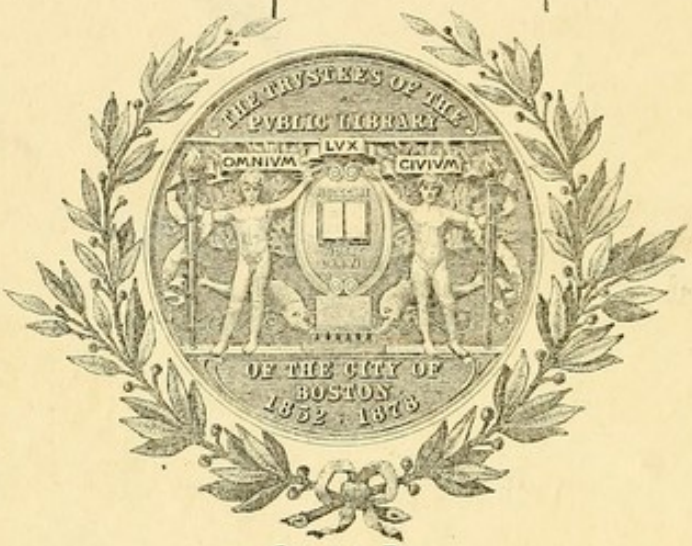
Epidemic cerebro-spinal meningitis / by Arthur H. Wentworth.



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EPIDEMIC CEREBRO-SPINAL MENINGITIS.

(From the Sears Pathological Laboratory of the Harvard Medical School.)

BY

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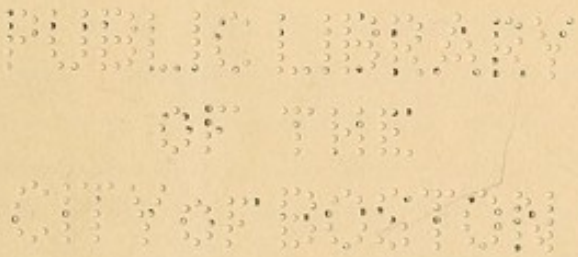

EPIDEMIC CEREBRO-SPINAL MENINGITIS.

HISTORY.

THE earliest epidemic of Cerebro-Spinal Meningitis which has been reported occurred in Geneva in 1805, and was described by Viesseaux. In 1806 the disease occurred in epidemic form in Massachusetts, and was described by a committee appointed for the purpose by The Massachusetts Medical Society in 1809. Since then epidemics have been described in various parts of Europe and America.

ETIOLOGY.

In 1887 Weichselbaum described a diplococcus which he obtained at autopsy from six cases of epidemic cerebro-spinal meningitis. This organism, which very closely resembles the gonococcus morphologically, he found in the protoplasm of the pus-corpuscles, and to a limited extent free in the inflammatory exudation in the meninges. The chief difference between it and the gonococcus is that it can be grown on ordinary culture media. The best culture medium is Loeffler's blood-serum. Weichselbaum called this organism the diplococcus intracellularis meningitidis.

During the last three years the diplococcus intracellularis has been found repeatedly by many other observers both in epidemic and sporadic cases of the disease.

As a rule inoculation experiments have been unsuccessful. Injections of pure cultures in the pleural aad peritoneal cavities of animals have produced sero-fibrinous inflammations,

and death in some cases. Meningitis has been produced in goats, in a few instances, by injections of cultures of the diplococcus into the spinal canal, and the organism has been recovered from the exudation in the meninges.

The organism appears to be very susceptible to outside influences, and it is often difficult to obtain more than a few colonies from the exudation in the meninges at autopsy. Better results are obtained when cultures are made from the spinal fluid obtained during life by means of lumbar puncture.

On culture media the organism rapidly loses its power of growth, and to maintain this power it is necessary to make fresh cultures every day. There have been no cases reported of general blood infection by this organism.

PREDISPOSING CAUSES.

There appears to be little or no influence exercised upon the spread of the disease by bad hygienic surroundings. Most epidemics have occurred in the winter and spring, and sporadic cases have been observed throughout the year. A very large proportion of all the cases have occurred between the ages of two and thirty years. Both sexes appear to be equally susceptible to the infection.

METHOD OF INFECTION.

Most observers are agreed that the disease is but slightly, if at all, contagious. The way in which infection takes place is not known. The organism has been found in the nose in some cases. The period of incubation has not been determined.

PATHOLOGY.

