

THE OPTICAL ACTIVITY OF CEREBROSPINAL FLUID IN SUPPURATIVE MENINGITIS, AND ITS LACTIC ACID, SUGAR, AND CHLORIDE CONTENT

By SYDNEY L. WRIGHT, JR.,¹ ELIZABETH F. HERR AND JOHN R. PAUL

(From the Ayer Clinical Laboratory, Pennsylvania Hospital, and the John Herr Musser Department of Research Medicine, University of Pennsylvania, Philadelphia)

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This study deals with the concentrations of lactate, chloride, and reducing substances, and with the optical activity of ultrafiltrates from 49 specimens of cerebrospinal fluid from 9 patients with meningitis. In 6 instances comparisons of the concentrations of lactate, chloride, and reducing substance in blood and spinal fluid are given. The change in concentration of lactate, and reducing substances, and in the optical activity in four specimens of cerebrospinal fluid during incubation at 37° for 1 or 2 days is reported.

In an earlier study (1) we showed that the greatest part of the levorotatory substances detected in protein free ultrafiltrates from blood, consists of the salts of d-lactic acid present in the blood or formed in vitro as the result of the glycolysis of the sugar. In this study, when sufficient fluid was available, polarimetric observations were made to determine whether changes in the rotation observed are correlated with the lactates found in the cerebrospinal fluid in meningitis.

LITERATURE

Normal cerebrospinal fluid

An examination of the literature has revealed analyses for sugar or lactate in cerebrospinal fluid from individuals supposedly quite normal in 28 subjects by 5 observers. The results are shown in table 1. In addition to these there can be gathered from the literature data from various authors on patients in whom it was reasonably assumed by the authors that the disease from which the patient suffered would not be associated with abnormal values for the constituents of the cerebrospinal fluid under consideration.

¹ National Research Council Fellow in Medicine.

Reducing substance. The amounts of reducing substance (calculated as dextrose) found in cerebrospinal fluids supposedly normal in this respect, vary from 27 to 100 mgm. per 100 cc. By far the greater number, however, are within the range from 45 to 80 mgm. and the average value lies between 60 and 70 mgm. per 100 cc. (4-12, 22-25). The reducing substance of cerebrospinal fluid has been found lower than that of blood. The ratio has been reported as from 0.40 to 0.81 where fluid and blood have been obtained at approximately the same time (11-13, 24). It has been reported that the reducing substance of cerebrospinal fluid varies with that of blood (11-16, 25), rising after meals (12-13), falling after insulin (26), and maintaining a high level in diabetes and other conditions attended with hyperglycemia (14, 23). On the other hand the range of the ratio given above indicates that the correlation is subject to considerable variation. Whereas 10 to 30 mgm. per 100 cc. of the reducing substance of blood appears to be not glucose

TABLE 1
Lactate and reducing substance in normal cerebrospinal fluids

| Reducing substance | | | Lactate | | | Observer and reference |
|---------------------|------------------|------------------|---------------------|------------------|------------------|-----------------------------|
| Number of specimens | Range | Mean | Number of specimens | Range | Mean | |
| | mgm. per 100 cc. | mgm. per 100 cc. | | mgm. per 100 cc. | mgm. per 100 cc. | |
| 3 | 64-83 | 72 | | | | Coope (23) |
| 6 | 53-74 | 61 | | | | Thalhimer and Updegraff (2) |
| 6 | 35-78 | 63 | 6 | 6-11 | 9 | Osnato and Killian (8) |
| 8 | 54-82 | 70 | 8 | 6-11 | 8 | Nishida (3) |
| 5 | 48-59 | 54 | 5 | 13-17 | 15 | Geldrich (21) |

(29-32), the non-glucose reducing substance of the cerebrospinal fluid is much less in amount (27, 28). However, most of the non-glucose reducing substance of the blood is contained in the cells (30-33) and if, as has been claimed (31, 32, 34), the glucose of the blood is in higher concentration in the plasma than in the cells, the ratio of glucose in cerebrospinal fluid to glucose in plasma is probably smaller than the figures given above.

Lactate. Nishimura (36) found amounts from 11.7 to 18.0 mgm. per 100 cc. in the apparently normal fluids from cases of encephalitis and cerebrospinal syphilis. Glaser (37) analysing thirteen rather carefully selected fluids found values from 11 to 27 mgm. and averaging 19 mgm. per cent. Several others besides those mentioned above and in table 1 have determined the lactate content of normal or nearly normal fluids (15, 20). The changes of blood lactate due to muscular exercise and other causes have recently been reviewed by Jervell (38). Wittgenstein and Gaedertz (39) showed that the cerebrospinal fluid responds to increases in blood lactate resulting from exercise, though the response in the fluid is delayed in a man-

ner similar to that observed by Halliday (12) and Goodwin and Shelley (13) in the case of changes of sugar content. The changes of blood and fluid lactate content in eclampsia appear to resemble those following exercise (40).

