A STUDY OF THE CEREBROSPINAL FLUID IN ACUTE POLIOMYELITIS.*

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In a paper published last year Draper and Peabody reported on the examination of the cerebrospinal fluid in sixty-nine cases of acute epidemic poliomyelitis in the Hospital of The Rockefeller Institute for Medical Research. The present study deals with their findings and, in addition, with the results of the examination of fifty-seven more cases that were admitted to the hospital during the summer of 1912. The purpose of this study was to ascertain whether the examination of the spinal fluid may be of aid in early diagnosis and whether the abnormalities present have any relation to the severity of the disease, the localization of paralysis, and the prognosis.

In all, 362 examinations have been made in 126 cases. The points to which attention was paid were the macroscopic appearance of the fluid, the number and type of cells present, the presence of globulin, and the power of reducing Fehling's solution. In all cases lumbar puncture was performed as soon after admission as possible, and at varying intervals afterwards, in some cases on successive days. The period covered extends from the preparalytic stage to the twelfth week after onset. The amount of fluid withdrawn varied from a few cubic centimeters to thirty, and although no special precautions were taken in limiting the amount withdrawn, no inconvenience was suffered by the patients, who, as a rule, slept quietly for a few hours after being returned to bed. Manometric estimation of the pressure of the fluid was found to be unsatisfactory, as the patients were usually crying, and this rendered observations as to the rapidity of flow also unsatisfactory; but as far as

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could be judged from the rate of flow in the quieter or very ill
patients, an especially high pressure was not usually present. In
these patients a continuous stream lasted usually only a few seconds,
following which the flow from the needle was in a steady stream
of drops. The fluid was always examined immediately after
withdrawal.

The following method of estimating the number of cells was em-
ployed: The fluid was mixed with acetic acid in a hematocytometer
pipette for white blood corpuscles. 50 per cent. acetic acid was
drawn up to the “1” mark on the stem and the pipette was
then filled with the spinal fluid. After a thorough shaking two
counting chambers were filled immediately and counts were made.
The globulin was estimated by the butyric acid method of Noguchi,
and the intensity of the reaction was noted as very slightly plus
(v. s. +), denoting a faint cloud; slightly plus (s. +), a definite
cloud settling to a fine precipitate; plus (+), a precipitate forming
immediately; and double plus (++), a heavy flocculent precipitate.
The reaction with Fehling’s solution was tested by boiling one cubic
centimeter of spinal fluid with one cubic centimeter of Fehling’s
solution and allowing the mixture to stand for ten or fifteen
minutes. No quantitative estimation of the reducing power was
attempted. Reduction took place with every fluid examined.

The macroscopic appearance of the fluids was constant; nearly all
were clear and colorless, a few showed very slight opalescence, and a
few contained small white flakes. Those containing the small white
flakes were usually obtained in the later stages of the disease. On
standing, a delicate clot formed in a very small number of cases, but
no relation between this property and the globulin reaction, cell
count, or severity of the disease could be made out.

Owing to the lack of precise knowledge of the character of the
spinal fluid in normal children and in children suffering from other
acute infections, it was necessary to adopt a somewhat arbitrary
standard as to the changes to be regarded as pathological. A globu-
lin reaction noted as slightly plus (s. +) or more has been con-
sidered abnormal, while all those noted very slightly plus (v. s. +)
and negative (−) have been considered normal. Cell counts of
over ten cells to the cubic millimeter have been considered as ab-
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Text: FIG. 1. Curves showing variation in cell count and in globulin content in the cerebrospinal fluid in acute poliomyelitis. —— = per cent. of cases with cell count above normal; ——— = per cent. of cases with globulin content above normal.
normal, and those of ten or less as normal. With these standards it is improbable that a normal fluid has been classed as abnormal.

In text-figure 1 are shown two curves; the continuous line indicates the percentage of cases that showed abnormal cell counts in each week of the disease, while the interrupted line indicates the percentage of cases that showed abnormal globulin reactions in each week. The percentage was calculated from the number of cases examined in each week, but if the fluid from a given case was examined more than once during a week, only the highest figure was taken. From the curves it is seen that while the number of cells was highest early in the disease and gradually diminished later, the globulin reaction was at a maximum in the third week of the disease and then gradually diminished. Of the fluids from the eighty-four cases examined in the first week, seventy-eight, or 93 per cent., showed cell counts of over ten per cubic millimeter, and forty-one, or 49 per cent., showed a globulin reaction of slightly plus (s. +) or over; of the fluids from the seventy-nine cases examined in the second week fifty-one, or 65 per cent., showed abnormal cell counts, and fifty-four, or 68 per cent., showed abnormal globulin reactions; of the fluids from the fifty-six cases in the third week eighteen, or 32 per cent., gave abnormal cell counts, and thirty-nine, or 70 per cent., abnormal globulin reactions; of the fluids from the thirty-seven cases in the fourth week ten, or 27 per cent., gave abnormal cell counts, and twenty, or 54 per cent., abnormal globulin reactions. After the fourth week examinations were made only on cases showing persistent abnormalities, so that the figures for the later weeks have not been included; twenty-five cases were examined in the fifth week and twenty-four in the sixth week or later.