The lesions consist of an inflammation of the pia-arachnoid. The exudation is confined to the meshes of the pia; none is found on the surface of the arachnoid. In the most acute cases the exudation is slight in amount and purulent. In acute cases of longer duration there is more fibrin

in the exudation. The pus cells are contained in the distended meshes of the pia. Large cells, derived from proliferation of the cells of the lymph spaces and from the connective tissue corpuscles, appear. These cells are phagocytic, and often enclose numbers of the exudation cells within them. In the very chronic cases the membranes are thickened, the exudation is slight in amount, and is marked only by circumscribed whitish foci. The cells in these foci are degenerated and do not stain well. The ventricles are always distended. The ependyma is softened and frequently ragged. The fluid is cloudy and a small mass of fibrin or pus is always found in the posterior cornua of the lateral ventricles if the body has lain on the back.

The changes in the brain consist of softening and infiltration of the cortex with pus cells, which extend in from the meninges, and of foci of softening in the interior of the brain. There is also some proliferation of the neuroglia cells of the cortex. The exudation extends along the cranial nerves. The nerves most affected are the second, fifth and eighth pairs. The meninges of the cord are always affected, and the exudation is found chiefly in the meninges of the lumbar cord over the posterior surface. The inflammation extends along the spinal nerves to the spinal ganglia. The changes in the interior of the cord are not so marked as in the brain. Degenerations are found in the cranial nerves and in the spinal nerve roots.

(The above description is a brief abstract of the pathological anatomy of the disease as given by Councilman, Mallory and Wright, "Epidemic Cerebro-Spinal Meningitis," etc.—Report of the Massachusetts State Board of Health.)

SYMPTOMS.

In considering epidemic cerebro-spinal meningitis, it is very important to remember that the frequent variations

which occur in this disease depend not so much upon the presence or absence of certain symptoms as upon differences in their intensity and the period at which they occur.

Strumpell has said that perhaps the most striking feature in the disease is the constant variation in the intensity of the nervous phenomena, not only from day to day but oftentimes in the same day.

Certain symptoms which are almost constant in their occurrence are headache, pain in the neck, retraction or rigidity of the head, pain in the spine, and some degree of mental disturbance. Other symptoms which are not so constant but which occur very frequently, are vomiting, hyperæsthesia, herpes, changes in the pupils, and conjunctivitis. The moderate and irregular type of fever is very characteristic and forms a striking contrast to the severe nervous symptoms.

To obtain a clear impression of the disease, it is necessary to consider it in its entirety; the onset; the sequence of symptoms and the variations in their intensity; the peculiar temperature and pulse; and the course of the disease. The picture thus presented is characteristic, and in a large number of cases is unlike any other disease.

In order to give an adequate and at the same time a clear impression of the variations in the symptoms, the latter will be described in detail, and the different types of the disease will be briefly alluded to afterward. These types have been classified clinically as foudroyant, acute, intermittent, chronic, mild and aborted.

ONSET.

Epidemic cerebro-spinal meningitis almost always begins suddenly. A number of observers have reported cases in which prodromal symptoms occurred and lasted for several days, in some cases for two weeks. These symptoms consisted of malaise; pains in the extremities and

headache. From the character and distribution of the lesions in the meninges, and from the severity and rapidity with which the symptoms develop in most cases, it is not improbable that in some of these cases, at least, the apparent prodromal symptoms were merely coincidences.

INITIAL SYMPTOMS.

The earliest symptoms are, as a rule, fever and severe headache. In quite a large proportion of cases vomiting is one of the earliest manifestations, especially in children. In a small proportion of the adult cases the disease begins with a chill, which may be repeated. Convulsions are quite uncommon in adults, but in children they are by no means infrequent as one of the initial symptoms. These symptoms will be considered in detail.

Fever.—There is no definite and constant relation between the height of the temperature and the severity of the other symptoms. This is one of the most characteristic peculiarities of the disease. Very often the temperature is moderately elevated at the onset and may remain so for several days, or throughout the disease in acute cases. If a four hour chart is kept remissions will be found to occur, oftentimes of several degrees.

Not infrequently the initial fever is very slight, although the nervous symptoms which rapidly supervene may be very severe; these cases usually occur in adults. Quite a number of cases have been reported in which there were severe headache, pain in the neck and spine, and mental disturbance, and the temperature remained normal for several days in the early part of the disease. In children, as a rule, the temperature at the onset is higher than in adults, not uncommonly 104° F. It shows the same tendency to remit as in adults. It is quite rare to find only a slight elevation of temperature in children in the initial stage. After the first few days there are usually marked irregularities in the

height of the temperature from day to day. It is rarely more than moderately elevated later in the disease, and very often the exacerbations and remissions occur independently of the other symptoms. Occasionally the temperature assumes an intermittent character for several days. There may be no parallelism between the fever and the other symptoms at these times. In the chronic form of the disease, after three or four weeks, the temperature is very apt to be normal or subnormal, with now and then slight elevations. The nervous symptoms, however, continue with exacerbations and remissions. Antemortem rises in temperature are not uncommon, but many patients die with little or no fever. The above description is by no means a complete one of the many variations which occur in the temperature, but enough has been said to indicate how little relation exists between the fever and the nervous symptoms in many cases.