In view of the above, and the paucity of data on resting subjects, lactic acid concentrations from 6 to 30 mgm. per cent must be considered within the normal range, though the upper part of the range is probably too high for subjects at rest. Chevassut (41) denies the presence of lactates in cerebrospinal fluid in vivo, but the weight of evidence seems against her interpretation.

Chloride. The normal average chloride content of cerebrospinal fluid as determined by different observers is remarkably consistent. Hamilton (42) found 124 m.Eq. per liter, Becker (5) 125, while Stewart (24) and Neale and Esselmont (10) found 124 and 125 respectively in children over five years of age. The great majority of the analyses on normal or supposedly normal fluids lie between 121 and 130 m.Eq. per liter.

The history of investigation into the origin of cerebrospinal fluid has recently been outlined by Levinson (35). Fremont-Smith (43) has summarized the evidence favoring the view that the fluid is a dialysate or filtrate.

Cerebrospinal fluid in meningitis

Reducing substance. It has long been known that in certain diseases the amount of reducing substance in the cerebrospinal fluid is greatly diminished. It is almost invariably low in purulent meningitis (2, 3, 7-11, 13, 17-23, 44) and occasionally in syphilis of the central nervous system, especially in untreated cases (5, 13). Neale and Esselmont (10) following the changes in concentration of reducing substance during the course of several types of meningitis reported characteristic changes in the various types. Geldrich (21) noted that in tuberculous meningitis there is occasionally a rise in the concentration from a low value to normal or nearly normal figures shortly before death.

Lactate. Comparatively few studies have been made on the lactate content of cerebrospinal fluid in meningitis. Nishimura (36) reported a slight increase in tuberculous meningitis, and Killian (19) and Osnato and Killian (8) noted high lactic acid concentrations (up to 84 mgm. per 100 cc.) in cases of several different types of meningitis. They found that in subjects responding to treatment the values became normal previous to discharge, while in those terminating in death the lactic acid content remained high. Glaser (37) reported 91 mgm. per 100 cc. in a case of influenzal and 150 mgm. per 100 cc. in a case of streptococcic meningitis, and Scheller (20) found an elevation of lactic acid in five cases of tuberculous and one of pneumococcic meningitis. Nishida (3) reported elevation of the lactic acid content of cerebrospinal fluid in cases of meningococcic, tuberculous and pneumococcic meningitis. More recently, Geldrich (21) published a series of cases of tuberculous meningitis in which the lactic acid was consistently elevated. Fasold and Schmidt (45) and Margreth (46) also have reported an elevation of lactic acid in cases of meningitis.

All investigators agree that the lactic acid content of cerebrospinal fluid is increased in suppurative and tuberculous meningitis, the amount of increase reported varying with the severity of the disease. Geldrich (21) and Garcia, Killian, and De Sanctis (47) agree that the lactic acid content of the fluid is of value as a guide to the patients progress, and of more value in this respect than the sugar content of the fluid. Geldrich observed that during a large part of the illness, the sum of glucose and lactic acid tends to remain within or close to normal limits, but as a fatal termination approaches, the sum usually increases. He found a rather steady but slow increase in lactic acid of the cerebrospinal fluid during the progress of tuberculous meningitis, until during the last week it would rise more rapidly, often to 120 mgm. per 100 cc.

Chloride. A lowered chloride concentration in cerebrospinal fluid in tuberculous meningitis seems generally recognized. Nowicka (48) found in sixty cases of tuberculous meningitis, values ranging from 87 to 116 m.Eq. per liter with a mean of 102, in general falling in the final stages nearly to the lower figure. In meningococcic meningitis the range was 108 to 120 m.Eq. per liter. Wilcox, Lyttle and Hearn (11) find a mean concentration of about 109 for tuberculous meningitis, and report the blood chlorides also lowered though not to so great an extent. Linder and Carmichael (49), however, find that the ratio of cerebrospinal fluid chloride to blood chloride is unaltered in meningitis and conclude that the fall of chloride concentration in the cerebrospinal fluid in meningitis is dependent on a similar fall in the chloride concentration of the serum. Neale and Esselmont (10) find that the changes in the chloride concentration of the fluid during the progress of the disease show special features in each type of meningitis. The range of values they report are, however, similar to those referred to above.

