THE pH AND LACTIC ACID CONTENT OF THE CEREBROSPINAL FLUID

By

I. HARRIS, E. WYN JONES * AND C. N. ALDRED,
LIVERPOOL HEART HOSPITAL

Recently we have been engaged in an investigation in regard to the relationship of blood pH to that of tissue. Spinal fluid was used as tissue for the purpose of this inquiry. Our observations proved that the current teaching according to which the spinal fluid is more alkaline than blood is erroneous. We believe that our figures are reliable because we employed a method for the determination of pH which is superior to those available to previous workers in the same field.

The majority of authors give pH reading of cerebrospinal fluid in normal cases without referring at all to the acid base balance in the blood. The majority of figures recorded are rather on the high side. Weston 1 gives it as 7.9–8.3; Felton, Hussey and Bayne-Jones, 2 7.7–7.9; Vogt, 3 7.4–7.6; Shearer and Parsons, 4 7.8–7.4; Levinson, 5 7.4–7.6; Eskuchen and Lickint, 6 7.36–7.5; Beaumont and Dodds, 7 7.45.

Cameron and Gilmour 8 give expression to the current teaching by stating that the pH of the spinal fluid is slightly more alkaline than that of the blood. McQuarrie, 9 however, believes that within the limits of experimental error the pH of spinal fluid always approximates to that of the blood. Cernatescu and Mayer 10 apparently were the first to observe greater acidity in the spinal fluid than in the blood. The figures given by these authors for spinal fluid are extremely low. They use, however, the Quin-hydrone electrode—an electrode which is unreliable for fluid containing protein. 11 Previous to their work, however, Parsons and Shearer concluded that cerebrospinal fluid is more alkaline than blood only at a low carbon dioxide tension.

There is no doubt that in many instances the high pH readings were due to the employment of methods which disregarded the CO₂ loss of the fluid, and other erroneous conclusions have been arrived at owing to disregard of the temperature factor. So far as we are aware, none of these investigators used the glass electrode.

* Working as British Medical Association Scholar, 1934, and as Maurice Stern Fellow.
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METHOD

The glass electrode was employed and was adapted for the use of blood and spinal fluid. As is generally recognized, it is superior not only to the colorimetric but also to other electrometric methods. There are two main difficulties with these methods so far as cerebrospinal fluid is concerned. It is not possible to use paraffin for the purpose of avoiding CO₂ loss, since the contact of paraffin with the glass membrane fouls the electrode. The other difficulty is that of temperature. If determination is made in room temperature a correction factor has to be used which is variously given by different authors. In addition it is essential for various reasons to make determinations in the shortest possible time. In such circumstances it would be difficult to be sure that a proper equilibrium between fluid and buffer solution has been established. To avoid the difficulty the whole investigation was made in a room heated to body temperature. To avoid CO₂ loss the method used was as follows: The ordinary canula in use for cerebrospinal work was employed. Connected to it was a piece of fine rubber tubing of a narrow bore, about 3 inches in length. The distal end of the tubing was inserted in the inner chamber of the electrode. This chamber fills up with fluid and overflows, so that the fluid whose pH was taken never came in contact with air. A detailed account of this method will be found in the Journal of Physiology (1934, vol. 81, p. 197).

Twelve cases were investigated altogether. They were all in-patients of the Heart Hospital. The majority of these patients did not exhibit any evidence of heart failure, and from the point of view of composition of the blood and the spinal fluid they must be considered as normal cases. There were, however, cases which exhibited definite evidence of heart failure. One case suffered from pronounced hyperthyroidism. These patients had been mostly resting in bed for a considerable time. However, a few minutes before the specimen of the spinal fluid was taken they were subjected to a slight exertion. They were taken from the wards by a wheel-chair and transported by means of a lift to two flights of stairs below, where they had to walk a few yards to a couch. It seems unlikely that there could have been an appreciable rise in the lactic acid of blood as a result of this exertion, so far as the great majority of cases were concerned.

