POLIOMYELITIS, WITH ESPECIAL REFERENCE TO TREATMENT WITH ROSENOW'S SERUM *

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Acute poliomyelitis is an infectious disease occurring either in endemic or epidemic form, and since the time its epidemic nature was recognized and commented upon by observers in Sweden, in 1868, and in Norway in 1881, there have been numerous epidemics, worldwide in distribution, the most severe in the United States occurring in New York and the Middle West in 1907, and in New York and Massachusetts in 1916. During these years, less severe epidemics occurred in various states.

It is the general consensus of opinion that epidemics are becoming more frequent with more or less periodicity. In 1916, there were 13,000 cases in New York, with 3300 deaths, a mortality of approximately 25 per cent. The percentage of patients to population is of interest; there were 1.6 cases per thousand in New York City, and in the rural districts 2.6 per thousand patients, and the average age at the time of infection was 2.8 years.

Why a more or less periodicity should occur is not known. Flexner, Amoss, and Clark have carried a single strain of virus through monkeys for a period of four years. This strain was of low virulence in the beginning; rose to a maximum for three years, and then decreased suddenly to the initial level of virulence. The same transformation in virulence of the virus present in a community may be a factor due to children who are non-immunized. Considering the rarity of the disease in children under 1 year of age, and the relative immunity of children past the age of 5, it seems that we must be dealing with a problem in which the age is an important factor. Children under 1 year of age seem to have acquired an immunity from the mother which affords them a reasonable degree of protection.

There are many interesting things observed in the study of experimental poliomyelitis. Landsteiner and Popper, in 1909, were able to produce in monkeys a typical anterio-poliomyelitis by the intraperitoneal injection of an emulsion of the brain and cord of a fatal human case. The next year Flexner and Lewis succeeded in passing the virus through a series of monkeys, using the intracerebral route.

Flexner and Noguchi cultivated a minute organism from a .15 to .3 microns in diameter from the nervous tissue of human beings and monkeys with acute poliomyelitis, and upon injection of these cultures produced the disease in monkeys, and they believed that they had fulfilled the requirements for proving the specificity of this organism.

Rosenow has isolated an organism which he designates as a pleomorphic streptococcus from material collected from cases occurring in widely separate parts of the country, the organism being found in large numbers in the various lesions of the central nervous system, mesentery glands, tonsil and adenoid tissue. He and his co-workers have proved its absence in various organs showing no lesions, and on the other hand have used hundreds of animals in proving that this particular organism has an elective affinity for nervous tissue.

He also used hundreds of animals, in determining whether or not various bacteria from different sources had an elective affinity for a nervous tissue, and concluded that bacteria from various sources did not have.

In their studies they found the organisms described by them, as well as the ones described by Flexner, occurring in the same cases, as well as in the same organs, and from experimental data conclude that the globoid organism isolated by Flexner, and the pleomorphic streptococcus isolated by them, were one and the same; that the organism varies in size and shape, depending on the method used in cultivation. Under aerobic conditions, resembling the ordinary green producing streptococcus and under anaerobic conditions becoming smaller in size, filterable, and corresponding to the "globoid" organism of Flexner and Noguchi.

As to the route of infection, it is believed by the majority of observers that the virus passes directly by the perineural lymph spaces through the cribiform plate of the ethymoid directly to the pia arachnoid and adjacent nerve structures.

Flexner and Clark observing that after intranasal innoculation the olfactory lobe might contain the virus, while none was present in the medulla and cord, concluded that the virus passes directly into the nervous system and is not carried by means of the blood stream. On the other hand, considering the fact that the tonsil and adenoid tissue always contain the organism, one might really conclude that, in some cases at least, the infection is carried by the blood stream.

The virus rapidly disappears from the blood stream when injected, being found in the spleen and bone marrow, lymph glands, and posterior spinal nerve roots. The nasal washings contain the virus; it has been demonstrated in cases six days before the onset of symptoms, is usually not found after the tenth day of illness, but has been found in carriers months afterward.

