THE REACTION OF THE SPINAL FLUID DURING CEREBRO-SPINAL FEVER

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THE reaction of the cerebro-spinal fluid during health and disease has been recently the subject of considerable investigation, and widely different results have been obtained. In large part they are to be explained by the fact that most of the investigators in this subject have taken no precautions to prevent the escape of the carbon dioxide from their fluids, before or during examination. Most of the figures so far given for the reaction of this fluid are, therefore, for this reason, too much on the alkaline side. In another communication (Parsons and Shearer, 1920) (1), it has been shown that the spinal fluid in man is slightly more acid in reaction than the blood, and that at the normal tension of carbon dioxide in the body it may have a P_h as low as 7.2-7.3.

Recent work, on the whole, has shown that in non-meningitic disease the cerebro-spinal fluid undergoes little change in reaction from that of the normal condition; even in such diseases as tubercular meningitis, lateral sclerosis, and syphilis of the cord and brain, little or no change can be demonstrated in this respect.

In epidemic cerebro-spinal fever, however, as Levinson (1916 and 1917) (2) has shown, a very marked change in reaction usually takes place. In the titration of 1 c.c. of spinal fluid in 20 c.c. distilled water with N/100 H_2SO_4 , using methyl red as an indicator, normal fluid required 2.0-2.4 c.c. of H_2SO_4 to give a neutral tint, while the fluid from a case of cerebro-spinal fever required only 0.7-1.3 c.c. acid. By the Sorensen colorimetric method he found normal fluid to have a P_h of 7.4-7.6, in cerebro-spinal fever it had usually a P_h of 7.3-7.4, and in some cases was even as low as 7.1. These determinations were made on fluid immediately after withdrawal from the body, and presumably before much of the carbon dioxide had escaped. He noted that the alkalinity of the fluid rapidly increased on standing in contact with air. Thus, in one sample, the P_h of which on withdrawal from the body was 7.4, at the end of twenty-four hours in contact with air its P_h had changed to 8.2. We have here an explanation of the high

figures given for the P_h of the cerebro-spinal fluid by many previous workers, such as Bisgaard (1914) (3), Weston (1916) (4), Hurwitz and Tranter (1916) (5), Felton, Hussey, and Bayne Jones (1917) (6), and other investigators.

Beyond the fact that he examined the fluid immediately on withdrawal from the body, Levinson (1917) (8) took no special precautions to prevent his fluid from coming in contact with air, for it was allowed to drop directly from the end of the lumbar puncture needle into the test-tube in which it was examined. We now know that in the case of blood collected in a similar manner a very considerable portion of its carbon dioxide is given off under such conditions. In the following estimations, for this reason, care was taken not to let the spinal fluid come in contact with air during collection and so to part with its carbon dioxide. It was a simple matter to attach a short length of thin rubber tubing to the end of the lumbar puncture needle, and by means of this run the spinal fluid into the bottom of a test-tube under a considerable quantity of paraffin oil. The indicator could then be added to the fluid by means of a long pipette passed down through the floating oil, so that it was never necessary to expose the fluid to the air at any time before or during examination. The fluid was received in the first place directly into a colorimetric test-tube, which was immediately placed in the comparator and the standard buffer solutions matched against it. These were prepared after the manner recommended by Clark and Lubs (1916) (7). Bromthymol blue and phenol red were used as indicators. It is worthy of note that all samples of spinal fluid examined in this way invariably gave a lower P_h value than samples of the same fluids examined after coming in contact with air in the manner adopted by Levinson (1917) (8).

In another paper it has been shown (Parsons and Shearer, 1920) (1) that with the spinal fluid we are dealing with a carbonic acid-bicarbonate system, in which the fundamental assumptions of Hasselbalch (1916) (9) hold, with reference to a solution in which the whole of the combined carbon dioxide of the solution is in the form of sodium bicarbonate, where the P_h of the fluid, the concentration of combined carbon dioxide (Bik), and the dissolved carbon dioxide (CO_2) are related by the formula:

$$P_h = pk_1 + \log. \left(\frac{Bik}{CO_2} \right)$$

where pk_1 is the magnitude involving the first dissociation constant of carbonic acid and the degree of ionization of the sodium bicarbonate in the solution. Our measurements would seem to show that the whole of the combined carbon dioxide in the cerebro-spinal fluid is in the form of sodium bicarbonate. In addition to this, there are probably present in the fluid small quantities of substances that increase its buffer efficiency above that of a sodium bicarbonate solution of the same alkali reserve.

In the following observations the alkali reserve of the spinal fluid was determined by the method recommended by McClendon (1918) (10), a N/10 HCl being used with bromcresol purple as an indicator. Three titrations were made on each fluid, the mean of the three being taken as the final reading.

The three following cases give the results of determinations on what may be considered normal fluids, using the above-described methods.