Table I shows that only once did the pH exceed 7.4—all the others were below this figure. It will also be seen that there is a definite relation between the pH of spinal fluid and that of blood, and that the latter is more on the alkaline side than the former. Incidentally, it shows that it is impossible to establish absolute values for pH of spinal fluid unless the acid balance of the blood is also determined. As is to be expected, there is no relationship between lactic acid and pH reading.

An explanation why the cerebrospinal fluid is more acid than blood may be found in the difference of behaviour of CO₂ in these two fluids.
Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>pH Blood</th>
<th>pH C.S.F.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>20</td>
<td>7.45</td>
<td>7.41</td>
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<td>2</td>
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<tr>
<td>4</td>
<td>M</td>
<td>53</td>
<td>7.42</td>
<td>7.38</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>39</td>
<td>7.39</td>
<td>7.37</td>
</tr>
<tr>
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<td>M</td>
<td>47</td>
<td>7.44</td>
<td>7.37</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>67</td>
<td>7.46</td>
<td>7.39</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>69</td>
<td>7.42</td>
<td>7.34</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>23</td>
<td>7.43</td>
<td>7.36</td>
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<td>10</td>
<td>F</td>
<td>54</td>
<td>7.40</td>
<td>7.30</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>55</td>
<td>7.42</td>
<td>7.36</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>47</td>
<td>7.42</td>
<td>7.37</td>
</tr>
</tbody>
</table>

Average readings: 7.42  7.36

Parsons and Shearer have shown that 'the reaction changes occurring in spinal fluid with increasing carbon dioxide tension are much more pronounced than those occurring in normal blood.'

LACTIC ACID

It appears again that the findings of different investigators in regard to lactic acid in cerebrospinal fluid are variable. Greenfield and Carmichael 12 state that lactic acid is normally absent from cerebrospinal fluid, or present only in minute traces. Cameron and Gilmour, in discussing the relative concentration of the constituents of human blood plasma and cerebrospinal fluid, do not mention the presence of lactic acid. De Sanctis, Killian and García 13 state that the normal lactic acid content of blood is 16 to 22 mg. per cent., and that the fluid figure is about 75 per cent. of that of blood.

Wittgenstein and Gaedertz 14 investigated the relations between blood lactic acid and that of spinal fluid in animals and man, and they found that at rest the lactic acid contents of the blood and cerebrospinal fluid were approximately equal—plasma at rest, 15 to 18 mg. per cent., cerebrospinal fluid at rest, 13 to 16 mg. per cent. In cases where the lactic acid is low, blood plasma and cerebrospinal fluid equal each other. Where lactic acid increases in the blood it also increases in the spinal fluid.

Zweifel and Scheller 15 state that lactic acid disappears more slowly in the cerebrospinal fluid than in the blood, and they also assume that the acid rises more slowly in the fluid.
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METHOD

The estimation of lactic acid in blood and fluid was carried out by the iodometric method introduced by Clausen[16] and modified by Friedemann, Cotonio and Shaffer,[17] and later by Friedemann and Kendall.[18] The principle of the method is the formation of acetaldehyde from lactic acid when the latter is oxidised by heating with potassium permanganate. The aldehyde is collected, by a process of aeration, into sodium bisulphite solution, and titrated by Clausen’s method.

The protein was removed from the blood by the Folin-Wu method, while sugar and other interfering substances were precipitated by means of the Van Slyke[19] copper-lime treatment. In the case of spinal fluid, protein precipitation was carried out according to the modification of the Folin-Wu technique suggested by Beaumont and Dodds,[20] while the sugar was dealt with as in the case of blood. Application of the old and new protein precipitation methods to spinal fluid showed no significant difference as far as the lactic acid content is concerned.