Of the eighty-four cases seen in the first week, in fifty the number of cells in the spinal fluid was fifty or more per cubic millimeter, while in six the number of cells was not increased. In one of the cases, seen on the seventh day of the disease and the third of paralysis, the spinal fluid contained but seven cells per cubic millimeter and gave a + globulin reaction. There was respiratory involvement and the patient died a few hours after the examination was made. Another one of the cases was classed among the abortive cases and the spinal fluid was never abnormal. In another the cell count was
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never abnormal, but a $\pm$ globulin reaction was present. In three other cases the spinal fluid later became abnormal. In one abortive case, seen on the second day of the disease, the number of cells in the spinal fluid was not increased, but on the following day the fluid contained sixty-two cells per cubic millimeter. Seventy-nine fluids from patients in the second week of the disease were examined, and in fourteen, or 18 per cent., the cells numbered fifty or more per cubic millimeter. Counts as high as this were found only once or twice among the fluids that were obtained in the later weeks. Of the fluids obtained during the third week, only 32 per cent. showed abnormal cell counts, while 70 per cent. showed abnormal globulin reactions. The most usual type of fluid examined was one with a moderate increase in the number of cells and a definite increase in the amount of globulin, but many fluids, especially in the earlier stages, showed a great increase of cells and only a slight increase of globulin that would be noted as s. $\pm$ or v.s.$\pm$. Another quite distinct type is that of fluids containing less than ten cells per cubic millimeter and giving a globulin reaction of $\pm$ or $\pm$. The highest cell count noted was one of 1,221 per cubic millimeter on the second day of the paralysis; three other fluids contained over 500 cells per cubic millimeter, and twenty-seven contained between 500 and 100. Of these thirty-one fluids only twelve, or 39 per cent., gave a globulin reaction of $\pm$ or $\pm$. Sixteen cases at no time showed an abnormal cell count and of these nine, or 56 per cent., showed a globulin estimation of $\pm$ or $\pm$, while in one fluid it was noted as $\pm$. The globulin estimation has been of great value in cases seen for the first time late in the disease or in cases where the number of cells was never very high.

The increase in the number of cells was due in nearly every case to mononuclear cells. A comparison of the results obtained by examining the cells in the hematocytometer chamber and in a stained dry preparation showed that while the chamber method gave an approximate idea of the proportion of polymorphonuclear cells present, it was quite inefficient for differentiating the various kinds of mononuclear cells. The dry preparations were made by centrifuging a mixture of one part of spinal fluid and two parts of carefully centrifuged sterile serum, pouring off the supernatant fluid,
collecting the deposit in a fine capillary glass tube, and spreading it between two cover-glasses as in preparing a blood film. The staining method employed was similar to the May-Giemsa method of Pappenheim for blood films. The cover-glass preparations were fixed in Wright's or Hasting's solution for three minutes, and stained by the addition of an equal quantity of water for one minute. The fluid was then poured off and without washing the film was stained in Giemsa solution (1 to 15 dilution) for ten to fifteen minutes, the last stages of the process being watched under the low power of the microscope. By this method the cells were obtained well spread and in an apparently undamaged condition. The most common type of cell was the lymphocyte,—large, small, and intermediate. Almost all the cells in the fluid might be of this type. Large mononuclear cells with cytoplasm that was relatively more basophilic and a regular or an irregular or sometimes even a lobed nucleus were always present and might account for at least half the cells. Polymorphonuclear cells were usually absent, but were present in all the fluids obtained on the second day of the disease and in 80 per cent. of those obtained on the third day. The average differential count of these cells was 34 per cent. on the second day and 6 per cent. on the third. Endothelial cells like those seen in smears from the surface of the meninges were rare. In every fluid degenerating cells were found that showed no cytoplasm or only ragged shreds of cytoplasm and a nucleus that was breaking down. These cells were probably mononuclear in type, but classification was usually impossible. They were present in some fluids to the extent of 20 to 30 per cent. A few plasma cells could also be identified in some of the fluids. In the more acute stages large cells with very irregular nuclei and a faintly basophilic and vacuolated cytoplasm were present in considerable numbers. Large phagocytic cells were very rare. Accurate differential counts were not attempted in all cases, for an exact classification of the cells was difficult, every grade of transition from one type of mononuclear to another being found. In the examinations made, the following were the maximal and minimal proportions of each type:
Polymorphonuclear ........................... 0 to 85 per cent.
Lymphocytes (large, small, intermediate)...... 17 to 89 per cent.
Endothelium of meninges ........................ 0 to 6 per cent.
Other types of mononuclear cells .............. 3 to 70 per cent.
Degenerating cells ............................ 4 to 24 per cent.

The cases that showed many polymorphonuclear cells in the early stages later showed the usual mononuclear excess.