Headache.—The disease almost always begins with headache. It is often very severe and persistent, and in some cases it the most marked symptoms for several days. It is rarely absent.

Vomiting-—Vomiting is frequently one of the initial symptoms, although it may not appear for a day or two. It may persist for several days, but usually is of short duration. In chronic cases it is apt to recur at intervals, and may become a dangerous symptom.

Chill.—This may be one of the initial symptoms, and may occur later with exacerbations of the disease. It is not so constant as the other symptoms, and is not common in children.

Convulsions.—Convulsions are quite uncommon in adults, but are by no means infrequent in children at the onset of the disease.

The occurence of convulsions is by no means an index of the severity of the disease. They may occur in some

cases which are rapidly fatal, but they also occur in cases in which the disease pursues the usual course. Convulsions are rare late in the disease under any circumstances.

LATER SYMPTOMS.

Retraction of the head and pain and tenderness in the neck.—These are constant symptoms, and usually appear early. It is somewhat exceptional for them to be delayed for several days. Marked variations are observed in the intensity of the pain and tenderness, not only in different cases, but in the same case from day to day. There is the same pronounced tendency to exacerbation and remission which takes place in the other nervous symptoms. In many cases these symptoms are but moderately severe at any time, in others they are so severe as to cause opisthotonos for a time. There appears to be no constant relation between the quantity, character and location of the exudation in the meninges and the degree of pain and retraction. This has been demonstrated at autopsy, and I have examined spinal fluid which contained many organisms, and in which a purulent sediment formed in the bottom of the test-tube in a number of cases which had but moderate pain or tenderness in the neck, and only a mild degree of stupor throughout the disease. In other cases the above symptoms were very much more severe, and the fluid was only moderately turbid. In some patients the symptoms of spinal irritation are more pronounced than the cerebral.

Mental disturbance.—Some degree of mental disturbance always occurs in the course of the disease, and varies from apathy to unconsciousness. This is one of the early symptoms in most cases, and usually occurs within a day or two of the onset, in many cases in the first day. In some of the rapidly fatal cases the patients became comatose within a few hours. In some severe acute cases there may be temporary unconsciousness early in the disease, and sub-

sequently these patients may show varying degrees of apathy or stupor. Often the degree of mental disturbance is milder, and varies from apathy to stupor. Delirium is not uncommon and may assume at times a violent character. As the disease continues, marked changes occur in the mental condition at short intervals, frequently in the same day.

Hyperæsthesia.—This is not a constant symptom, but is nevertheless of frequent occurrence. It usually appears at an early stage of the disease, and may occur later when there are exacerbations. It varies from moderate general tenderness to extreme sensitiveness.

Efflorescences.—Herpes occurs very frequently. The lesions are usually confined to the lips and face. Rarely they have been found on the neck and shoulders. The herpetic efflorescence usually appears between the third and sixth days and is not an index of the severity of the meningitis.

Other efflorescences are not so common, although roseola have been observed and petechiæ and ecchymoses occur at times. The latter are oftenest seen in severe cases. It would seem from the literature as if efflorescences occurred more frequently in the earlier epidemics than at the present time. It is not impossible that this may be due to greater accuracy in diagnosis at the present time.

Pupils.—Dilatation of the pupils and incomplete reaction to light occur quite frequently, oftentimes early in the disease. These conditions are not necessarily associated with lesions of the eyes and often show the same tendency to variations as the other nervous symptoms. At times the pupils are unequal.

Nystagmus.—Nystagmus is not an uncommon symptom.

Strabismus.—Strabismus occurs frequently. It may be either convergent or divergent, and appears to have no con-

nection with the severity of the disease. The condition is almost always a temporary one, and both varieties of strabismus may occur in the same patient.

Paralyses.—Paralyses are not so common as the other nervous symptoms. They may occur early in the disease, and usually affect the extremities and at times the face. Ptosis is seen in some cases. The paralyses are not often complete, and are very apt to be temporary, sometimes only lasting for a few days. Patients who have had paralytic symptoms, and who recover from the disease, rarely show evidences of paralysis at the time when they are discharged from observation. It is uncertain whether paralyses recur later in these individuals. General cerebral and spinal symptoms are much more common than localized ones.

Reflexes.—The reflexes vary a great deal. The deep reflexes may be increased, absent, or normal. There seems to be no connection between the reflexes and the severity of the meningitis.

Emaciation.—This is a constant symptom if the disease lasts longer than a week or two. In chronic cases the patients are always extremely emaciated; in some cases they are reduced literally to skin and bones.