All the estimations were commenced almost immediately after the removal of the blood or fluid, so as to ensure that no extra lactic acid was

TABLE II

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Lactic Acid</th>
<th>Diagnosis</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Blood</td>
<td>C.S.F.</td>
</tr>
<tr>
<td>1</td>
<td>M</td>
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<td>37</td>
<td>Not done</td>
</tr>
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<td>M</td>
<td>50</td>
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</tr>
<tr>
<td>4</td>
<td>M</td>
<td>53</td>
<td>37</td>
<td>22</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>39</td>
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<td>25-5</td>
</tr>
<tr>
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<tr>
<td>8</td>
<td>F</td>
<td>69</td>
<td>59</td>
<td>45</td>
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<tr>
<td>9</td>
<td>F</td>
<td>23</td>
<td>31-5</td>
<td>31-5</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>54</td>
<td>26</td>
<td>24</td>
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<tr>
<td>11</td>
<td>M</td>
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<tr>
<td>12</td>
<td>F</td>
<td>47</td>
<td>33</td>
<td>28</td>
</tr>
</tbody>
</table>

Average readings: 34-5 31-2
formed by autoglycolysis of the sugar present. Double estimations were carried out on nearly every specimen of blood and fluid.

Here again (Table II), it is clear that the lactic acid content of the spinal fluid stands in definite relation to that of the blood. It must be kept in mind in analysing the table that the method of determining lactic acid has a maximum margin of error of, say, +5 per cent. —5 per cent.

In six cases out of eleven the lactic acid content of the spinal fluid was lower than that of blood; in three cases it was higher. In the latter the difference in the lactic acid content of the two fluids was so small as to come within the limits of the margin of experimental error. On the other hand, in some instances the lactic acid content of the fluid was so definitely below that of the blood that the difference between the two fluids in this respect cannot be accounted for by any experimental error. We may safely assume therefore that there are cases where the lactic acid content in the fluid is definitely lower than that in the blood. We may assume that if the patient is completely at rest for a considerable time an equilibrium between these two fluids will approximately be established. However, if lactic acid is being actively formed in the organism one of two things may happen. As long as the lactic acid blood level continues to rise this level may be higher than that of the fluid, because the latter can only increase its lactic acid store by a process of relatively slow diffusion from the blood. On the other hand, lactic acid disappears from the blood at a much quicker rate than does the acid from the spinal fluid. It is therefore possible that immediately after exercise there may be a higher percentage of lactic acid in the spinal fluid than in the blood. The difference in level between the lactic acid content of blood and spinal fluid in the case of exophthalmic heart failure is easily explained. We know that in such cases the oxygen consumption is very high and the oxygen ‘debt’ also high, which means a high level of blood lactic acid. Moreover, as this patient suffered from pronounced heart failure it is likely that a slight exertion was sufficient to raise the lactic acid level to a considerable degree. For reasons stated before, the lactic acid level in the spinal fluid would rise in such circumstances but slowly. However, the pronounced difference of lactic acid content of blood and fluid in the case of the patient suffering from partial heart block is less easily explicable on these grounds. It is true the patient had suffered from degenerative myocarditis, but the lactic acid in the blood is apparently within normal limits.

The figures also suggest that in heart failure the lactic acid level in blood and fluid is raised, as was to be expected.

CONCLUSIONS

(1) The pH of the cerebrospinal fluid is lower than that of blood.
(2) The lactic acid contents of cerebrospinal fluid and blood are approximately the same, provided sufficient time is allowed for an equilibrium between the two fluids to be established.
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We wish to express our indebtedness to Mr. Shutt, Lecturer in Chemistry in the University of Liverpool, for valuable help given in this investigation.

REFERENCES

2. Felton, Hussey and Bayne-Jones, ibid., 1917, 19.
7. Beaumont and Dodds, Recent Advances in Medicine, 1934, 370.
11. Personal communication by Mr. Shutt.

APPENDIX

CASES—BRIEF SUMMARY

(1) McMerryman. Subternal pain and flatulence with palpitation—6 months. Aortic regurgitation and mitral stenosis. B.P. 140/75. No congestive failure.


(9) HANNAKIN. Exhaustion, dyspnoea and swelling of feet—6 months. Auricular fibrillation. Rate 90. B.P. 125/760. No gross valvular lesion. Slight œdema of legs. Liver enlarged 2 inches below costal margin.


(12) CULLIGAN. Giddiness and precordial pain of anginal type—4 years. Normal rhythm. Rate 74. B.P. 200/100. No gross arteriosclerosis. No congestive failure.