Amoss, in an excellent article, describes the mechanisms of defense against this infection, as follows:

The virus, having been transferred to the nasal mucosa of a second human being, may lodge there, remain active (there are no indications that it multiplies) or it may be destroyed. That the latter may happen is shown by experiments on the neutralization of virus by nasal washing. In general, the nasal washings of healthy adults, but not children, neutralize the virus. This power of the nasal secretions to neutralize may, therefore, be regarded as the first line of defense of the human body against the entrance of the virus. If this were the only line of defense, infection or non-infection would be a relatively simple matter. However, there are other obstacles in the way of the virus, so that if the neutralizing power is absent from the nasal secretions, infection does not always result, but the person on whose nasal mucosa the virus falls becomes a carrier. Flexner, Clark, and Fraser have detected the virus of poliomyelitis in healthy adults who never showed

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signs of infection, and the Swedish observers believe that carriers are quite common.

A third mechanism of a decisive nature is the presence of immune bodies in the serum, as shown by neutralization tests. Anderson and Frost noted the presence of immune bodies in the serum of 66 per cent of the persons who had been in close contact with poliomyelitis cases but who had not contracted the disease.

Whether or not the virus gains access directly from the mucous membrane of the nose to the nervous system, or is carried by the blood stream, it is believed that the protective mechanism of the choroid plexus must be broken down before the virus can cause widespread involvement of the nervous system, and I am forced to conclude, considering the onset and course of a series of cases, that the route of infection is not always the same.

Cases developing a paralysis, before any but the slightest evidence of systemic infection occurs, followed later by severe and intense systemic reaction, producing the so-called dromedary type of case, might well be considered as those in which the infection of the nervous system occurs before general systemic involvement. The following case illustrates this particular type. This little child of eighteen months had had no previous illness, and, while playing with the other children one evening, it was noticed that she limped on her left foot. The mother thought that there might be sand or a wrinkling of her stocking in her shoe to account for this, removed the shoe and found nothing, and did not attach any importance to it at the time. During the night, the child awakened, was rather fretful for a few minutes, apparently did not have any temperature, and in the morning, when she was taken out of the crib by her mother, she was unable to stand because of weakness in the left leg. At this time the rectal temperature was 99 degrees, pulse 90, leucocyte count, 8000; there was loss of all the deep reflexes of the left leg; there was no complaint of pain; there was no tenderness upon movement of the spine; there was no evidence of meningeal involvement upon flexing the chin upon the chest. Within thirty hours there was marked evidence of meningeal irritation, the body was in a typical opisthotonus, temperature 103 degrees, pulse 130, the spinal fluid showing seventy-six cells per ccm., positive globulin, reduced Fehlings, negative to culture. These stormy symptoms persisted for five days, being relieved, temporarily, by lumbar puncture. This child, after being ill for ten days, and her life having been despaired of, recovered, but with a paralysis of moderate severity from the tenth dorsal downward. This child was treated with Rosenow's serum, the first injection a few hours after paralysis was observed.

The above is typical of those cases which develop paralysis, with but little evidence of the presence of a general infection; there being no apparent reaction on the part of the defense mechanisms of the body ordinarily shown by increased temperature, rapid pulse, leucocytosis, etc. In such cases, involvement through the nasal mucosa might be considered as the most probable. Those cases in which the child is acutely ill for a number of days preceding involvement of the nervous system suggest that the portal of infection is through the tonsil or adenoid tissue, since it is well known that this tissue always harbors the organism which experimentally produces the disease. One might easily reach the conclusion that this mode of entrance is more common than most authors would lead us to believe.