METHODS

The specimens of spinal fluid, except where otherwise noted, were obtained by lumbar puncture and were taken immediately to the laboratory. When the puncture was made at night, the fluid was kept in the refrigerator until the following morning, but ordinarily not over an hour elapsed between collection and analysis. For polarimetric readings it was necessary to remove proteins. Ultrafiltration through collodion sacs was the method used, and for the sake of uniformity this procedure was carried out preliminary to all analyses. The filtration was rapid and only occasionally required over twenty or thirty minutes.

Reducing substances ("sugar") were determined by the method of Folin and Wu after appropriate dilution, and chlorides by that of Van Slyke (50). The lactic acid determinations were made by the method of Friedemann, Cotonio and Schaffer (51), and were carefully controlled by determinations made on blanks and on known quantities of pure zinc lactate. The green light of a mercury vapor lamp was used for polarimetric readings. The optical activity is expressed in terms of the milligrams of dextrose per 100 cc. required to give the same rotation, using 63.03° as the specific rotation of dextrose for a wave length of 5416\AA . Details

regarding the instrument and the method of preparing and using the collodion sacs are given in the earlier papers (1, 52, 53). By expressing the optical activity in terms of dextrose either plus or minus, comparison between the optical activities of fluids of differing actual dextrose content (as determined by reduction) can be made more conveniently than when rotation is expressed in degrees.

The fluids were tested with phenol red before the polarimetric observations to be certain that they were not acid in reaction. This was necessary in view of the change which marked variations in the pH exert upon the optical activity of lactates (1).

RESULTS

Normals

A few determinations were made on cerebrospinal fluids collected in the Out-Patient Department for Wassermann determinations. While obviously none were from persons in perfect health, fifteen of them were apparently normal fluids from persons suffering from a variety of diseases but with presumably normal chemical composition of the cerebrospinal fluid. Among them are patients admitted for diagnostic study as well as patients suffering from heart disease, paralysis agitans, chronic maxillary sinusitis, and cerebrospinal syphilis.

In these fifteen cases the sugar concentration in the fluid varied from 43 to 95 and averaged 66 mgm. per 100 cc., and the lactic acid varied from 12 to 31 and averaged 19 mgm. per 100 cc.

Meningitis

Our data include one case of pneumococcic, one of tuberculous, three of streptococcic and four of meningococcic meningitis. A total of 49 specimens of cerebrospinal fluid from these nine cases were examined. Except for one case of streptococcic and three of meningococcic infection, data are not available before the day previous to death. Forty of the fluids examined were from these four cases.

In neither of the cases showing eventual recovery did we secure suitable specimens for analysis during the period of improvement and return to normal. In Case 6, no punctures were made later than those here recorded. In Case 1 a few were made but the fluids were not analyzed as treatment at this period was by irrigation of the entire canal with saline.

It was contended by Goodwin and Shelley (13) that a low sugar

concentration in the cerebrospinal fluid after intraspinal administration of antimeningococcus serum is of no diagnostic value. Analyses of serum prepared by two manufacturers, showed reducing values of 12 and 12 mgm. per 100 cc., lactic acid concentrations of 70 and 50 mgm. per 100 cc. and chloride concentrations of 95 and 100 m.Eq. per liter respectively. This is a deviation from the normal values for spinal fluid in the direction reported in cases of meningitis. A comment as to the serum treatment is therefore in order. In Cases 1, 2, and 6 from 12 to 30 cc. of antimeningococcus serum were injected usually twice daily immediately after removal of the specimen for analysis. Thus an average period of 12 hours elapsed between serum treatment and removal of the specimen. In Case 7, 15 cc. of sera were injected on each occasion, but at longer intervals. The specimens recorded were collected from one to nine days after the last previous treatment. In Case 9, one injection of 25 cc. of antistreptococcic serum was made, five hours previous to the collection of the last antemortem specimen.

Reducing

The sugar content in our series of cases is generally lowered, half the specimens showing a sugar content of 20 mgm. per 100 cc. or less. The only marked exception is in Case 5 where the sugar in the fluid was 90 mgm. per 100 cc. In this patient the blood sugar was 254 mgm. per 100 cc. and a relatively high fluid sugar was therefore to be expected.

Lactic acid

The lactic acid concentration increased in some cases eight to ten fold, four times becoming greater than 150 mgm. per 100 cc. in the last specimen prior to death.

Only seven observations showed less than 30 mgm. of lactic acid per 100 cc. Of these, six are during the favorable period of Case 1.

