fed on any particular day, nor how many fed before infection.

In nature 300 bites are impossible as are 200, 100, or even 50. Twenty seem improbable to me, while any number up to 10 is quite possible. *Stomoxys* seems very fond of feeding around the ankles, and I have seen two feeding on a child who was so intent on something or other that he did not notice the flies at all. In the case of heart-water, a disease of sheep, goats and cattle, which resembles Poliomyelitis in many ways, it has been found that one can be reasonably sure of getting the disease from the bites of three infected ticks. If such could be shown to be the case with *Stomoxys* in Infantile Paralysis, I think it would be a very important addition to the knowledge of the subject.

MR. C. T. BRUES: Just a word in regard to the fact that it actually takes a large amount of blood to transfer the disease from one animal to another by inoculation in this way. I do not think that a large number of flies would be necessary to transfer it in this way, much less that a single bite would produce disease in a merely mechanical way. I very much doubt if any of these monkeys could have been bitten by many infected flies.

MR. BRAIN: In connection with the inference that there is a cycle, part of which occurs in the body of the fly, from the fact that it requires a large amount of blood to cause the disease, it seems to me that I have heard of a similar case where a very small, or a very large amount of blood was necessary. I do not think the case is quite understood. That there is anything like a ten days' incubation period in the body of the fly seems to be disproved by the experiments of Anderson and Frost, for they inoculated the first monkey with the virus on October 3d, and the second on October 5th. Flies were fed a few hours after inoculation, and by October 13th they had two monkeys down from the inoculation and two from fly transmission.

MR. E. P. FELT: We have with us Dr. C. F. Hodge of Clark University, Worcester, Mass., who has developed a very successful flytrap and I think it would be very interesting if we could hear from him at this time.

PRESIDENT W. D. HUNTER: If there is no objection we will allow Dr. Hodge five minutes in which to discuss his flytrap.

A NEW FLY TRAP

By C. F. HODGE, *Clark University, Worcester, Mass.*

In our present war on the flies the quick, easy and effective method is to catch the breeders, or let them catch themselves. One pair put out of business in the spring may mean bushels less through the summer and fall.