Constipation.—Constipation is a very common symptom, and often requires periodic treatment to relieve it.

Retracted abdomen and the tàche cerèbrale.—These symptoms are present in many cases, especially in children, but are of no diagnostic importance.

Urine.—The urine often contains a slight trace of albumin, and occasionally a few hyaline casts. Retention of urine is not uncommon in adults, but is much less so in children.

Pulse.—In adults there is usually a striking contrast between the rapidity of the pulse and the other symptoms. In a large proportion of cases the pulse is slower than normal in spite of the elevation of temperature and severe

nervous symptoms. This symptom is not often observed in children, in whom the pulse is often very rapid. In both adults and children there is a marked variability in the pulse-rate at different times in the day. The variations may exceed twenty or thirty pulse-beats in a minute. In cases which terminate fatally there is usually a marked increase in the pulse rate.

Respiration.—There is usually nothing striking about the respiration. It may be somewhat increased in rate, but is often within normal limits unless there is some complication in the lungs.

Spleen.—The spleen is rarely more than slightly enlarged by percussion, and is not often palpable.

COMPLICATIONS.

Eyes.—Conjunctivitis is such a constant symptom that it can hardly be considered a complication. It usually occurs within a few days of the onset. Severe lesions of the eyes are not rare. They may be caused by degeneration of the nerves, or by extension of the inflammation from the meninges into the retina and choroid. Of these severe lesions, optic neuritis occurs most frequently, and may be followed by atrophy of the disc. The inflammation of the retina may be mild or severe, and in some cases produces partial or total blindness. Some cases in which the lesions are severe recover their sight later. A few cases have been observed in which moderately good vision has been restored after some degree of atrophy of the discs. Irido-choroiditis occurs more rarely. Councilman claims that it is caused by direct extension of the inflammation from the meninges and is not metastatic in this form of meningitis. Optic neuritis may occur without showing external evidence of its presence and without much disturbance of vision.

Ears.—Lesions of the auditory nerves and internal ears are quite common, and are caused by extension of the inflammation from the meninges along the auditory nerves to the labyrinth. These lesions are severe and often cause permanent and complete deafness. Acute suppurative inflammation of the middle ear occurs quite frequently. It may be caused by direct extension from the brain, or in some cases may be produced by other pathogenic organisms which reach the ears by way of the eustachian tubes.

Joints.—There is much variation in the frequency of joint complications in different epidemics. In the epidemic in Nauplia, reported by Kotsonopolus, this complication occurred in almost all cases. In most epidemics the number was limited. The symptoms consist of acute swelling, redness and pain, which subside after a few days. The knees, ankles, wrists and elbows are the joints most often involved. In many cases only one joint is affected. But little is known of the nature of the lesions. Still claims that the disease is not in the joints, but is in the sheath of the tendons in the neighborhood of the joints. He has found the diplococcus intracellularis in one case.

Lungs.—Complications in the lungs do not occur so frequently as in the eyes and ears. Focal pneumonias are not uncommon, and are caused in some cases by the diplococcus intracellularis. In others, they are due to a mixed infection by the pyogenic organisms. Croupous pneumonia caused by the pneumococcus is much rarer than focal pneumonia.

Heart.—Lesions of the heart are very uncommon. A few cases of acute endocarditis have been reported in which the cause was not determined.

Kidneys—Nephritis is a very rare complication.

Septicæmia.—The writer has found no record in the literature of cases of septicæmia caused by the diplococcus intracellularis.

CLINICAL TYPES.

Foudroyant cases are not very common. They appear to have been much more frequent in earlier epidemics. These cases prove fatal in a few hours—usually from twelve to thirty-six. The onset is sudden and severe, beginning with fever, headache and vomiting, and at times with convulsions, more especially in children. The initial symptoms are rapidly followed by stupor and unconsciousness. The temperature may be high; the skin becomes gray, and there are usually multiple small hemorrhages in the skin of the body and extremities. The spinal symptoms may not develop, and the clinical picture may resemble septicæmia more than meningitis.

Acute cases run their course in from two days to two weeks. Although the general type of these cases is similar, there are many individual variations. In some cases almost all of the symptoms which have been enumerated may occur; in other cases several of them may be absent. The cases differ also in the sequence and time of occurrence of some of the symptoms. There are also marked differences in the intensity of certain symptoms. Quite a large proportion of the cases show characteristic remissions and exacerbations in the severity of the symptoms at short intervals, but there still remain quite a number of cases in which exacerbations and remissions do not occur; these patients continue in about the same condition for a varying number of days, and then the symptoms either gradually subside, and recovery takes place, or severe symptoms supervene and prove fatal, or a chronic form of the disease develops.