The various clinical forms of the disease are dependent upon the localization and extent of the changes in the nervous system. The pia arachnoid invariably shows a round cell infiltration of varying degree, and the perivascular lymph spaces are infiltrated with the lymphoid cells. The cut section of the cord shows a decided swelling, with small hemorrhagic areas in the region of the anterior horn cells. The degree of destruction of the nerve cells varies from simple swelling to complete degeneration, probably due to a toxic feature in addition to the anemia, edema, and minute hemorrhages constantly present. The posterior spinal root ganglions are involved in the same process, and it is interesting to recall that these structures show changes in experimental animals in which the brain and cord are not involved. The entire lymph glandular system of the body shows hyperplasia, especially the mesenteric glands.

The clinical picture is so varied, depending upon the nervous tissues most involved, that, unless one constantly keeps the classification of Wickman in mind, he is apt to have difficulty in recognizing the clinical manifestations, because we are all influenced by our conception of the disease acquired by observation of a typical case.

Wickman, who has commented upon the abortive form, has described eight definite typical types, which are as follows: (1) Spinal poliomyelitis; (2) the ascending, or Landry's type; (3) the bulbar; (4) the cerebral; (5) ataxic; (6) polyneuritic; (7) meningitic; and (8) abortive. All of which may occur in any epidemic.

To have in mind a clear clinical picture of this disease, one must remember that we have an acute infection, characterized by a toxemia with its accompanying fever and malaise to which, in some instances, are added symptoms suggestive of respiratory and gastro-intestinal involvement. In those cases which go on to paralysis, there is a reaction on the part of the nervous system, depending upon the localization of the infection.

The recognition of the abortive type is of the most importance, from the standpoint both of the treatment of the patient and the protection of the community. It is this type, rather than the one with a frank paralysis, which, if unrecognized, spreads the infection. During epidemics, children who complain of vague symptoms should be isolated for one week, which is considered the incubation period.

Before paralysis has occurred, when only signs of toxemia are present, such as malaise, headache, fever of a moderate degree, with perhaps evidence of a mild respiratory or gastro-intestinal disturbance, one should consider the child carefully, as there are rather distinctive signs which might suggest something more than merely a reaction to teething, a

cold, or gastro-intestinal infection. He is more prostrated than usual, with a relatively slight fever, he voluntarily goes to bed and lies quietly, becomes peevish and irritable when disturbed, and many times assumes a position on his side with knees reflexed and head slightly retracted. There is something about the clinical picture out of the ordinary. If one places the child on its back, or flexes the leg on the thigh, in many cases pain is produced, due to extension of the spine. Spinal tenderness is one of the earliest evidences of involvement of the nervous system, and is often present before evidence of general cerebrospinal involvement occurs. One can readily appreciate the value of this symptom.

Another valuable diagnostic point is evidence of the meningeal involvement as shown by a positive Brudzinskis' sign elicited by flexing the chin on the chest. It is positive in the greater number of cases. A careful examination of the reflexes should be made, as any inequality or any deviation from normal has decided value.

Any suspicion of infantile paralysis should prompt lumbar puncture, as valuable information can be obtained. The fluid is clear, usually under moderate tension, with a cell count rarely exceeding 200. In the majority of cases the globulin is positive, Fehlings solution is reduced, no pellicule forms upon standing, and the colloidal gold reaction is in the syphilitic zone. This latter reaction is very important, as it has been shown by Ragan, in a series of cases, to be constantly present, affording a means of differentiating the fluid of poliomyelitis from that of meningitis and lethargic encephalitis. The fluid shows a reduction in ascending dilutions, starting in the reddish-blue area in 1 to 10, extending into the lilac and purple in 1 to 80, being expressed by 1, 1½, 2, 2, 2, 1, 0, 0, 0, 0. Such a reaction is quite distinctive from that found in meningitis, which is usually expressed as 0, 0, 0, 0, 1, 1, 2, 3, 3, 4, or tubucular meningitis, which is usually 0, 0, 1, 2, 3, 2, 2, 0, 0, 0. He has found that the length of the reaction corresponds clinically to the height of the activity, fading after three or four weeks, and that the reaction does not have any definite relationship to the number of cells or amount of globulin.

