

## ACUTE POLIOMYELITIS.

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This subject is deemed worthy of discussion in detail because of the extensive outbreak of Infantile Paralysis in the United States in 1916, especially the eastern part.

In 1840 a detailed description of the symptoms of Infantile Paralysis was published by Heine, an orthopedic surgeon, of Cannstadt, Germany, although previous to this several cases of the disease had been reported. He suggested that the seat of the disease was a serous exudate in the spinal cord.

Medin after studying forty-three cases in the Swedish epidemic in 1887 came to the conclusion that this was an infectious disease because of the accompanying symptoms of fever, headache, gastro-intestinal disturbances, etc. Wickman, who suggested Heine-Medin as the name of the disease, after studying the epidemic of 1905 in Sweden in which over one thousand cases occurred, first called attention to the fact that an abortive form may occur without paralysis or any of the other symptoms. He also noted the fact that the so-called Landry's type was most fatal.

A great many authors describe their results of bacteriological findings, especially in the cerebrospinal fluid. A typical example of the latter is that of Geirsvold who was able to cultivate a gram positive diplococcus on ordinary nutritive media. Upon injection of suspensions of this organism into animals, he was able on several occasions to produce paralysis. His work and that of others who also isolated cocci cannot be taken as authentic because noted investigators like Wickman, Landsteiner, Popper and Römer could not duplicate results of their experiments.

Attempts were made to reproduce similar processes characteristic to poliomyelitis by injecting different micro-organisms such as streptococci, staphylococci directly into the blood current but the results were not satisfactory and in no case were the histological changes similar to those of poliomyelitis. This was also true of Wickman's streptococcus strain which he isolated from the spinal fluid of a poliomyelitis patient and exalted by successive animal passage. Injecting rabbits with the serous exudate in the spinal cord from known positive cases gave absolutely negative results according to Bülow-Hansen and Harbitz.

All such attempts to determine the causative agent were unsatisfactory until Landsteiner and Popper while studying the epidemic in Vienna in 1908, were able to reproduce the disease with typical clinical symptoms and pathological findings by injecting monkeys with spinal cord from cases of poliomyelitis. From these successful experiments conclusions were made which

showed that Poliomyelitis is not as we were heretofore lead to believe caused by different kinds of micro-organisms, but by a specific virus which can not be demonstrated by the ordinary bacteriological methods. This work gave impetus to a host of experiments upon monkeys and made it possible for the previously mentioned authors and Flexner, and Lewis, and Levaditi to carry out successive animal passages. These experiments also demonstrated that the virus was filterable and resistant toward glycerin and in these respects resembled the virus of Rabies.

Uniformly negative results are obtained when mice, rats, guinea-pigs, cats, dogs, sheep, goats, pigs, horses, calves, chickens, and doves are injected. Of the different species of monkeys used for this work the *macac cynomolgus* seems to be the most susceptible. This is especially true of young, half-grown animals. The symptoms of infected monkeys are essentially the same as those of the human type of the disease. According to the experiments conducted by Flexner and Lewis the inoculation is followed by a symptomless incubation period which may be from two to forty-six days, usually one or two weeks in duration. This latter is largely dependent upon the size and virulence of the test dose. The incubation period is followed by premonitory symptoms which consist of nervousness, shaking of the head and of the extremities, general weakness, spasmodic condition, and possibly unconsciousness, followed in a comparatively short time, from a few hours to one or two days, by the characteristic paresis and crippling. Paralysis of the hind quarters, seldom front, follows and in sever cases the muscles of the trunk, neck, and back are affected and the animals die with disturbed breathing. The disease is much more fatal for monkeys, seventy-six per cent, than for humans, five to twenty per cent. Flexnor and Lewis noticed that some of the monkeys after intraperitoneal or subcutaneous injection of the suspected material developed no paralysis but showed marked signs of drowsiness, weakening, and diarrhea. However, if fresh clean monkeys were injected with spinal cord suspensions which were obtained from these latter cases, they would become infected with the typical type of the disease. From analogy, in all probability we have the same occurring in humans; also it is quite probable that monkeys may suffer from the abortive type as man does.