Intermittent cases differ from acute cases in having one or several acute exacerbations with intervals of several days during which the temperature may be normal, or more or less elevated, but the cerebral and spinal symptoms dis-

appear, and the patient appears to be convalescing. This is followed by a return of the acute symptoms which may last for several days as before. Sometimes two or more of these exacerbations occur. The intervals between the acute attacks rarely exceed a few days, but several cases have been reported in which the intervals lasted for from two to three weeks. Some cases die during an acute exacerbation; others recover after one or more attacks; and in some cases a chronic form of the disease develops which may terminate fatally, or in recovery. Emaciation is a marked symptom in the intermittent cases.

Chronic cases begin with the usual acute onset and succession of acute symptoms. After a varying number of days the temperature subsides and may remain normal, subnormal or slightly elevated for weeks. The cerebral and spinal symptoms persist with varying degrees of severity. Sometimes the patients show little or no evidence of meningitis for several days, and then the symptoms recur. The increase in severity of the symptoms may be accompanied by rises in temperature, although the latter often remains normal, or subnormal. At times elevations of temperature occur without any marked symptoms. The symptoms are generally more or less mental disturbance; headache; pain and tenderness in the neck and spine, and retraction of the head. Emaciation is very marked. The patients usually take but little food, and gradually grow weaker. At times there is temporary improvement in the cases that end fatally. In the cases which recover there is usually a gradual cessation of the symptoms. When the disease ends fatally, death usually takes place suddenly and quietly. When lesions of the eyes and ears occur in chronic cases they do so in the early stage of the disease at a time when the acute inflammation is present in the meninges.

Mild cases may begin with the same sudden onset as the

other varieties, so that in the beginning it may be impossible to determine that the disease is going to pursue a mild course. In general, however, the symptoms are milder and subside after a varying number of days.

Aborted cases are described by Strümpell as beginning with sudden and severe symptoms which rapidly subside after a day or two.

DIAGNOSIS.

Many of the symptoms of epidemic cerebro-spinal meningitis are so constant and characteristic that the diagnosis is not difficult in a large proportion of the typical cases, if one takes into consideration the whole picture of the disease; the sudden onset; the constant occurrence of cerebral and spinal symptoms early in the disease; the tendency to variation in the intensity of the nervous symptoms from day to day; the absence of correllation between the nervous symptoms and the temperature and pulse; the eye and ear complications and the frequent occurrence of the herpes. Chronic cases when seen late in the disease are the most difficult to diagnosticate, and the diagnosis may depend upon obtaining an accurate history of the onset and earlier symptoms. In several instances a diagnosis of chronic cerebro-spinal meningitis has been made by means of lumbar puncture when all other methods of diagnosis had failed. The diagnosis may be difficult or impossible in the early stage of the disease and in mild cases, without the aid of lumbar puncture. Furthermore it is important, as Councilman has pointed out, to obtain all the information possible about the different varieties of meningitis with regard to their etiology, frequency of occurrence and termination. This can only be accomplished by means of an accurate method of diagnosis, such as is furnished by lumbar puncture.

LUMBAR PUNCTURE.

When symptoms of any variety of active meningitis are present it is very rare to obtain spinal fluid in which, after standing for several hours, one cannot find fibrin or cells microscopically. In many cases it is even possible to find slight evidence of inflammatory exudation when the patients are convalescent. This method of examination fails at times, as do all methods of examination, but I believe that it does so less frequently than any other clinical means of diagnosis, such as the examination of the sputum, urine and blood; Vidal's serum test, etc. This belief is based upon work done by me during the past three years, and includes upwards of two hundred punctures. The technique of obtaining and examining the cultures, and of making the microscopic examinations of the fluid, have been systematically and carefully performed during this period. The results obtained warrant conceding a higher place to this than to other methods of clinical diagnosis. There are fewer sources of error to modify the accuracy of this test than in the others. The spinal fluid either contains cells and fibrin which denote inflammation of the meninges, or else the fluid is perfectly clear, and contains neither cellular elements nor fibrin. In the other tests various diseases or pathological conditions may give similar results, or at least so modify the results as to make a positive diagnosis impossible in many cases, in addition to the negative results which are obtained in a relatively large number of cases.

Sources of Error.—It is not necessary to describe again the technique of the operation. It may be well, however, to allude to some of the sources of error. In some cases one fails to obtain any fluid. This may be due to several causes; the needle may not enter the spinal canal; the needle may be in the spinal canal but outside the dura—that is, between the dura and the wall of the canal; the needle may be in

the sub-arachnoid space, but may be occluded by a blood-clot or a small particle of skin; the needle may be in the sub-arachnoid space, but its point may be buried in the dura on the opposite side, or the lumen of the needle may be obstructed by resting against one of the nerves. To control these sources of error it is necessary to have a wire which is large enough to fill completely the lumen of the needle. This wire of course should be sterile. If the wire is much smaller than the lumen it is likely to pass through, or to one side of, an obstruction in the lumen, and may not remove it.