The spine symptoms and Brudzinski's sign were of value, in making a diagnosis of the following case:

Case No. 9—J. C. This boy was taken ill August 7, 1922, with very severe vomiting, complained of headache; his mother stated that he had a very high temperature. The next day he had a still higher temperature, wanted to be let alone, would not eat, and his mother said that it was very difficult to arouse him. Because of the vomiting, he was treated on this day by a doctor for some gastro-intestinal disturbance. The next day he had a great deal of pain upon flexing the chin upon the chest, was lying in bed with his knees drawn up, and any effort made to straighten out his legs caused a great deal of pain. The knee-jerk could not be elicited. At 10 a. m. on the 9th, which was three days after the onset of the illness, his temperature was 99.6 degrees, pulse 120, and respiration 36. Lumbar puncture showed a clear fluid under pressure, twenty-three cells per cm. m., and a positive globulin. At this time 30 cc. of Rosenow's serum were given intramuscularly. On August 10, he had improved so that he could talk and take some light nourishment; 20 cc. of serum again administered. The next day there was a little stiffness of the spine remaining, and there was a very weak response of the deep reflexes. He complained of seeing double when he looked upward, and he was very weak. This boy recovered within a few days with a residual sixth nerve involvement. There were no other neurological findings.

Intestinal disturbances, manifested by vomiting and diarrhoea which persists for a number of days, are not unusual, and the following short synopsis illustrates such a case:

This patient was 7 years of age. The symptoms began August 29, 1922, with severe vomiting and diarrhoea; these symptoms lasted for four days, he became much better, and was permitted to be up and dressed. Four days after the onset of the trouble it was noticed by the parents that he staggered and could not control his legs; this became rapidly worse, and in a few hours he was unable to walk. He showed improvement for two days, and then did not feel so well, and was admitted to the hospital September 3 at 2:30 p. m., showing at that time a marked weakness of the right leg with a loss of the k. j. and t. a., Brudzinski's sign was positive, and there was stiffness of the neck. His temperature was normal, his pulse was 90. He objected to being examined. Spinal puncture was done, eighteen cells per c. cm., globulin plus, 14 cc. of Rosenow's serum were administered intramuscularly, and by the next day he was so much improved that he voluntarily flexed his chin upon his chest. Within two weeks the power of his legs was better, and within a few months the child had been restored to normal.

The bulbar type is ordinarily fatal, and the following case illustrates a rather typical case of this type:

Case No. 2—S. T., male, age 5, had been in contact with an active case six days before. On August 7, 1922, at 9 p. m., his temperature was 100.5 degrees, rectal; there was no complaint. The following day his temperature and general condition were the same. The patient was seen at 10 a. m.; there was slight tenderness of the muscles of the neck; loss of the knee reflexes; no fever. At this time, 15 cc. Rosenow's serum were administered intramuscularly. At 2 p. m. his temperature was 100 degrees R., at 6 p. m. 100 degrees, and at this time an aphonia had developed so he could not make himself understood. Spinal fluid was negative as far as cell counts was concerned, with a positive globulin; his respiration was 30, he vomited frequently, with marked accumulation of mucus in the throat and larynx, which caused him to gag very often. At 10 p. m. his temperature was 101 degrees R., his respiration 36, pulse 112, there was decided rigidity of the neck, he did not complain of headache, he could not speak, and had difficulty in swallowing; 15 cc. Rosenow's serum were again administered. On August 9, he became gradually worse, the temperature was 104 degrees, there were twitching of the muscles all over the body and slight convulsive movements, 20 cc. of Rosenow's serum again administered. He became rapidly worse and died on August 10 at 1:30 p. m., two and a half days after the onset.

The ataxic type may present some diagnostic difficulties.