We do not find the constancy in the sum of lactic acid and sugar concentrations reported by Geldrich. In Case 1 for example the sum fell below the normal range and in Case 6 the sum exceeded 100 on two successive days but the patient eventually recovered. The sum does, it is true, rise to a high figure previous to death.

Chloride

Thirty chloride determinations were made and the results range from 77 to 126 m.Eq. per liter being under 121 in 83 per cent of the observations and under 110 in 50 per cent. We therefore find, in agreement with others, that the chloride concentration is lowered, sometimes very considerably, in suppurative meningitis. Only five observations fell within the range 121-130 m.Eq. per liter and three of these occurred in a patient (Case 6) who finally recovered.

TABLE 2
Comparison of concentrations in blood and cerebrospinal fluid*

| Case | Day | Lactic acid | | | Reducing | | | Chloride | | |
|----------------|-----|-------------------------|-------------------------|---------------------|----------------------------------|----------------------------------|---------------------|-------------------------|-------------------------|---------------------|
| | | Blood | Fluid | Ratio $\frac{F}{B}$ | Blood | Fluid | Ratio $\frac{F}{B}$ | Serum | Fluid | Ratio $\frac{F}{S}$ |
| | | <i>mgm. per 100 cc.</i> | <i>mgm. per 100 cc.</i> | | <i>mgm. dextrose per 100 cc.</i> | <i>mgm. dextrose per 100 cc.</i> | | <i>m. Eq. per liter</i> | <i>m. Eq. per liter</i> | |
| 2 | 2 | 40 | 115 | 2.9 | 74 | 15 | 0.20 | | | |
| 5 | 1 | | | | 254 | 90 | 0.39 | | | |
| 6 | 9 | 29 | 69 | 2.4 | 100 | 22 | 0.22 | 94 | 113 | 1.20 |
| | 10 | 25 | 71 | 2.8 | 91 | 18 | 0.20 | 94 | 116 | 1.23 |
| 8 | 2 | 35 | 156 | 4.5 | 179 | 10 | 0.06 | 92 | 109 | 1.19 |
| | 3 | 23 | 171 | 7.4 | 152 | 20 | 0.13 | | | |
| Average. . . . | | 30 | 116 | 4.0 | 142 | 29 | 0.20 | 93 | 113 | 1.21 |
| Normal. . . . | | 23 | 19 | 0.8 | 100 | 66 | 0.66 | 103 | 124 | 1.20 |

* Lactic acid and reducing on whole blood; chloride on serum.

Ratio of concentrations in blood and cerebrospinal fluid

On six occasions we examined blood and cerebrospinal fluid taken almost simultaneously from cases of meningitis. The results of these determinations are shown in table 2, together with the approximate mean normal values. In the case of lactic acid, the ratios vary from 2.4 to 7.4 contrasted with a normal value of 0.8. The normal ratio for sugar is about 0.66 but in our cases of suppurative meningitis the ratios were from 0.06 to 0.39. In the case of chloride, the ratio found by us is normal, a confirmation of the observations of Linder and Carmichael mentioned earlier (49).

Optical activity

Few observations of the optical activity of cerebrospinal fluid have been recorded and none to our knowledge, have previously been made on fluids from patients with meningitis. Lundsgaard and Høllboll (54) reported six fluids from patients with normal carbohydrate metabolism. The glucose content varied from 68 to 83 mgm. per 100 cc. as determined by reduction and from 18 to 37 mgm. per 100 cc. by optical activity. On allowing the fluids to stand for 48 hours, the reducing values remained nearly constant, while the polarimetric values increased to approximate agreement with them. Hagedorn (55) in similar experiments in a larger series of fluids found reduction values corresponding to from 43 to 70 mgm. of glucose per 100 cc. The optical activities were, however, nearly zero, and standing for 48 or 72 hours did not alter the findings. The increase of optical activity of cerebrospinal fluid on standing, described by Lundsgaard and Høllboll could not be confirmed.

In view of the above disagreement of results, Gram, Nielsen and Rud (56) made a similar study. In three out of eleven specimens an increase of optical activity greater than the experimental error, was observed on standing. They suspected that the small amount of protein present in cerebrospinal fluid might be altered or precipitated on standing and cause an increase in rotatory power. Their results in four fluids of patients with normal carbohydrate metabolism from which the proteins were precipitated by means of lead acetate together with a series in which the glucose was removed by dialysis, readings made, and the protein then precipitated, indicated to them that the wide discrepancy between the polarimetric and reducing methods of determining glucose was caused by the presence of proteins, and that alteration or disappearance of the proteins was the cause of the rise in optical activity reported by Lundsgaard and Høllboll. Their data showing the results of polarimetric observations after the precipitation of proteins, are the only ones comparable to our results after ultrafiltration. They report glucose contents, based upon the optical activity, of 50, 58, and 61 mgm. per 100 cc., whereas those estimated by reduction were 65, 76, and 64 respectively.