If the lumen is shown to be clear by passing a wire, and a slight withdrawal of the needle does not cause the fluid to flow, than in most cases it will be found that the needle has not penetrated the dura, but is outside of it. To obviate this it is necessary to withdraw it for a distance, not sufficient for it to leave the spinal canal, and then to thrust again directing the point more towards the median line. If these various procedures be performed one will rarely fail to obtain fluid.

The chief source of error in the examination of the fluid is a reliance upon the macroscopic appearances of the fluid alone, although in many cases they are characteristic. A very slight admixture of blood will render the fluid cloudy. The quantity of blood may not exceed the fractional part of a drop, and still will produce a diffuse cloudiness. In most cases even this small quantity imparts a slight tinge of yellow to the fluid, and after the fluid has settled the blood collects in a small drop at the bottom of the test-tube. When such a small quantity of blood as this is present there is no formation of fibrin, and it is usually easy to exclude the presence of inflammatory exudation microscopically from the absence of fibrin and leucocytes. If therefore blood appears at the end of the needle it is necessary to allow a certain quantity of the fluid to escape until the

latter appears to be clear. It seldom is necessary to allow more than one cubic centimetre to escape in this way. The fluid, after this is done, is still very likely to contain a trace of blood, but not enough to interfere with the later examination. If the spinal fluid does not become clearer at once it is generally because the point of the needle is scratching the membranes, and it is necessary to withdraw it a little or to slightly alter its position. If considerable blood is mixed with the fluid there will be a formation of fibrin later.

The fluid may be slightly cloudy from particles of dust which may be in the tube, or come from the cotton at the upper part. The microscopic examination readily detects this, even if one is not certain from the macroscopic appearances.

Not unfrequently larger white particles of epidermis are present in the fluid; they should never be mistaken for the very fine diffuse cloudiness due to cells.

Sometimes a faint diffuse cloudiness may be caused by the presence of bacteria and their products, in cases of septicæmia. In these cases the cultures will show the organisms, and there will be no evidences of inflammatory exudation microscopically.

Technique of examining the fluid.—The technique of the microscopic and bacteriological examinations of the spinal fluid are important. After it has stood for some time there is a formation of fibrin in cases in which the fluid is slightly or moderately turbid and a precipitation of pus when the exudation is more purulent. In some instances the quantity of the fibrin is small, and may adhere to the bottom of the test-tube. The supernatant fluid is left perfectly clear under these circumstances, and unless the fluid is carefully examined this sediment may be overlooked. It is necessary in all such cases to scrape the bottom of the test-tube with the platinum wire in order to dislodge the

fibrin. If the test-tube has been allowed to remain in a slanting position, and only a small quantity of exudation is present, it adheres to the side, and may not be noticed. This may account for some of the negative results obtained in cases of meningitis in which the fluid was said to have been perfectly clear like normal fluid. In many cases even when the quantity of fibrin is small it adheres to the bottom of the tube by its lower end, and the remainder floats in the fluid like a web. The fibrin contains the cells in its meshes.

Cover-glass preparations of the fibrin should be made; dried by passing them through the flame of a Bunsen burner, or alcohol lamp; and stained. Lœffler's methylene blue gives the best results. By means of this stain the nuclei of the cells are very clearly defined, so that the character of the exudation can readily be detected. In addition, it stains any organisms that may be present.

To differentiate the diplococcus intracellularis from other organisms, a second cover-glass preparation should be stained by Gram's method. (By this method the diplococcus intracellularis becomes decolorized.)

Cover-glass preparations may also be stained for tubercle bacilli, by appropriate methods of staining, but the organisms are so few in number that more accurate results are obtained by inoculating guinea-pigs with the spinal fluid. In cases of tubercular meningitis this produces tuberculosis in the guinea-pig in from four to six weeks.

Character of the cells.—The cells in the spinal fluid from cases of epidemic cerebro-spinal meningitis are chiefly polymorphonuclear leucocytes—"pus corpuscles." In addition there are found a varying number of small mononuclear cells—"lymphoid cells"—and large phagocytic endothelial cells. These latter cells are very large, and have large oval or round nuclei. In the protoplasm of some of them one finds leucocytes, blood-corpuscles and particles of

cell detritus. In the protoplasm of some of the "pus-corpucles" one usually finds one or more diplococci. Sometimes a leucocyte contains large numbers of them. In this variety of meningitis the majority of the organisms are contained within the "pus-corpuscles," and are found only in limited numbers outside of the cells.