Case No. 24—J. A., male, age 9. He complained of not feeling well. His mother thought he was bilious and gave him a cathartic. The next morning he had difficulty in dressing himself, the mother chiding him for being so clumsy in using his arms, for he couldn't lace his shoes. She attributed this to the fact that he was probably sleepy, and after dressing him, she helped him to the table, and after preparing his food for him she observed that he could not find his mouth with his fork. She then decided that he was ill, and it was found that he had marked involvement of the

right sixth and seventh nerve, partial involvement of the right eleventh and twelfth. At this time his temperature was 99 degrees, he walked with legs adducted to steady himself, and complained of seeing double. There was marked adiadochocinesis and asynergy. It was impossible for him to hold his head erect, the reflexes of the lower extremities were a trifle active, with a decided Babinski and ankle clonus on the left and none on the right. He did not complain of pain, headaches, nor did he vomit, nor was there any mental change. When he came under my observation two weeks later, spinal puncture showed a normal fluid. Examination of the boy three months after the onset of symptoms showed marked improvement in the involvement of the cranial nerve, he could hold his head erect, and there was nothing noticeable in the use of his legs, but the reflexes of the lower extremities were slightly increased.

The ascending type is of interest, and is ordinarily fatal. The progression of the symptoms is well illustrated by the following:

Case No. 17—Male, J. H., age 15. On September 5, 1922, he developed a severe headache, without temperature. On September 6, his headache was treated by a chiropractor, and he was permitted to go to school as usual. On the morning of the 7th, upon getting out of bed, it was found that his left leg was so weak that he could not use it, and he complained of some stiffness in his neck. At 8:30 of this day his temperature was 101 degrees, he showed a marked stiffness of the neck, and a marked weakness of his left leg (most marked below the knee), the k. j. were lost, the t. a. were normal. Forty cc. of Rosenow's serum were administered. On September 9, there was some weakness of his left shoulder, and slight ataxia upon movement of his arm; 40 cc. of Rosenow's serum were administered. Within a few days the acuteness of his illness subsided, leaving him with a well-defined weakness of his left leg.

Rosenow has shown that the serum of horses immunized with aerobic cultures of the pleomorphic streptococcus from both poliomyelitis in man and experimental poliomyelitis in monkeys will develop specific antibodies, agglutins, and complement deviating properties. He has utilized this fact in the production of a serum which, unquestionably, is of value in the treatment of these cases. During the epidemic of 1916, in Yellowstone County, Montana, I observed twenty-four cases, eighteen of which were treated with this serum. In this series of cases there was one death. The number of cases recovering with paralysis was eight, or 47 per cent, and the number of cases recovering without paralysis was 9, or 52 per cent. Of the eight cases paralyzed, five were moderately severe, and three were very mild.

When one considers that in various epidemics the general mortality rate is 25 per cent, but in this series only one death occurred, he must conclude either that the administration of Rosenow's serum was of value, or that the disease was unusually mild. However, during the same year in the same state, the State Epidemologist, in tabulating cases, reported a death rate of 40 per cent in those cases with paralysis in which Rosenow's serum was not used.

The dose of serum is, roughly speaking, 5 cc. to 10 cc. for each 5 to 10 years of age, depending upon the urgency of symptoms, and it should be repeated in twelve, eighteen, or twenty-four hours, depending upon the urgency of the symptoms, and if there is no fall in temperature within twelve hours after the first injection. Rosenow formerly advised intravenous injection in conjunction with intramuscular injection, but now his advice is that the serum be given intramuscularly.

Generally speaking, one might look for a decided improvement within eighteen hours following the injection of serum, though it usually requires two to three injections before the temperature is reduced to normal. If a child has had asthma or horse serum previously, one should determine by minute injections if there is any degree of hypersensitiveness present. I have never seen any immediate reaction resulting from its use, but in about 50 per cent of cases, serum sickness will develop in eight or nine days, is often severe, and ordinarily can be relieved promptly by the injection of adrenalin chloride.

Rosenow has treated a series of patients with this serum. Of 60 treated in the pre-paralytic stage, all completely recovered without residual paralysis. In a second group of 61, with slight paralysis at the time of treatment, all but one recovered completely. In a third group showing advanced paralysis, 18 out of 123 died, 30 had residual paralysis, 61 recovered completely, and in 14 the late results were not known. In the 259 cases reported by Rosenow, the mortality rate was 7.3 per cent, which is a favorable comparison with the usual death rate of from 22 to 27 per cent.