In our cases of suppurative meningitis, the cerebrospinal fluid was found to be actually levorotatory in 13 of 19 instances. This fact,

together with the high lactate content of the fluids and the absence of proteins, suggests that the lactates are present in the form of salts of d-lactic acid, all of which are levorotatory. We have found this to be the case in ultrafiltrates of glycolysed blood. In order to show the

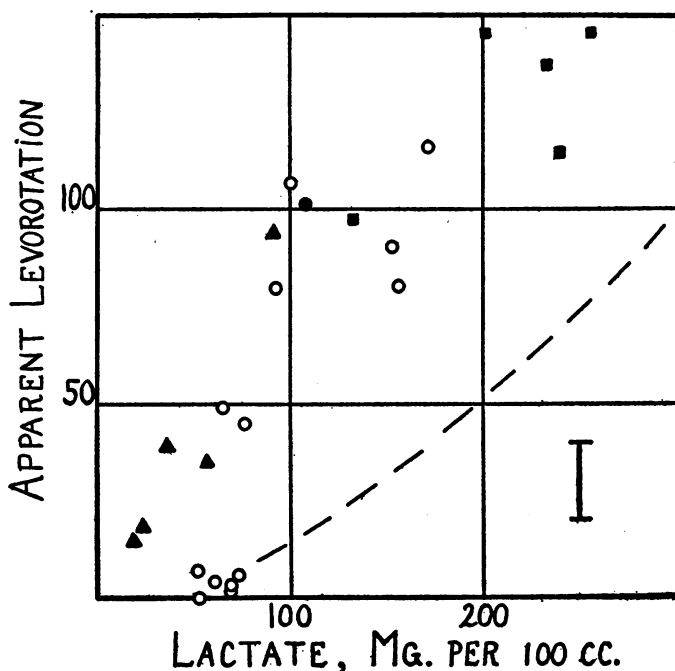


FIG. 1. THE APPARENT AMOUNT OF LEVOROTATION (EXPRESSED IN MILLIGRAMS OF DEXTROSE PER 100 CC.) IN SPINAL FLUID COMPARED WITH ITS LACTATE CONTENT

Circles represent fluids from lumbar puncture; shaded circles, from cisternal puncture; squares, postmortem, and triangles, after incubation. The approximate line for blood is indicated by dashes, and the error of the polarimetric reading (± 10 mgm.) by the vertical line.

relation between the lactate concentration and the apparent amount of levorotation, the data bearing upon it are plotted in figure 1. The apparent amount of levorotation is a calculated value, being the milligrams of dextrose it would be necessary to add to 100 cc. of the fluid to make the optical activity of the fluid equal that of a pure solution of

dextrose of the concentration indicated by the reducing determinations. It will be observed that the points tend to fall along a curve similar to, but not identical with that drawn for blood in our previous paper (1). The six points lying together somewhat apart from the others are those (five of them from Case 6) in which the total optical activity was dextro-rotatory. In the curve drawn from blood we obtained, by glycolysis, a figure for the non-glucose reducing substances and subtracted this from the reducing value in computing the apparent levorotation. In calculating the apparent levorotation of the spinal fluid as shown in figure 1, no allowance is made for non-glucose reducing substances. That they are absent is probably not true but they can hardly introduce an error that invalidates our conclusion drawn from figure 1 that there is a relationship between the apparent levorotation and the lactate concentration.

Glycolysis

Specimens of normal cerebrospinal fluid handled in a manner to avoid contamination, showed no alteration in reducing substance on standing at room temperature or in the incubator as long as 48 hours. This is in agreement with the recent report of Nielsen (57) who found that the loss of sugar frequently did not begin until a much longer time had elapsed than we allowed. Chevassut (41) found glycolysis occurring promptly and rapidly in normal fluid. Fasold and Schmidt (45) found insignificant changes of sugar and lactate in fluids from cases of meningitis.

Four specimens of fluid from a case of meningococcic meningitis were allowed to stand for 24 or 48 hours in an incubator. The concentration of reducing substance was small at the start and remained virtually unchanged. The lactate content, however, originally large, became less, and the optical activity showed a correlated diminished amount of levorotation. The data are shown in table 3 and are included in figure 1 as triangles. The fluids were allowed to stand as drawn, but the protein and cells were removed by ultrafiltration before the polarimetric reading.