Toward the end of the disease in acute cases which terminate in recovery the "pus-corpuscles" show evidences of degeneration. The nuclei do not stain sharply, and many of the cells appear to be disintegrated. This appearance indicates that the acute inflammatory process has subsided, at least for a time, and may have some prognostic value.

In chronic cases there are fewer "pus-corpuscles." The majority of the cells have single round nuclei. Some of them are smaller than "pus-corpuscles"; have very little protoplasm, and are evidently "lymphoid cells." Others are about the same size as "pus-corpuscles," with large round nuclei and considerable protoplasm, and are probably "plasma cells." (Both lymphoid and plasma cells are present in large numbers in the meninges in chronic cases.)

Technique of obtaining cultures.—Cultures should be made on blood-serum, *at the time* of puncture, by allowing one or more cubic centimetres of the spinal fluid to drop into the culture tube. Care must be taken to prevent the fluid from running down the side of the tube at its upper part in order to avoid contamination by wetting the portion of the tube which comes in contact with the cotton. The operator should handle the end of the needle over which the fluid runs as little as possible. After obtaining the fluid in the serum tube, allow it to flow over the surface of the serum and to remain in contact with it for at least a minute or two. In a number of earlier cases in which organisms were present in the cells, and in which symptoms of active meningitis were also present, I have failed to obtain cultures by the use of a small platinum loop

filled with exudation, because the quantity was too small. Furthermore, it seems probable that in a number of cases failures to obtain a growth of the intracellular diplococcus have resulted from making cultures from the sediment after the fluid has stood for several hours, even when considerable quantities of the exudation were used.

Variations in the turbidity of the spinal fluid and their relation to the severity of the symptoms.—The following results are derived from the examination of the spinal fluid from thirty cases of epidemic cerebro-spinal meningitis. In many of these, two punctures were made at different times and in some cases three or four.

Within certain limits there is some relation between the degree of turbidity of the spinal fluid and the severity of the symptoms. The acute cases almost always show a markedly turbid fluid during the early part of the disease when the symptoms are severe. In some cases there is an immediate formation of purulent sediment in the bottom of the test-tube, but in the majority of cases the fluid is simply very turbid, and after standing contains considerable fibrin and many cells. The cases in which a purulent sediment forms may prove fatal within a few days, but on the other hand the same kind of fluid may be obtained in cases which are only moderately severe at the time when the puncture is made.

Moderately severe cases may show well marked turbidity at first, and later punctures, made at intervals of several days, may show a diminution in the turbidity of the fluid, and yet the symptoms may be severer than they were at the time of the first puncture. In other cases the diminution in turbidity may correspond to some extent with the improvement of the patient's condition. If the fluid in acute cases is obtained late in the disease, at a time when the acute symptoms have for the most part subsided, it may be clear in some cases, and the microscopic examination may

fail to detect evidences of meningitis. In other cases the cloudiness may be very slight, and very little fibrin and only a few lymphoid cells and "pus-corpuscles" may be found by microscopic examination. So that beyond certain limits there is no constant relation between the degrees of turbidity and the severity of the symptoms.

In the intermittent cases the spinal fluid may be clear during the intervals that the patient is without symptoms, and become turbid again during the exacerbations. This is by no means constant however. The fluid is very likely to show a slight degree of cloudiness in these cases in spite of the absence of symptoms.

It is impossible to say how long a slight cloudiness may persist in chronic cases. I have found more or less cloudiness due to cells in a number of chronic cases in which the disease had lasted for several weeks. From my experience thus far I would attach more importance to the results obtained by lumbar puncture than to any other means of diagnosis in the doubtful chronic cases seen late, in which even slight cerebral or spinal symptons still persisted.

In mild cases, the exudation may disappear from the spinal fluid in a few days. In the questionable cases in which the fluid appears to be perfectly clear, it is necessary to make a very thorough examination of the bottom of the test-tube with a platinum wire, after the fluid has stood for several hours.

Relation of the number of organisms to the severity of the disease.—There is no constant relation between the severity of the disease and the number of organisms present in the spinal fluid. If cultures are carefully made *at the time* of puncture, and if the blood-serum is good, one may expect to obtain a growth of the diplococcus intracellularis in the majority of acute cases, provided the patient has symptoms of active disease. In a number of cases I have obtained a growth of the diplococcus after the disease had

lasted for more than two weeks. In one case, which lasted for five weeks, I obtained growths in every one of five punctures made at intervals of one week. On the other hand there have been cases in which the spinal fluid was very turbid and in which a purulent sediment formed, and no colonies were visible on the serum after twenty-four hours, although a moderate number of diplococci were present in the water of condensation, and a very few were obtained by scraping the surface of the serum with the wire. In one such case lumbar puncture was performed three days after the onset of the disease, at a time when the cerebral and spinal symptoms were intense. In this case in addition to the very slight growth on the serum, no organisms were found in the "pus-corpuscles," although the exudation was purulent.

