CEREBROSPINAL FLUID AND SERUM.

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Cerebrospinal fluid has been analyzed chemically by a number of investigators (1). These have confined themselves usually to the quantitative estimation of well known organic constituents or of the inorganic constituents as a whole. Mestrezat (2) determined the concentration of the individual inorganic elements in cerebrospinal fluids, using for the purpose standard gravimetric and volumetric methods. For these methods large amounts of cerebrospinal fluid were required. It was therefore necessary to pool the fluid from several individuals. Recent improvements in analytical technique have made possible the accurate quantitative estimation of the concentration of all the well known elements (sodium, potassium, calcium, chlorine, phosphorus, and bicarbonate), in such a volume of cerebrospinal fluid as may readily be obtained from a single patient. Depisch and Richter-Quittner (3) in a very elaborate study determined the concentration of a number of substances in the cerebrospinal fluid of normal individuals as well as in that of individuals suffering from various diseases. They also simultaneously determined the concentration of some of the substances in the serum of the same patients. The variation in the concentration of certain of the inorganic elements as found by these workers is so great as to justify serious scepticism as to the accuracy of their determinations. It is now well known from studies on serum that the concentration of the inorganic constituents of serum is remarkably constant during health and varies but little in disease. Where
definite variations are found they are usually associated with definite clinical symptoms. It has been conclusively shown that the calcium concentration of the serum of the normal adult is constant, varying only within the narrow limits of 9.5 and 10.5 mg. per 100 cc. of serum. In no condition is the calcium concentration of serum increased above the normal level. Depisch and Richter-Quittner report 14.84 mg. per 100 cc. as the calcium concentration of the serum of a normal adult. For pathological sera values ranging from 19.6 to 53.53 mg. per 100 cc. of serum are given. It is quite impossible to explain such results.

The work which furnishes the basis of this report was undertaken to determine:

1. The concentration of the cations (sodium, potassium, and calcium) and the anions (chlorine, phosphate, and bicarbonate) in normal cerebrospinal fluid.

2. The changes in the concentration of these elements with disease.

3. By analyzing the serum and cerebrospinal fluid obtained simultaneously from the same patient we attempted to determine the nature of the equilibrium that prevails between these two body fluids, the former with its high protein content, the latter protein-free.

We have studied the cerebrospinal fluid and serum of thirteen patients. Three of these patients were normal. The others were suffering either from some general constitutional disease or from some specific involvement of the central nervous system.

Method.

Lumbar and venous punctures were performed in the usual manner. Four of our adult patients were in the sitting position, the remainder were lying down during the procedure.

Cerebrospinal fluids and sera were examined at once. Only fluids free of blood were examined. Hemolyzed sera were rejected.

Sodium, calcium, and potassium were determined by the methods devised by Kramer and Tisdall (4). Phosphorus determinations were made by employing the Brigg's modification (5) of the Bell-Doisy method. We used Whitehorn's method (6) in our chlorine and Van Slyke and Cullen's method (7) for our CO₂ determinations.
TABLE I.*

Concentration of the Inorganic Constituents of Blood Serum and Spinal Fluid of Normal Individuals.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Ca Serum</th>
<th>Ca Spinal fluid</th>
<th>P Serum</th>
<th>P Spinal fluid</th>
<th>Cl (NaCl) Serum</th>
<th>Cl (NaCl) Spinal fluid</th>
<th>K Serum</th>
<th>K Spinal fluid</th>
<th>Na Serum</th>
<th>Na Spinal fluid</th>
<th>CO₂ Serum</th>
<th>CO₂ Spinal fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. B.</td>
<td>Male</td>
<td>60</td>
<td>Normal</td>
<td>10.5</td>
<td>5.0</td>
<td>3.2</td>
<td>1.8</td>
<td>570</td>
<td>720</td>
<td>20.0</td>
<td>12.8</td>
<td>340</td>
<td>370</td>
<td>59</td>
<td>62</td>
</tr>
<tr>
<td>A. T.</td>
<td>&quot;</td>
<td>29</td>
<td>&quot;</td>
<td>10.5</td>
<td>5.0</td>
<td>3.2</td>
<td>1.1</td>
<td>613</td>
<td>710</td>
<td>21.0</td>
<td>10.0</td>
<td>340</td>
<td>370</td>
<td>59</td>
<td>62</td>
</tr>
<tr>
<td>A. B.</td>
<td>&quot;</td>
<td>20</td>
<td>&quot;</td>
<td>10.6</td>
<td>4.4</td>
<td>2.3</td>
<td>0.8</td>
<td>574</td>
<td>235</td>
<td>24.2</td>
<td>16.6</td>
<td>336</td>
<td>336</td>
<td>60.5</td>
<td>57</td>
</tr>
</tbody>
</table>

* The results, except those for CO₂, are expressed in mg. per 100 cc. of fluid.
### TABLE II.