This change in optical activity is in the same direction as reported by Lundsgaard and Højboell and in three instances by Gram, Nielson and Rud. No lactic acid determinations were made in those studies.

While the presence of proteins would be a disturbing factor in any study of optical activity, our experiments indicate that alterations in lactic acid content may be of considerable significance.

TABLE 3
The effect of incubation in cerebrospinal fluid in meningitis. Case 7

| Day of disease | Incubated | Lactic acid | Reducing value (dextrose equivalent) | Rotation (dextrose equivalent) | Apparent levo- rotation (dex- trose equivalent) |
|----------------|-------------|-------------------------|---|-----------------------------------|---|
| | <i>days</i> | <i>mgm. per 100 cc.</i> | <i>mgm. per 100 cc.</i> | <i>mgm. per 100 cc.</i> | <i>mgm. per 100 cc.</i> |
| 15 | Fresh | 65 | 15 | -34 | 49 |
| | 1 | 36 | 10 | -29 | 39 |
| 21 | Fresh | 108 | 24 | -77 | 101 |
| | 1 | 93 | 20 | -73 | 93 |
| | 2 | 19 | 15 | 0 | 15 |
| 27 | Fresh | 93 | 18 | -61 | 79 |
| | 1 | 23 | 18 | 0 | 18 |
| 30 | Fresh | 172 | 15 | -101 | 116 |
| | 1 | 56 | 15 | -20 | 35 |

DISCUSSION

Insufficient evidence is available to satisfactorily establish the mechanism of formation of normal cerebrospinal fluid and the relation between the concentration of its chemical constituents and the same constituents of the plasma, although evidence for the importance of dialysis or filtration through the membranes of the choroid plexus is impressive. The explanation of pathological observations is obviously even more complex. The apparently greater disturbance of glucose and lactic acid equilibrium than of chloride equilibrium between plasma and fluid may be due to the conversion of glucose to lactic acid by leucocytes and bacteria, probably especially the former.

CONCLUSIONS

1. Lactic acid determinations on the cerebrospinal fluid give striking evidence of abnormality in cases of suppurative meningitis and the lactic acid concentrations are more or less related to the severity of the clinical symptoms.

2. In suppurative meningitis the ultrafiltrate of the cerebrospinal fluid is usually levorotatory. The parallelism between degree of levorotation and lactic acid concentration suggests that the latter is present in the form of levorotatory d-lactates, which is the same form that has been found in glycolysed blood.

3. The ratio of the concentration of chloride in the blood to that in the cerebrospinal fluid in suppurative meningitis was not found altered from the normal.

4. The sugar and lactic acid ratios were markedly altered, the cerebrospinal fluid being relatively high in lactic acid content and low in sugar content

PROTOCOLS

Case 1. Unit history number 8658. White male, age 20. Admitted December 25, 1928, called the 2nd day of disease, complaining of headache, fever and occasional chills. Lumbar puncture revealed a cloudy fluid, pressure 22 mm. Hg, cells 12,500 per cubic millimeter largely polymorphonuclear, few organisms. Antimeningococcic polyvalent serum was introduced. The following day a positive Kernig's sign and distinct rigidity of the neck were noted. Under serum treatment the fluid cell count fell to as low as 300; his temperature became normal on the fifth day of disease and improvement was noted for several days thereafter. His general condition then steadily grew worse until the 21st day of disease when improvement was again noted. Vision was clear, no headache; he looked and talked better. That afternoon the fluid from the lumbar puncture ran slowly and showed 14,400 cells. On the 22nd day no fluid could be obtained; apparently there was a block. On the 23rd day, cisternal and lumbar punctures were made and the canal irrigated with saline. This was repeated the following day, and from that point recovery was rapid and continuous. Patient discharged March 12, 1929. Temperature during stay in hospital was 37.5 to 39.8°C. Spinal fluid culture showed meningococci. Our data include the early improvement and later decline, but do not include any figures during the final improvement and recovery.

Case 2. Unit history number 8881. White male, aged 41. Onset was sudden. Admitted in the afternoon of January 9, 1929, having worked as usual the previous day. Patient was unconscious. Physical examination was negative except for rigidity of neck and a temperature of 40.0°C. Spinal fluid turbid with 20,800 cells, many diplococci. Blood leucocyte count was 16,400. Patient never recovered consciousness and died following a generalized convulsion on January 11. Blood culture showed many colonies of meningococci.