By injecting young rabbits of a certain species with enormous doses Marks was able to infect and to pass the virus successfully from rabbit to rabbit. Marks also produced typical infection in monkeys by injecting the latter with the virus which had undergone successive rabbit passage.

The infected rabbits died between the eighth and tenth days and just before death showed symptoms of weakness and cramps. However, characteristic pathological changes were not found on post-mortem. Therefore, that rabbits are susceptible to the virus, although not developing the characteristic symptoms, can be demonstrated by injecting the rabbit strain into monkeys, the latter develop the characteristics of the disease.

As previously stated the presence of the virus in suspensions made from spinal cord and its filterability was first positively demonstrated by Landsteiner and Popper and soon after by Flexnor and Lewis. The virus passed readily through Pasteur-Chamberland, Berkefeld, and Pukall filters, although the virulence is decreased after such treatment, as is noted by a longer incubation period. In this connection it would be interesting to know if the virus could be made to pass through collodium sacs. The rabie virus which resembles the poliomyelitis virus in some respects can be filtered through collodium.

A temperature of 50° C. to 55° C. for one-half hour will destroy the virus, whereas it will retain its virulence for several days at room temperature, 22° C. to 25° C. Freezing does not injure the virus but on the contrary it seems that at a temperature of minus ten or minus fifteen degrees Centigrade the virulence is best preserved, as it is retained for months under these conditions.

The virus of Poliomyelitis is resistant to glycerin. Therefore, in order to conserve its virulence it is advisable to keep it in 33% to 50% glycerin in the ice-box. In this condition it will survive for more than six months. The virulence of the virus remains after drying over caustic sodium or potassium for twenty or thirty days. It is destroyed by the ordinary disinfectants.

Although the characteristics of the virus of Poliomyelitis were fairly well worked out, they were not free from objection until its presence was demonstrated by microscopic and cultural methods. Cultivation experiments were undertaken by Flexnor and Lewis, and Levaditi. They noticed that when serum bouillon was inoculated with filtered virus and incubated at 37½°C. for fifteen days that a slight cloudiness developed and that if a small amount of this cloudy fluid was transferred to a similar medium cloudiness appeared in these tubes. However, Römer by using the same medium could not duplicate these results. The latter investigator also obtained negative results by placing collodium sacs containing suspensions of the infecting material in the intraperitoneal cavity of animals. New attempts were pursued by Flexnor and Noguchi and positive results were obtained in 1913 by using a medium similar to that used by Noguchi in cultivating the spirochaete of syphilis. The medium used consists of aseptic fluid, sterile fresh tissue, usually kidney of a rabbit, although brain tissue may also be used. Oxygen must be excluded and is mechanically accomplished by paraffin oil. The technique employed is as follows; about 15 cc of aseptic fluid and a piece of sterile fresh kidney obtained from a rabbit is placed in a sterile tube. This is inoculated with a physiological salt emulsion of brain. The tubes are incubated at 37° C. and are not disturbed for seven to twelve days. Tubes revealing the presence of growth in a few days are discarded because of contamination. A faint opalescence should, however, appear just around the tissue in about five days. Cultures were also obtained using a solid medium which was prepared in a similar manner as above plus 2% agar. The

opalescence also just appears in the immediate vicinity of the tissue and then gradually disseminates throughout the medium. This condition soon gives rise to macroscopically visible, grayish colored colonies. These colonies may obtain the size of  $\frac{1}{3}$  millimeter in diameter. In the cultivation of the virus of Poliomyelitis ascitic fluid, fresh sterile tissue, anaerobic conditions, and 37° C. are essential. Examination of these colonies under the dark-field microscope revealed the presence of small globular bodies which are often in pairs or small groups. The forms described by Flexnor and Noguchi are .15 to .3 microns in diameter and are similar to the bodies found by Noguchi in spinal cord obtained from cases of Poliomyelitis. Similar bodies were observed by these investigators and others by examining Berkefield filterates of brain and spinal cord emulsions. The bodies stain with the polychrome dyes, and Löffler's flagella and Gram's method is applicable.

