The constant presence of the tubercle bacillus in the cerebrospinal fluid of tuberculous meningitis : with a study of the cerebrospinal fluid in other forms of acute meningitis / Josephine Hemenway.

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THE CONSTANT PRESENCE OF TUBERCLE BACILLI IN THE CEREBROSPINAL FLUID OF TUBERCULOUS MENINGITIS

WITH OBSERVATIONS ON THE CEREBROSPINAL FLUID IN OTHER FORMS OF ACUTE MENINGITIS *

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A systematic effort has been made since March, 1906, in the laboratory of the Babies' Hospital, to determine the presence of tubercle bacilli in the cerebrospinal fluid in cases of tuberculous meningitis. One hundred and thirty-eight patients have been admitted to the wards of the hospital since that time, but fluids for examination were obtained from 137 only. In all but two, tubercle bacilli were demonstrated in the cerebrospinal fluid. The technic which was followed in demonstrating the bacilli has given such satisfactory results that it is herewith given in detail.

TECHNIC

The cerebrospinal fluid is collected in several test tubes, allowing about 20 c.c. to a tube. The last fluid withdrawn after the child has been raised to the sitting posture is considered the most important, as the bacilli are usually found more readily in this. Care must be taken not to shake the tubes. It has been found that a fibrin coagulum, the so-called "film," forms more often in tubes which have not been agitated. The fibrin coagulum is at first very delicate and friable. It forms with greater regularity and becomes firmer in fluids which have been placed in the incubator over night. After ten hours it is usually so firm that the entire film can be removed with a platinum loop. It is then carefully spread with fine needles on a glass slide. This is stained by the carbol-fuchsin Gabbett method. Bacilli were found with comparative ease in every case in which the film formed. In several cases in which the question of immediate diagnosis was extremely important, there was a sufficient coagulum after the fluid had stood three hours to enable one to find the bacilli.

In about 4 per cent. of the fluids examined this coagulum did not form at all. One of the following devices was then used: The sides of the test tubes were scraped with a platinum loop and any material

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removed, superimposed, drop by drop, over a small area on a glass slide, each drop dried in the air and fixed in the flame before another was added. Or with a fine capillary tube, the sediment from the test tube was superimposed in the same manner. In a few cases the sediment from centrifuged fluid was used. If the fluid drawn early in the disease showed no coagulum and if no bacilli were found, then at the second puncture, before the needle was withdrawn, it was pushed slightly forward so as to touch the anterior surface of the spinal canal, and one or two drops of blood allowed to flow into the last fluid withdrawn. With the addition of the blood a coagulum would often form, when the other tubes of fluid, drawn at the same time, remained clear.

The length of time required to find the tubercle bacilli varied greatly in different cases. Often they were found in a few minutes. If not readily discovered, careful search through the entire film was made. When a moderate number of bacilli were present, a thirty to forty minute search was usually rewarded by the finding of isolated organisms or several in clumps. In no case was a single bacillus considered conclusive. The films from all the tubes sometimes had to be used, and the bacilli were then found after a two- or three-hour search. The average time consumed was about an hour. The amount of fluid removed has averaged 60 c.c. although frequently twice as much has been obtained.

FINDINGS

The cerebrospinal fluid in tuberculous meningitis is usually as clear as distilled water, and often, although not invariably, there are seen floating in it, very small white flecks. In only one case was there a distinct cloudiness. In this the film showed far more polymorphonuclear cells than usual, and also a very large number of tubercle bacilli in each field. Repeated cultures and examinations made in this case, however, revealed the presence of no other organism. In all the other cases the predominating type of cell was the mononuclear, with very few scattered polymorphonuclear cells.

Of the 138 cases of tuberculous meningitis, tubercle bacilli were found in the fluids of 135. Of the remaining three, in one only was an early puncture possible, because the child was removed from the hospital during the first week of illness. No bacilli were found in this fluid, but a guinea-pig was inoculated and eight weeks later showed characteristic lesions of tuberculosis. Another child was brought to the hospital moribund. The diagnosis of tuberculous meningitis was evident from the history obtained from the physician. Only 2 c.c. of clear fluid could be obtained by lumbar puncture, not enough for a satisfactory examination. In the third case no puncture was made, as the child died a few minutes after admission. The diagnosis rested on the clinical symptoms.

Bacilli were therefore missed but once when a satisfactory amount of fluid could be obtained for examination, and that was from a puncture made very early in the disease.

There is little doubt that the bacilli are more numerous late in the disease, yet they were found in the first puncture in 117 cases; in the second in thirteen; and in the third puncture in four cases. Most hospital patients are not admitted until symptoms are tolerably well marked. It is therefore somewhat difficult to say how early in the disease bacilli may regularly be found. On the average, the first puncture was made about ten days before death. The larger amount of fibrin found in the fluid late in the disease, as evidenced by the constant formation of a film, renders the discovery of the bacilli easier at that time. The four cases in which a third puncture was necessary were admitted with symptoms suggesting meningitis. The early puncture showed only an excess of clear fluid, under slightly increased tension, and a few mononuclear cells.