A recent article by Aycock and Amoss, utilizing the observations of Weed and co-workers that the intravenous injection of hypertonic sodium chloride solution in normal animals caused a reduction in the volume of brain and cord, with a marked reduction of cerebrospinal fluid pressure and an aspiration of fluid from subarachnoid spaces into the perivascular spaces of the brain and cord, have recently reported a case in which this fact was utilized in conjunction with the giving of convalescent serum, with apparently excellent results. Any method which facilitates the passing of serum from the blood stream through the chloride plexus into the subdural spaces certainly might well be considered of value in the treatment of this disease.

GENERAL MANAGEMENT

In the acute stage, in addition to the serum treatment, everything possible must be done for the child to prevent restlessness and irritability. The child should be at complete rest until all pain has disappeared, and every precaution taken to prevent muscular contractions. I am convinced that the only way to place the paralyzed muscles at absolute rest is by the use of the cast. Every child following its acute illness should be placed in the care of a competent orthopedic surgeon.

In every case, numerous questions are always asked. Will my child die? Will my child have paralysis? Will the paralysis be marked? Will it recover from the paralysis, and will there be any shortening of the leg? It is very difficult to answer the first question within three or four days, inasmuch as the mortality rate in certain epidemics has been 27 per cent. One must necessarily be rather cautious in making a positive statement. As to whether or not the paralysis will be marked cannot be determined in an individual case until a sufficient time has elapsed to permit one to judge. As

to whether the child will recover from its paralysis depends entirely upon the degree of loss of function, but as we know that every child who receives intelligent treatment following paralysis will show a great deal of improvement during the following year. As to whether or not there will be shortening of the leg, one might conclude, after reading the observations of Nathan, that unless the gastrocnemius is involved, the shortening of the limb will not occur. He has found that in seventy cases, five years after the onset of the paralysis, all children with shortening had gastrocnemius involvement alone or in association with the tibialiposticus.

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DISCUSSION

Cleon C. Mason, M. D. (219 East Tenth Street, Long Beach, Calif.)—It is with great pleasure that I make these few remarks on Dr. Clarke's paper. I was present when it was originally read, and can testify as to its reception.

As Dr. Clarke has pointed out, the first essential in the handling of the disease is a diagnosis. In the presence of an epidemic this is comparatively easy, but when isolated cases spring up, often out of season, and manifesting rather bizarre symptoms, it becomes almost impossible to arrive at a correct diagnosis until paralysis sets in. Two very valuable points in the early diagnosis were brought out; both I have found of the greatest value. First, the child seems much sicker than the physical findings would warrant, and second, the presence of a positive Brudzinski sign. This last, in the cases I have seen, is most constantly present, and usually absent in other acute meningeal conditions. A third, quite constant finding is a persistent diarrhoea in the presence of an acute gastro-intestinal upset. Certainly, finding all three would be strong evidence in favor of poliomyelitis.

I feel it is still too early to draw any definite conclusions regarding the value of Rosenow's serum. There is considerable evidence, which seems to indicate that the pleomorphic streptococci described by Flexner, Amoss, Noguchi, Rosenow, etc., are not primarily the cause of the disease, but are secondary invaders; especially the work of Bull seems to sustain this view. This should in nowise detract from the work now in progress. Dr. Clarke's figures are very convincing, especially when one bears in mind that, where not used, the mortality rate was close to that of the 1916 epidemic. Certainly, the serum should be given a thorough trial with carefully controlled cases.

Ellis Jones, M. D. (Medical Office Building, Los Angeles)—Dr. Clarke has most admirably covered the subject of poliomyelitis from the standpoint of the internist. The treatment of the acute phase, as he has indicated, should consist of rest and absence of irritation and the avoidance of meddlesome therapeutics.