Case 3. Unit history number 8322. White girl, age 13. Tonsillectomy early in December 1928. Readmitted in a stuporous condition January 12, 1929. Had

been troubled with chills and drowsiness for the past three weeks. A discharge from the nose, chronic for ten years, ceased January 8. Spinal fluid was clear, colorless, with cells 119 per cubic millimeter; 80 per cent lymphocytes, 20 per cent red blood cells, no polymorphonuclears. January 17, cells of fluid were 687. Became steadily worse and died January 18. Autopsy showed tubercles in lungs, brain, and along walls of the meningeal vessels.

Case 4. Unit history number 8715. Male, age 18. Admitted December 28, 1928 with a severe acute mastoiditis complicated by an acute nephritis and a gonococcal urethritis. Symptoms of meningitis developed January 20 and patient died January 22, 1929. Almost pure growth of hemolytic streptococci was obtained from spinal fluid and from swab of left ear. Blood leucocytes were 14,000 to 16,900 but blood culture was negative.

Case 5. Unit history number 9076. Colored laborer, age 29. Illness began on December 28, 1928 with pain in left eye and left side of head. January 2, 1929 was treated conservatively in Out-Patient Department for frontal sinusitis. January 23 convulsions began, beginning in right arm. Brought to hospital unconscious. Convulsions became generalized. Right arm and leg were paralyzed, with diminution or absence of reflexes. Lumbar punctures: pressure 4 mm. Hg, cloudy, 4,200 cells, 95 per cent polymorphonuclears. Blood sugar 254 mgm. per 100 cc., urea nitrogen 13.4. Temperature ranged from 37.4 to 40.4°C. Death occurred on January 24th, called the second day of meningeal involvement. Diagnosis at autopsy: left frontal abscess, which had extended into the ventricle to produce epidymitis and meningitis. Organism was reported as an hemolytic streptococcus.

Case 6. Unit history number 9088. White girl, age 7. Admitted to hospital January 23, 1929, called the second day of disease with classical picture of meningitis. Marked rigidity of neck, Kernig's sign and photophobia were present. Antimeningococcic serum was given intravenously and intraspinally. The fifth day, her condition was much better. The ninth day she was not improving, cough troublesome. On the twelfth day, a cisternal tap was made and from that date improvement was continuous. Discharged March 25. Temperature 37.8 to 40.4°C. during first eight days, normal later. Meningococci recognized in spinal fluid and cultured. Our data cover the decline and the beginnings of improvement.

Case 7. Unit history number 9204. White boy, age 8. Admitted January 30, 1929. Diagnosed acute appendicitis. Appendectomy was performed. Appendix found slightly enlarged. Bloody serous fluid was in peritoneal cavity. January 31, called the first day of disease, cheeks were flushed, patient apathetic, and photophobia and definite cervical rigidity were present. Heart and lungs were normal. Questionable Kernig's on left was demonstrated. Positive Babinski on

left. On lumbar puncture, 30 cc. cloudy fluid were removed, at pressure 26 mm. Hg, and containing 17,000 cells per cubic millimeter. Daily administration of antimeningococcic serum was given partly intraspinally and partly intravenously, with apparent mental improvement. The spinal fluid pressure steadily diminished, until by the seventh day when with the pressure at 12 mm. Hg, a little mental retardation was noted. Serum sickness developed. Serum was withheld until the twelfth day, with gradual disappearance of urticarial lesions and less mental apathy. On fifteenth day, he was irritable, head drawn to the left, neck rigid.

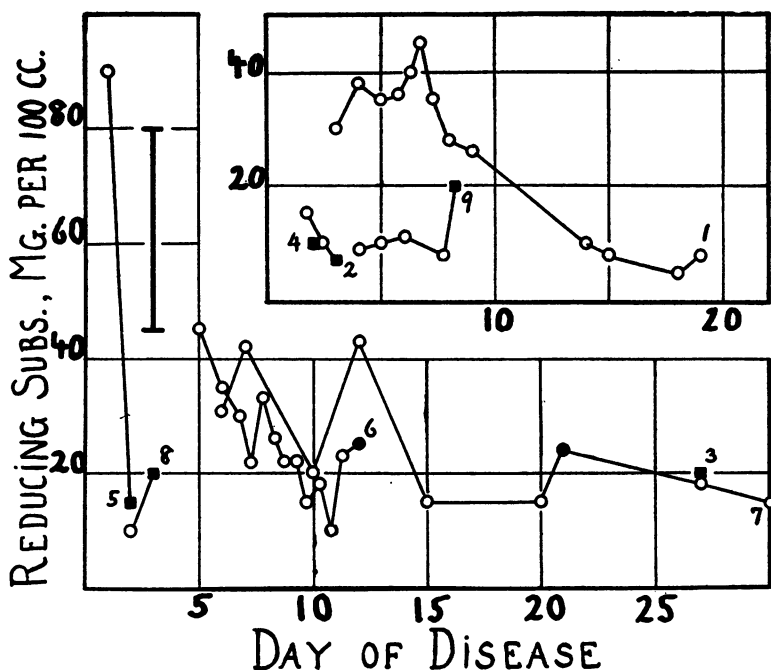


FIG. 2. REDUCING SUBSTANCE IN THE CEREBROSPINAL FLUID IN MENINGITIS

Normal range indicated by vertical line. Case numbers indicated. Other symbols as in figure 1.