Infection of monkeys was obtained by injecting with the fifth, sixth, and even the twentieth generation. From the infections thus produced true poliomyelitis symptoms develop and the virus can be recultivated from such culture infected animals, thus positively demonstrating the casual relationship of this organism to the disease. However, the virulence of the organism is not well retained. Considerable difficulty is met with in inoculating monkeys with material from human source. Several times monkeys were inoculated with original human material without effect; likewise passage of the virus from monkey to monkey failed. Levaditi calls attention to the fact that the virus from sporadic cases is less virulent than the epidemic form. Flexnor by continuous animal passage obtained a so-called "Fixed-virus" which would infect in a dilution of .001 cc.

Because of the similarity between Rabies and Infantile paralysis it would seem possible that "negri-like" bodies might be found. Bonhoff reports finding small round or oval bodies having a diameter of about 2 microns, although the size varies considerably in the nucleus of the neuroglia cells. According to Bonhoff these bodies are specific for Poliomyelitis.

The disease may present different clinical pictures, depending upon the different parts of the central nervous system that may be attacked. The disease, therefore, may be divided into several forms according to the parts affected which are as follows: 1, the spinal; 2, the ascending or descending Landry's type; 3, the bulbar, pontine, and midbrain; 4, cerebral; 5, the cerebellar (ataxic); 6, neuritic; 7, meningitic; and 8, abortive forms.

Excluding the latter type because of lack of definite data, the spinal form is most common. The symptoms of the disease may be of great variety. Clean-cut cases will usually occur suddenly, often with fever (102-103.5° F.), general weakness, gastro-intestinal trouble, vomiting, and severe headache and pains in the neck, spine and extremities.

Flexnor, Lewis, Levaditi, Landsteiner, Leiner and Wiesner observed that one attack of the disease usually brings about a condition of active immunity and the insusceptibility thus conferred includes the various forms of the disease. This has been demonstrated in monkeys and similar conclusions

were made by observations upon humans. Blood taken from monkeys or persons who have recovered from poliomyelitis when brought in contact with virulent virus has the power of rendering the latter inert, whereas the blood from normal animals has no effect.

Because of the similarity in some respects of the virus of poliomyelitis and rabies it was suggested and hoped that methods which are used to immunize against the latter could likewise be used against poliomyelitis. The Högyes antirabic method which is to inject with sub-lethal doses and gradually increase until lethal doses are used, has been attempted and has afforded monkeys protection and immune bodies have been demonstrated in their blood. The method however, is not applicable because in some instances immunity was not obtained and unexpected paralysis resulted. Levaditi and Landsteiner were able in some cases to produce immunity by repeatedly injecting suspensions of the spinal cord as per Pasteur method. The same condition of uncertainty followed when the virus containing material was heated to 55°-60° C. or treated with chemicals—phenol and formalin. Animals injected with immune serum plus virus according to Flexnor and Lewis do not become immune. Immunity experiments show that the poliomyelitis and rabies virus are not similar not only because of the above facts but also because animals immunized against Rabies are susceptible to the virus of poliomyelitis.

It was hoped that animals might be temporarily protected, rendered passively immune, by transferring the blood from immune persons or monkeys to healthy ones. It was found that this could be actually done but the artificial immunity was only of very short duration as well as somewhat uncertain and therefore this method is not practical from the prophylactic standpoint.

Flexnor and Lewis, and others, have obtained favorable results by repeated intra-spinal injections of immune serum into infected monkeys. This method is not practical because of the source and the very limited amount of immune serum. Anti-rabic serum showed no germicidal or protective action against the virus of infantile paralysis.

Attempts at serum diagnosis by the complement-fixation test have in general proven unsuccessful. Römer and Joseph; Gay and Lucas were not able to demonstrate complement-fixation substances in the serous spinal fluid or in the blood of persons or monkeys affected with the disease.

What can be said of serum treatment in general holds true for chemicals Hexamethylenamin is according to experiments performed on monkeys, sometimes effective if used very early in the course of the disease.

Apparently the best treatment to prevent paralysis is total rest.