Fixation of the neck, trunk, and limbs in a well-padded plaster of paris bed, is desirable in the most acute cases. There is no evidence that drugs are of any use, and nothing is to be expected from counter-irritation, electricity, heat, or hot or cold applications. Hexamethylenamin may delay infection in monkeys, but is no use after actual infection has occurred.

During the acute stage, immersion in a warm bath is agreeable; massage and muscular exercise during the acute process is not good physiology, since it irritates peripheral ends of nerves connected with hemorrhagic nerve centers. Rest is imperative to enable the damaged cord to repair without interference, and rest to the muscles is equally imperative to prevent stretching of paralyzed or paretic muscle groups and contractures of the non-paralyzed muscles.

It is extremely trying to the parents, and even to the experienced surgeon, to apparently do nothing else but restrict motion and prevent contractures during the stage of tenderness, but surgical impatience during this stage is disastrous.

It is routine with us to employ plaster fixation as soon as the diagnosis is established, in order to prevent deformity and muscle-stretching. Flexion deformities of the knees, of the hips, drop-foot, adduction contractures at the shoulder and lateral curvature of the spine are most efficiently prevented by the early employment of adequate plaster fixation.

The convalescent phase begins with the disappearance of tenderness, and during this period muscle-training is begun. It is not sufficient to delegate the re-education of damaged muscles to a nurse or an untrained parent. Muscle-training requires the technique of an expert and constant orthopaedic supervision. Fatigue and muscle-stretching will convert a partial paralysis into a total paralysis, and the disregard of proper muscular balance will perpetuate a lateral curvature.

Ambulatory activity is made possible by carefully fitted braces. With the use of apparatus, almost every paralytic can be made to walk. Orthopaedic surgery enables most of our patients to eventually discard all forms of braces.

If early treatment is adequate, deformities will not occur, and much of the surgery of the orthopaedic surgeon be made unnecessary.

Philip H. Pierson, M. D. (Physicians Building, San Francisco)—This paper has been of considerable interest to me, in that it has given a comprehensive view of the diagnosis, prognosis, and treatment of a disease which generally is seen by a pediatrician, neurologist, or orthopedic surgeon, but which should be at least recognized by the general clinician. It is strikingly evident what a paucity of pathognomonic signs there are in many of the groups, and how the symptoms present might be construed as due to an irritable disposition on the part of the child. The value of a careful routine examination in all such children is rewarded by an early correct diagnosis, the most significant signs being the positive Brudzinski and the diminished or absent knee-jerks.

The treatment by Rosenow's serum has met with sufficiently satisfactory results to warrant its more general use; but it is essential that those using it record the effects produced by the amount of serum used. It seems that a larger dose applied early would be more beneficial. Small doses of diphtheria antitoxin were originally used, but later much larger amounts produced the desired neutralizing effect, and if a superfluous amount was used it did no harm.

Dr. Clarke is to be congratulated on the clear presentation of this subject and the success he has encountered.

Heredity and Hypertension—James P. O'Hare, William G. Walker, and M. C. Vickers, Boston (Journal A. M. A., July 5, 1924), analyzed the family histories of 300 unselected cases of permanent hypertension. In 204, or 68 per cent of this group, there was a definite history of apoplexy, heart disease, nephritis, arteriosclerosis or diabetes in one or more members of the patient's family. The number of relatives with vascular disease averaged 2.5 per patient, with the minimum one and the maximum nine. The large bulk of the relatives that had vascular disease, had heart, cerebral or kidney disease. The authors feel that these cases demonstrate rather conclusively that a family history of heart, kidney, cerebral disease, etc., is almost twice as common in a patient with hypertension as in the ordinary patient who has no increased blood pressure. Nature very frequently sounds a warning as early as the second decade in life of the possible development of hypertensive disease in the fourth or fifth decade. Such symptoms include frequent epistaxis, abnormal flowing at menstruation, migraine, cold, sweaty and cyanotic hands, flushing, blushing, extreme sensitiveness, a high-strung and nervous temperament, etc.