Case I. Normal fluid. Collected from a man aged 37 years, who was lumbar-punctured under suspicion of being a case of commencing cerebro-spinal fever. Fluid was clear and transparent, showing no cellular elements, and was sterile on subculture. A few hours after the lumbar puncture was made the patient made a complete recovery.

$$P_h = 7.4, \text{ alkali reserve} = 0.025 \text{ N.}$$

Case II. Normal fluid. Case of early syphilis of the cord. Fluid clear and transparent, contained no cellular elements, and was sterile on subculture.

$$P_h = 7.4, \text{ alkali reserve} = 0.031 \text{ N.}$$

Case III. Normal fluid. Tubercular meningitis in a female child aged 8 years. Fluid clear and transparent.

$$P_h = 7.3, \text{ alkali reserve} = 0.025 \text{ N.}$$

Cerebro-spinal fever cases. Case I. Cerebro-spinal fever resulting in death. Fluid turbid, and showing the presence of the meningococcus.

$$P_h = 6.9, \text{ alkali reserve} = 0.012 \text{ N.}$$

Case II. Cerebro-spinal fever case resulting in death after the second lumbar-puncture. Serum administered. Fluid very turbid, showing the presence of the meningococcus.

1st lumbar puncture, 10 c.c. serum administered.

$$P_h = 7.0, \text{ alkali reserve} = 0.013 \text{ N.}$$

2nd lumbar puncture.

$$P_h = 6.9, \text{ alkali reserve} = 0.010 \text{ N.}$$

Case III. Cerebro-spinal fever with recovery. Fluid turbid, the meningococcus present.

1st lumbar puncture. Serum administered.

$$P_h = 6.9, \text{ alkali reserve} = 0.011 \text{ N.}$$

2nd lumbar puncture. Serum administered.

$$P_h = 7.1, \text{ alkali reserve} = 0.020 \text{ N.}$$

3rd lumbar puncture. Serum administered.

$$P_h = 7.3, \text{ alkali reserve} = 0.020 \text{ N.}$$

The second puncture was made twenty-four hours after the first, while the third was made three days after the second. In distinction to these cases in which all precautions had been taken to prevent the fluid from coming in contact with air after withdrawal from the body, it is interesting to compare with them a number of estimations on fluids collected in the ordinary way where these precautions had not been observed. These fluids had been collected in contact with air, the ends of the test-tubes in which they had been collected were then sealed in a blow-pipe flame, and the tubes dispatched through the post and examined about twenty-four to thirty-six hours after they had been taken from the body. Their alkali reserve was not determined.

Normal fluids.

Case I. $P_h = 8.3$

" II. $P_h = 8.4$

" III. $P_h = 8.5$

Cerebro-spinal fever fluids.

Case IV. $P_h = 7.8$

" V. $P_h = 7.4$

" VI. $P_h = 7.4$

" VII. $P_h = 7.5$

In both the normal and the cerebro-spinal fever fluids of these cases the rise in the P_h due to the loss of the carbon dioxide is clearly shown, when these values are compared with those of the previous ones where the carbon dioxide was present. It will be noticed that, despite this, the cerebro-spinal fever fluids were more acid than the normal fluids.

Conclusions.

It has been shown that if rigorous precautions are taken to prevent the cerebro-spinal fluid on withdrawal from the body from coming in contact with air, its P_h , as determined colorimetrically, has a much higher acid value than when these precautions are not taken. Levinson's (1917) (8) discovery that in cerebro-spinal fever there is marked acidosis of the spinal fluid is confirmed. This acidosis, however, is much more marked than that found by Levinson, if the escape of all carbon dioxide from the fluid is avoided on collection. The present observations show that the P_h of the fluid in this disease may sink as low as 6.9¹ with an alkali reserve of 0.010 N. This figure fixes the hydrogen-ion concentration of the fluid well on the acid side of the real point of neutrality.²

In consideration of the great sensitivity of the respiratory centre to slight changes in the P_h of the blood, it is of considerable interest to determine the effect of the administration of alkali with serum in cases where a marked acidosis is present. Levinson's demonstration that in this disease the alkali reserve and P_h of the spinal fluid rapidly improve under serum treatment when recovery takes place is also confirmed. In fatal cases, on the other hand, serum treatment would seem to have little influence on the P_h and alkali reserve.

This peculiar acidosis of the cerebro-spinal fluid in meningococcal infection, in contradistinction to what we find in other meningeal infections, is probably due to the ease with which this germ can attack the sugar present in the spinal fluid. The meningococcus can rapidly break down glucose, forming lactic acid, and this sugar is present in a variable quantity in the cerebro-spinal fluid.

In cerebro-spinal fever it has frequently been noted that there is often a striking difference between the clinical symptoms shown by a patient suffering from this disease and the degree of infection or number of meningococci found in the spinal fluid on lumbar puncture. It is possible that in such cases the degree of acidosis is the controlling feature. If the spinal fluid contains less than the normal amount of glucose or other substance from which the meningococcus may form acid, or the particular strain of the organism setting up infection does not possess the faculty of forming the usual amount of acid, then the patient's fluid will show but slight change in reaction from the normal condition, although large

¹ The buffer used for this determination was at the conclusion of the observations measured by the gas-chain method and its P_h value confirmed.

² It should be remembered that this value was determined in the laboratory at room temperature; at body temperature this fluid would be just on the alkaline side of the absolute point of neutrality.

numbers of the meningococci may be present. The absence of any marked acidosis of the spinal fluid in such cases would account for the mild clinical symptoms. It may prove that those types of the meningococcus responsible for fatal cases are always strong acid-forming strains.

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