Concentration of the Inorganic Constituents of Blood Serum and Spinal Fluid in Individuals Suffering from Various Diseases.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Ca Serum</th>
<th>Ca Spinal</th>
<th>P Serum</th>
<th>P Spinal</th>
<th>Cl (NaCl) Serum</th>
<th>Cl (NaCl) Spinal</th>
<th>K Serum</th>
<th>K Spinal</th>
<th>Na Serum</th>
<th>Na Spinal</th>
<th>CO₂ Serum</th>
<th>CO₂ Spinal</th>
</tr>
</thead>
<tbody>
<tr>
<td>R. S.</td>
<td>Male.</td>
<td>8</td>
<td>Acute nephritis.</td>
<td>8.8</td>
<td>5.4</td>
<td>6.16</td>
<td>1.7</td>
<td>614</td>
<td>674</td>
<td>300</td>
<td>298</td>
<td>50</td>
<td>47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. B.</td>
<td>Female.</td>
<td>36</td>
<td>Cerebrospinal lues.</td>
<td>9.9</td>
<td>5.3</td>
<td>4.0</td>
<td>1.0</td>
<td>561</td>
<td>709</td>
<td>296</td>
<td>310</td>
<td>57</td>
<td>55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. J.</td>
<td>Male.</td>
<td>33</td>
<td>&quot;</td>
<td>10.5</td>
<td>4.6</td>
<td>2.8</td>
<td>1.4</td>
<td>591</td>
<td>726</td>
<td>298</td>
<td>305</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. W.</td>
<td>&quot;</td>
<td>15 mos.</td>
<td>Tuberculous meningitis.</td>
<td>8.2</td>
<td>4.9</td>
<td>2.5</td>
<td>1.1</td>
<td>504</td>
<td>701</td>
<td>19.2</td>
<td>12.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L. D.</td>
<td>&quot;</td>
<td>40</td>
<td>Cerebrospinal lues.</td>
<td>10.2</td>
<td>4.6</td>
<td>3.1</td>
<td>1.0</td>
<td>570</td>
<td>709</td>
<td>20.5</td>
<td>15.8</td>
<td>58.6</td>
<td>60.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>W. B.</td>
<td>&quot;</td>
<td>37</td>
<td>Paresis.</td>
<td>9.4</td>
<td>4.6</td>
<td>3.6</td>
<td>1.1</td>
<td>556</td>
<td>705</td>
<td>23.6</td>
<td>16.3</td>
<td>57.0</td>
<td>58.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. H.</td>
<td>&quot;</td>
<td>65</td>
<td>&quot;</td>
<td>10.0</td>
<td>5.0</td>
<td>2.8</td>
<td>1.9</td>
<td>556</td>
<td>705</td>
<td>23.0</td>
<td>17.0</td>
<td>47.0</td>
<td>50.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J. B.</td>
<td>&quot;</td>
<td>36</td>
<td>Cerebrospinal lues.</td>
<td>10.0</td>
<td>5.0</td>
<td>3.0</td>
<td>1.8</td>
<td>597</td>
<td>742</td>
<td>19.8</td>
<td>13.6</td>
<td>354</td>
<td>360</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N. R.</td>
<td>&quot;</td>
<td>10</td>
<td>Paresis ?</td>
<td>10.0</td>
<td>5.0</td>
<td>2.2</td>
<td>1.5</td>
<td>612</td>
<td>723</td>
<td>19.1</td>
<td>12.0</td>
<td>327</td>
<td>359</td>
<td></td>
<td></td>
</tr>
<tr>
<td>W.</td>
<td>&quot;</td>
<td>13</td>
<td>Epilepsy.</td>
<td>10.0</td>
<td>5.1</td>
<td>4.1</td>
<td>1.3</td>
<td>550</td>
<td>752</td>
<td>19.0</td>
<td>12.9</td>
<td>337</td>
<td>345</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The results, except those for CO₂, are expressed in mg. per 100 cc. of fluid.
Table I gives the results of determinations made upon the serum and spinal fluid of three normal individuals. The calcium concentration of the spinal fluid is found to be 40 to 50 per cent of that of the serum of the same individual or 4.4 to 5.0 mg. per 100 cc. of spinal fluid. These figures agree very well with those obtained by Neuhausen and Pincus for the free calcium of serum. The inorganic phosphorus concentration of spinal fluid is much less than that of the serum of the same individual. The chlorine concentration, however, is much higher in cerebrospinal fluid than in serum. This is a regular finding not only with normal but also with pathological fluids. The potassium concentration is always less in spinal fluid than in the serum, varying from 12.8 to 16.6 mg. per 100 cc. of cerebrospinal fluid as compared with 20.0 to 24.2 mg. of the same element in serum. We are unable to explain the high results obtained by Depisch and Richter-Quittner who found as much as 72 mg. of potassium per 100 cc. of normal serum. In an unpublished report Kramer and Wilkins have shown that the potassium concentration of normal serum varies only from 18 to 24 mg. per 100 cc. The sodium concentration of spinal fluid is essentially the same as that of serum. The same applies to the bicarbonate concentration.