Recently a peculiar polymorphous streptococcus and its etiologic relation to poliomyelitis was described by E. C. Rosenow, Towne and Wheeler. Ascites media containing sterile tissue was used in the cultivation of this organism and pure cultures were obtained from throats, tonsils, abscesses in tonsils and from the central nervous system in cases of poliomyelitis. Flexnor

and Noguchi consider these cocci as contamination. Guinea-pigs, rabbits, dogs, cats, and monkeys after receiving intravenous or intracerebral injections of this pleomorphic organism became paralyzed and developed lesions in the central nervous system.

The serum of horses immunized with suspensions of this organism has specific antibodies, agglutinins and complement-deviating substances.

This serum, according to Rosenow, seems to have protective and curative power against the virus of poliomyelitis.

Nuzum and Herzog also describe an organism similar to the one isolated by Rosenow.

There have been several theories advanced as to the mode in which the virus of Poliomyelitis is spread. Our attention was called to this through the great opportunity of studying the epidemics occurring in Sweden, Norway, Germany, Austria, France, England, United States, Russia, Switzerland, Italy, Spain, Holland, Australia, Cuba, and in an island in the South Sea. The largest is that which is occurring at the present time in the United States, especially the eastern part, with some 20,000 cases involved up to September 30, 1916. There were 9,029 in New York City alone. In 1910 8,700; 1909, 2,300; 1907, 2,900 cases; and in Sweden in 1911 3,800, in 1905, 1,000 cases occurred.

Some of the most discussed theories as to the manner in which Poliomyelitis is spread are: (1) Contagious; (2) Insect-borne; (3) Dust-borne; (4) Alimentary infection. Wickman while investigating the Swedish epidemic in 1905, noticing the occurrence of sporadic cases, epidemic groups, and the abortive form, came to the conclusion that Poliomyelitis is a contagious disease and is transmitted not only by contact with sick individuals but by so-called healthy "carriers" and by persons having the abortive type of the disease. Kling and Levaditi came to the same conclusions while studying the epidemic in Sweden in 1911. Flexnor and Lewis expound the theory that the infection occurs by way of the mucous membrane of the nose and mouth and leaves the body in a like manner. These investigators were able to demonstrate the presence of the virus of poliomyelitis on the mucous membrane of the nose of monkeys which had been infected by an intracranial inoculation. Vice versa, they could infect monkeys by applying the virus on the unbroken mucous membrane of the nose. These experimentors also were able to demonstrate that the secretions of the mouth, nose, throat, and feces were virulent both from the sick and the diseased. During the extensive epidemic in Sweden in 1911, Kling, Wernstadt, and Pettersson not only came to the same conclusions but were able to demonstrate that in some instances the secretions of healthy people were infective. Monkeys can be infected therefore, not only with material from abortive cases where no symptoms present themselves but also with secretions from some healthy persons. The experimental demonstration of the presence of the virus in the secretions of the nose and mouth shows the contagious character of the

disease and how it may be spread in the immediate neighborhood of the infected one.

Flexnor, Clark, and Frazer have apparently positively demonstrated the part of the healthy "carrier" by infecting a monkey with washings of the mucous membrane of a parent of a child who was suffering from the disease. The question arises; are adults relatively immune because they have had the disease in a mild form in childhood. Likewise, this may explain the occurrence of few cases of the disease in densely inhabited localities.

Osgood and Lucas experimentally demonstrated the presence of the virus on the mucous membrane of a monkey five and one-half months after apparent recovery. They also proved its presence in a chronic "carrier" in man. Kling, Pettersson, and Wernstadt corroborated these latter findings.

In humans as well as in monkeys stomach and intestinal symptoms often occur previous to paralysis. Medin, Wickman, Krause, and Richardson, because of these symptoms, were lead to believe that there were other avenues of entrance for the virus than through the air passages of the nose and throat. However, Römer and Joseph called attention to the fact that monkeys which were injected intracranially develop gastro-intestinal symptoms.

The virus is widely disseminated in the body. It is constantly found in the central nervous system and cerebro-spinal fluid, mucous membrane of nose and throat, mesentery glands, lymph nodes, intestines and it has been found in the general circulating blood and internal organs.