Lumbar puncture was performed in ten cases that were either in the preparalytic stage or that never developed definite paretic symptoms. The fluids from two children seen on the second day after onset of symptoms contained 880 and 113 cells per cubic millimeter, and they developed typical paralyses one and two days later, respectively. The fluid from one case seen on the fourth day of symptoms contained 650 cells per cubic millimeter and gave a + globulin reaction. The child developed respiratory paralysis three days later and died. Another case seen on the sixth day, with a fluid containing thirty-seven cells per cubic millimeter, developed paralysis two days later. The spinal fluids of six abortive cases were examined and five of them contained an increase in the number of cells, the number varying from thirty-four to eighty-nine per cubic millimeter. The sixth abortive case was that of a child who suffered from fever and irritability, with tenderness and slight stiffness of the neck, and who was living in the same house with a child who, a few days later, developed typical paralysis. Lumbar puncture was performed on two occasions, the fourth and tenth days after onset of symptoms, but on both occasions the fluid showed no abnormalities. From one of the abortive cases a normal fluid was obtained on the second day after onset of the symptoms, and a fluid containing sixty-two cells per cubic millimeter on the following day. The large proportion of cases that gave abnormal fluids early in the disease is represented in text-figure 2, where the number of fluids abnormal in either cell count, globulin content, or both, examined on each day of the disease, is represented.

From this figure it is seen that nearly every fluid obtained during the first week after onset of symptoms was abnormal. During the second week the number of abnormal fluids diminished slightly, and at the beginning of the third week the percentage dropped to 62
TEXT-FIG. 2. Curve showing per cent. of cases with abnormal cerebrospinal fluids, on each day of the disease in acute poliomyelitis.
per cent. In the second half of the third week the percentage rose again. This rise was due to the number of fluids giving abnormal globulin reactions at this period of the disease. After the fourth week so few fluids were examined on any one day that the daily figures are of little value. From the point of view of estimating the value of lumbar puncture in making an early diagnosis, it is important to know on what day after the onset of symptoms the first signs of paralysis were noted. It was found that paralysis was noted on the same day as the first definite symptom; that is, on the first day of the disease in five cases, on the second day in thirty cases, on the third in thirty-two cases, on the fourth in sixteen cases, on the fifth in fourteen cases, on the sixth in seven cases, on the seventh in two cases, on the eighth in four cases, on the tenth in one case, and on the fifteenth in one case. In most cases, then, paralysis developed after two or more days of preparalytic symptoms. Of the spinal fluids examined on the second day after onset of symptoms, 86 per cent. were abnormal, and all of those examined on the third day showed definite abnormalities. It would appear, therefore, that in most cases the spinal fluid would give indications of pathological conditions before the onset of paralysis. In tuberculous meningitis and in syphilitic myelitis the clinical picture closely resembles that of acute epidemic poliomyelitis, and the characters of the spinal fluid are similar as regards the number and type of cells present and the character of the globulin reaction. The finding of the tubercle bacillus in the fluid in tuberculous meningitis and a positive Wassermann reaction in the spinal fluid in syphilitic myelitis is a sufficient differentiation, as the Wassermann reaction was performed on the fluids of all the poliomyelitis cases in the hospital in 1912 and was negative in every case.

The relation between the severity of the attack and the changes in the spinal fluid is not capable of accurate determination. While all the cases that died during the acute stages showed marked abnormalities in the number of cells present or in the globulin reaction, comparatively mild or even abortive cases were accompanied by just as marked abnormalities. Nor did the cases that showed the more extensive changes in their spinal fluids always give clinical
signs of more extensive meningeal involvement. The localization of the paralysis did not seem to affect the extent of the changes in the fluids; the cases that showed involvement of the lower limbs and thus of the lower segments of the spinal cord did not consistently show greater changes in the spinal fluid obtained by lumbar puncture, while those cases that showed clinical evidence of lesions confined to the upper part of the cord or to the bulb often showed as great changes in the fluid.

The prognosis as to life depends on the localization of the paralysis as well as on the severity, while the prognosis as to ultimate return of muscular power depends rather on the completeness of the damage done to any particular part of the spinal cord. The examination of the spinal fluid does not seem to offer evidence as to the localization or the severity of the damage.

CONCLUSIONS.

The spinal fluid in the cases of acute epidemic poliomyelitis examined was usually clear, colorless, and did not appear to be under any great increase of pressure. It showed changes in the number of cells present, or in the globulin content, or in both, in the majority of cases examined on the first few days after onset of symptoms. The number of cells was usually highest during the first week, and in one case reached the figure of 1,221 per cubic millimeter. The globulin reaction was usually most marked during the third week. The number of cells diminished rapidly and was above normal in only 32 per cent. of the cases in the third week. The increase in the globulin reaction persisted to the fourth week and might be present for a considerably longer period. The cell increase was due almost invariably to mononuclear cells of various types. The lymphocytic type of cell was the most common. A high polymorphonuclear count was noted in the very early stages. All the fluids reduced Fehling's solution. The examination of the spinal fluid may be of value in diagnosis in the preaparalytic stages and in abortive cases. It is not of value in prognosis as to life or ultimate recovery.