Table II contains the results of analyses of the blood serum and spinal fluid of ten patients suffering from various diseases. The calcium concentration of the spinal fluid remains remarkably constant even though that of the serum may at times be somewhat decreased. The inorganic phosphorus of the spinal fluid is regularly very low, quite independently of the concentration of the same element in the serum. As with normal individuals so we find here that the chlorine concentration of spinal fluid is much higher than that of the serum of the same patient. The relationship between the potassium, sodium, and bicarbonate of spinal fluid and serum is the same as in the normal individual.

In Table III the results for normal fluids are summarized.

DISCUSSION.

We have no desire to enter here into a discussion as to the nature of cerebrospinal fluid or the mechanism of its formation. These subjects have been reviewed at length by Dandy and Blackfan (8), by Weed and Cushing (9), and more recently by Becht (10).
Cerebrospinal fluid is considered by some to be a secretion, whereas others look upon it as being an ultrafiltrate or a dialysate. Normal cerebrospinal fluid contains the same electrolytes as serum, but practically no protein whereas serum contains 7 to 9 per cent of protein. The proteins of serum do not diffuse through a collodion membrane. Donnan (11) has shown that when a membrane

TABLE III.
Average Concentration of the Anions and Cations in Normal Serum and Spinal Fluid.

<table>
<thead>
<tr>
<th>Material</th>
<th>Ca</th>
<th>P</th>
<th>Cl (NaCl)</th>
<th>K</th>
<th>Na</th>
<th>CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>9.6</td>
<td>2.9</td>
<td>578</td>
<td>20.9</td>
<td>328</td>
<td>55.6*</td>
</tr>
<tr>
<td>(Adults.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Children.)</td>
<td>4.6</td>
<td>1.3</td>
<td>712</td>
<td>14.7</td>
<td>351</td>
<td>55.7</td>
</tr>
</tbody>
</table>
| * Concentration expressed in cc. of CO₂ gas per 100 cc. of serum at 0°C. and 760 mm. of Hg.

TABLE IV.
Concentrations of Anions and Cations in Cerebrospinal Fluid and Serum Expressed in Gram Molecules per Liter.

<table>
<thead>
<tr>
<th>Material</th>
<th>Sodium</th>
<th>Potassium</th>
<th>Calcium</th>
<th>Chlorine</th>
<th>Bicarbonate</th>
<th>Phosphate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>0.143</td>
<td>0.005</td>
<td>0.0025</td>
<td>0.102</td>
<td>0.032</td>
<td>0.001</td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>0.143</td>
<td>0.004</td>
<td>0.0012</td>
<td>0.124</td>
<td>0.032</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

Total concentration of cations = 0.163 molal

Total concentration of anions = 0.147 molal

Product = 0.024 molal

* Note.—If we assume that only 92 per cent of the serum is water and calculate the concentrations accordingly the agreement is much better.

Concentration of cations in serum = 0.163 molal

Concentration of anions = 0.147 molal

Product = 0.024 molal

separates two solutions of electrolytes, one of which contains one ion which cannot diffuse through the membrane while all the other ions can diffuse through the membrane, the result will be an unequal distribution of the diffusible ions on the opposite
sides of the membrane. At equilibrium the products of the concentration of each pair of oppositely charged diffusible ions are the same on the opposite sides of the membrane.

In Table IV are given the molal concentrations of the various anions and cations in serum and cerebrospinal fluid. When the figures for the concentrations of the oppositely charged ions in each fluid are multiplied by each other the results are approximately the same both for serum and cerebrospinal fluid. We are aware of the fact that no account has been taken of differences in ionization of different salts, but sodium and chlorine which constitute the major part of the electrolytes are both practically completely ionized in blood serum and very likely also in cerebrospinal fluid. In a study of the physical and chemical properties of serum, and serous effusions Loeb, Atehley, and Palmer (12) found the potassium content of serum to be always higher than that of the effusion. The chlorine content of the serous fluid is always higher than that of the serum, while the sodium and bicarbonate are equally distributed. When the serum and the effusion were dialyzed against each other the equilibrium between the electrolytes remained unaffected.

Table I shows that a similar equilibrium exists between serum and cerebrospinal fluid. Here also the chlorine concentration of the spinal fluid (protein-free) is higher than that of the serum, the sodium and bicarbonate concentrations are the same, whereas the potassium concentration is lower in the spinal fluid than in the serum. Some determinations of the calcium of serum and serous effusions have shown the calcium concentration to be about the same in both fluids, whereas here we find the calcium concentration of spinal fluid to be only about 50 per cent of that of the serum. However, serous effusions always contain a variable amount of protein, whereas normal spinal fluid is practically protein-free.

CONCLUSIONS.

The concentration of the various cations and anions in spinal fluid and serum of the same patient has been determined.

A study of the equilibrium between the concentration of these elements in the serum and spinal fluid suggests that the Donnan membrane equilibrium plays an important part.

1 Since practically all the ions are univalent, the gram equivalent and molal concentrations are the same.
We take pleasure in expressing our thanks to Dr. Franklin of Bay View Hospital for his assistance in securing much of the material for study.

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COMPARATIVE STUDY OF THE CONCENTRATION OF VARIOUS ANIONS AND CATIONS IN CEREBROSPINAL FLUID AND SERUM
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