Poliomyelitis has a seasonal prevalence which does not correspond to that of diseases spread by secretions or excretions of the nose and mouth. Its seasonal prevalence is during summer and fall and because of this fact it was thought that the disease was insect-borne. Experiments directed along these lines by Flexnor and Clark showed that flies which were allowed to come in contact with infected spinal cord could carry the virus at least for 48 hours. Flies that were caught in sick rooms according to Kling, Pettersson, and Wernstadt could not produce infection. Howard and Clark were able to experimentally produce the disease by injecting filtrates made from bed-bugs seven days after they were permitted to suck the blood from infected monkeys. However, transmission by the bite of bedbugs, mosquitoes, and lice proved uniformly negative. Rosenau and Brues were able to successfully transmit the virus from monkey to monkey by the bite of the stable fly (*Stomoxys calcitrans*). They believe this fly is the intermediate host. Kling and Levaditi seem to have positively proven that the disease is not insect-borne. They had occasion to allow flies, bedbugs, and mosquitoes to feed upon infected material and in no case were they able to produce the disease by injecting emulsions of them into monkeys. Also, in opposition to this view, is the fact that in order to infect a monkey from the blood of a monkey suffering from the disease Flexnor and Lewis had to take twenty cubic centimeters; with two cubic centimeters they failed. Leiner and Wiesner made six attempts using defibrinated monkey blood taken after

the appearance of paresis and one from the blood of a paralyzed child. Only in one case (from a monkey) did the infection succeed. This, of course, argues against the possibility of infection by any blood-sucking insect.

Because of the gastro-intestinal symptoms the possibility of it being carried by foodstuffs and milk is apparent. No outbreak of Poliomyelitis has been associated with milk, water, or any article of diet. Landsteiner and Levaditi have shown that milk and water which were inoculated with the virus remained infective for a month. Kling and Levaditi could not, however demonstrate the presence of the virus in milk or water used by families that were suffering from the disease. Breast nursed children also suffer from Poliomyelitis.

Infantile paralysis is considered by some to be a dust-borne disease and this is very probable when we recall the fact that the virus is resistant to drying. The best evidences of this are the very interesting experiments of Neustäder and Thro who succeeded in infecting monkeys by means of filtered extracts of dust collected from rooms in which patients had poliomyelitis. This experiment demonstrates the presence of the virus in the dust of the sick-room.

It was also suggested that poliomyelitis may be spread by some of the lower animals for it was noticed that domestic animals (horses, dogs, pigs, chickens) suffer from nervous diseases during poliomyelitis epidemics. In the cases reported we are not sure that rabies was excluded. In as much that the lower animals except the monkey and certain species of rabbits cannot be infected with the virus it is strong evidence against the theory of transmission by such animals. Flexnor, Lewis, Clark and Richardson could not by experimental methods transmit the affection suffered by the domestic animals and in all probability there is no connection between these diseases.

The manner in which the disease makes its appearance seems rather uncertain. Consequently specific methods of prophylaxis are difficult. In the present state of our knowledge the only thing that can be done is to fight the disease from every possible avenue of infection.

The patient should be isolated and other members of the family should be kept under quarantine for four to eight weeks. Above all children from such families must not be allowed to go to school. It may be advisable to close the latter and other places of assembly for children during epidemics.

Persons who have been directly exposed to poliomyelitis should be kept under observation for a period of two weeks.

Traveling in or out of infected areas especially children should not be permitted and unnecessary contact with persons known to have come from infected regions should be avoided.

Secretions and excretions of the nose and intestines of patients should be carefully disinfected. Local application of disinfectants may be applied to the nose and mouth regents.

Children should not kiss or be kissed by other persons during the prevalence of the disease.

Remnants of food, dishes, toys, books, towels, bed linen, etc., which have been in the room should be properly cared for.

Cats, dogs, or other pets must not be allowed in the sick room.

All cases should be reported to the health authorities. Houses should be placarded. Patients should be screened in and the breeding places of flies destroyed as far as possible. Suspicious cases should also be reported.

Dust on the streets should be allayed as well as in the sick room.

Sick rooms should be disinfected not only by gaseous fumigation but they should be given a thorough mechanical cleansing.

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