It is difficult to give a satisfactory explanation of such cases. It seems improbable that the organisms were dead, and therefore did not stain in the cells, or grow on the serum, three days after the onset with persistence of severe acute symptoms.

One rarely obtains a growth of the intracellular diplococcus in chronic cases. In some instances, however, a few diplococci are found in some of the "pus-corpuscles," and at times a limited number of organisms can be obtained by scraping the surface of the serum when there are no visible colonies. In mild cases the organisms are apparently not very numerous, and one would expect to obtain a negative result, so far as the cultures are concerned, unless the punctures were made soon after the onset.

SUMMARY.

1. There is no constant and definite relation between the severity of the symptoms and the degree of turbidity of the spinal fluid.

2. There is little or no connection between the number of organisms and the number of cells present in the spinal fluid.

3. In many cases there appears to be but slight connection between the number of organisms found in the spinal fluid and the severity of the disease.

4. Unless the subsequent examination of the spinal fluid is carefully performed no deductions as to the presence or absence of meningitis are justifiable.

PROGNOSIS.

It is impossible to say how long the disease will last, or what the termination will be in a given case until the lapse of a considerable interval of time during which the patient is free from symptoms. The length of this interval cannot be definitely stated, but in most cases two weeks is a safe estimate.

In acute cases it is impossible to say that the disease will not become chronic or intermittent in type later. Furthermore, the disease may be moderately severe at first and increase in severity later and prove fatal. In the intermittent type of the disease the symptoms during exacerbations may be more or less severe than those of the onset.

In chronic cases the mortality is estimated to be fully as high as in the acute variety. The patient may die from the results of the lesions produced early in the disease, or from complications, such as pneumonia, or persistent vomiting.

The mortality varies very much in different epidemics. Hirsch estimates it at from twenty to seventy per cent.

TREATMENT.

Prophylactic.—Nothing of practical value is known about the method of infection or about predisposing causes. The disease is a primary infection, and frequently attacks

apparently healthy people, therefore no definite prophylactic treatment can be formulated. Although the disease appears to be slightly, if at all, contagious, it can do no harm, in the absence of positive knowledge as to the method of infection, to isolate the patients.

Curative.— There is no known remedy which either checks the disease, or shortens its course. In a disease like cerebro-spinal meningitis in which such marked variations in the severity of the symptoms occur at short intervals, and in which so many types are observed, one must be very cautious, and not confound apparent therapeutic results with coincidences.

No effectual method of treatment has been suggested that I am aware of. The older methods, consisting of cautery of the spine; cupping; leeching; purging; ice-bags; mercurial treatment, all appear to have been faithfully tried. There is no evidence that any of these procedures accomplished anything more than to increase the patient's discomfort in some instances.

Symptomatic.— Some relief from the nervous symptoms has been obtained by the use of sedatives and analgesics. It is difficult to estimate their value in such a variable disease. Delirious and restless patients are sometimes quieted by the bromides. The pain and tenderness in the head and neck may require some preparation of opium at times. Antipyrin and allied drugs have been used, but have not proved of much value unless large doses were given. The danger to be apprehended from the depressant action of these drugs is well known, and it is safer not to use them. Salicylate of soda has been tried by various men in cases in which joint complications occurred. There is some difference of opinion as to its efficacy. In the cases which run a long course the most important indications are to sustain the strength of the patient by feeding and stimulation. It is important to keep a daily estimate of the

quantity of food taken by these patients. In the long-continued cases the patients often refuse food for several days at a time, and it is necessary to use a stomach tube in these cases at such times. This is especially the case in children.

Complications must be treated as they arise. The convalescent stage is often long, and requires careful supervision. The emaciation, weakness and anæmia demand appropriate hygienic, dietetic and tonic treatment.

In conclusion, a few words about the therapeutic value of lumbar puncture may not be amiss. The value of this procedure is purely diagnostic. One reads from time to time of recoveries from meningitis following the operation, and of other cases in which the symptoms were ameliorated. I have never seen any such cases, although constantly on the watch for them. A temporary relief, lasting for a few hours, has followed the operation in a few cases, but the same remissions frequently occur without any treatment. The fact that in almost all cases no change of any kind is visible in the patient's condition after the operation is strong evidence against its therapeutic value.

(An extensive bibliography may be found in Councilman, Mallory and Wright's work entitled, "Cerebro-Spinal Meningitis," etc.—Report of the Massachusetts State Board of Health, 1898.)