FINDINGS IN OTHER FORMS OF MENINGITIS

Examination of the cerebrospinal fluid was made in twenty-two cases of pneumococcus meningitis. The fluid in twenty of the cases could not have been distinguished macroscopically from turbid fluids in other forms of meningitis. It varied from a slight cloudiness to such a turbidity as to cause a thick deposit of pus in each tube. The cells were chiefly polymorphonuclear; the organisms were plentiful in the smears, and grew readily in cultures.

In contrast to these typical cases, it may be of interest to mention the findings in some other cases, which were quite exceptional. A child with lobar pneumonia showed definite meningeal symptoms. An excess of clear fluid under increased tension was obtained twice by lumbar puncture, and from both fluids the pneumococcus was grown in pure culture. The disease terminated by crisis, the nervous symptoms disappearing with the fall in temperature, the child making a prompt recovery. The case was certainly not one of meningitis.

In twelve other cases of pneumonia with very pronounced nervous symptoms, punctures were made, but in none was the pneumococcus found. In cases of pneumonia with a high temperature, if a puncture was made, the cerebrospinal fluid was usually found to be under increased tension and in excess of the usual amount. This has later been observed to be true in many other diseases in which lumbar puncture has been done on children with nervous symptoms suggesting meningitis, the true diagnosis being made later. In one case, which was proved by autopsy to be one of pneumococcus meningitis, three punctures showed normal fluid in the acute stage. This finding, which was a very remarkable one, sug-

gests that one cannot draw the conclusion that because the cerebrospinal fluid is negative, there is no meningitis present.

The cerebrospinal fluid in the four cases of influenza meningitis all showed great turbidity, the cells were practically all of the polymorphonuclear variety, and the influenza organism was readily cultivated. An examination of a smear from the fresh fluid shows at once that the organism is not the meningococcus, and a culture on blood agar should therefore immediately be made. Cultures on ordinary media would show no growth and one would easily be misled if one relied on them. The organisms are not numerous in the smears, in marked contrast to the great numbers of organisms in cases of pneumococcus meningitis.

In a series of twenty-four meningococcus cases, the fluid from twenty-two showed the usual turbidity, great numbers of polymorphonuclear cells and the presence of the meningococcus in the smears and by culture. In two cases the findings were unusual. One was that of a six months old child admitted in the second week of illness with a history strongly suggesting meningitis. By lumbar puncture 15 c.c. of clear fluid was obtained, which was negative by smear and culture. A very few polymorphonuclear cells were found. The fever and nervous symptoms increased with such severity that a second puncture was made seven days later, and 20 c.c. of slightly turbid fluid obtained, in which the meningococcus was easily demonstrated. From this time the course of the disease was that of a rather mild cerebrospinal meningitis.

An almost identical history was that of a nine months old child, admitted after an illness of four weeks. The symptoms were rather indefinite. The first puncture in this case also showed clear fluid and no organisms of any kind could be found. Two weeks later the fluid was that of a typical cerebrospinal meningitis and the meningococcus was grown from fluids obtained at four subsequent punctures. From a study of these histories the question arises whether there may not be a definite meningeal inflammatory lesion present with, at the same time, a clear cerebrospinal fluid from which no organisms can be cultivated.

In the ten cases of streptococcus meningitis the fluid from each showed great turbidity. There were many polymorphonuclear cells present. The streptococci were present in large numbers and grew readily on ordinary media.

There were three cases in which more than one type of organism was found. In one case tuberculous meningitis occurred six weeks after recovery from a meningococcus meningitis. In another, tubercle bacilli and streptococci were both present during the acute stage. In the third, pneumococci and meningococci were both isolated from the thick, purulent fluid.

OTHER TESTS OF CEREBROSPINAL FLUID

Tests with Fehling's solution were made on 111 fluids to determine the diagnostic value of the presence of a reducing substance. The results were so inconstant that no reliance could be placed on this test in differentiating between tuberculous and other forms of acute meningitis. The results are embodied in the following table:

Form of meningitis	Reduction	No Reduction	Total
Tuberculous	24	26	50
Meningococcus	3	29	32
Pneumococcus	2	2	4
Streptococcus	.	1	1
Normal fluids	23	1	24

These findings suggest that a reduction in normal fluids is the rule, and yet there is reduction in so many cases of tuberculous meningitis that the test is of no value in diagnosis.

The globulin test of Noguchi has been used only recently. It consists of a precipitation of an excess of globulin by means of a solution of butyric acid in normal salt solution, and the addition of a sodium hydrate solution. Seventeen cases of meningitis—eight tuberculous, five meningococcus and four influenza—all gave typical positive reactions. Of twenty-two normal fluids tested, all but two gave a negative reaction. Of the two apparently normal fluids giving a positive test, one was from an acute case of enterocolitis with toxemia and a temperature of 107 F. The cerebrospinal fluid, which was clear, was injected into a guinea-pig and ten weeks later no evidence of tuberculosis or other disease could be found. The other fluid was also from a case of colitis, the autopsy in which showed no meningeal lesion. This test appears to be of great value in differentiating normal from abnormal fluid.