fluid pressure 36 mm. Eighteenth day, pressure 56 mm. Hg; he seemed better. On the nineteenth day he asked for food. On the twenty-seventh day the canal was irrigated with saline between cisternal and lumbar punctures. Thirtieth day: pressure 20 mm. Hg, fluid bloody and ran slowly. The respiration became labored and death occurred on March 5th, the thirty-fourth day of disease. Temperature in hospital, 37.2 to 39.4°C. Spinal fluid showed pure culture of meningococcus. Our data include the recovery from serum sickness and the final decline.

Case 8. Unit history number 9303. White male, age 44. Admitted in delirious state February 6, 1929, called the second day of disease. Had sustained severe injury in left frontal region of the head. Reflexes were hyperactive. Kernig's sign positive, Babinski negative. Blood leucocytes were 29,000. He died the following day. Pneumococcus, Type IV, was cultured from blood and spinal fluid.

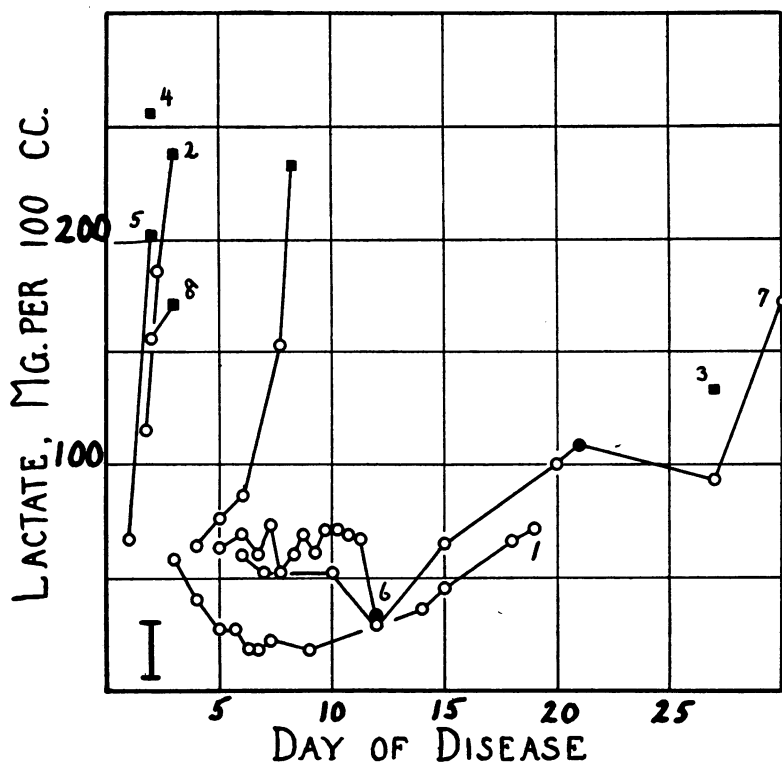


FIG. 3. LACTATE CONTENT OF CEREBROSPINAL FLUID IN MENINGITIS

Symbols as in figure 2

Case 9. Unit history number 9397. White boy, age 8. In latter part of December 1928, he had a gastro-intestinal attack and at this time the right ear commenced to discharge. February 8, ear stopped draining. Admitted February 12, 1929, called the second day of disease. Thigh was flexed on abdomen, subject irritable with rigid neck, positive Kernig's, photophobia, no tenderness over mastoid. Anterior cervical lymph nodes were palpable. Impression: meningitis, secondary to middle ear disease. Lumbar puncture: fluid turbid with 2,700 cells

chiefly polynuclear cells, many streptococci, at pressure of 12 mm. Hg. Mastoidectomy was performed on the third day; bloody pus was found in right mastoid. He became progressively worse. On the sixth day antistreptococcic serum was injected; fluid pressure 24 mm. Hg. Died February 18. Temperature in hospital was 39.4 to 40.0°C. Spinal fluid culture showed hemolytic streptococci.

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