# DENSITIES OF CEREBROSPINAL FLUID OF HUMAN BEINGS * †

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MANY anesthesiologists control the level of spinal analgesia with the aid of baricity, that is, the degree of heaviness or lightness of the spinal anesthetic solution compared to that of the cerebrospinal fluid of the patient. The term, "baric gravity," has been introduced in order to quantitate this ratio, and the densities of certain spinal anesthetic solutions at 37 C. have already been reported (1). In this paper the remaining fact is supplied necessary to determine the baric gravity of these solutions, namely, the mean density of cerebrospinal fluid of man at 37 C.

Density is preferred to specific gravity, because density is more fundamental and requires only one temperature report, that of the measured solution. The reference water temperature, so frequently omitted in specific gravity reports, need only be the concern of the original investigator.

The density of a theoretically dilute solution, in which the volume of the solutes is nil, is the sum of the density of the solvent and the concentrations of the solutes, all expressed in the same units. Human cerebrospinal fluid is not such a dilute solution, however, and its density is proportional only to the sum of the concentrations of its constituents. Table 1 lists the normal range of concentrations of the contents of cerebrospinal fluid, except the variable number of lymphocytes.

As can be seen in table 1, water, chlorine, sodium and carbon dioxide affect the density of cerebrospinal fluid to the fourth or less significant figure; § whereas protein (albumin and globulin) affects it only to the fifth. Under abnormal conditions, the fourth significant figure can be more affected by clinical variations in urea (2b), in glucose (2b), and in the temperature of measurement (as it affects the density of water, table 2), than by protein. Clinically, specific gravities of cerebrospinal fluid do not correlate with protein concentrations (4) in the manner that

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§ Significant figures are arbitrarily numbered: 1.23456.

TABLE 1

RANGE OF CHEMICAL COMPOSITION (GRAMS PER CUBIC CENTIMETER) OF LUMBAR CEREBROSPINAL FLUID OF HUMAN BEINGS *
[MODIFIED FROM LEVINSON (2) AND KOLMER (3)]

| | Low | | High |
|---|---|---|---|
| Water | 0.98300 | to | 0.99660 |
| Chlorine (as $Cl^-$) | 0.00364 | | 0.00455 |
| Sodium | 0.00323 | | 0.00382 |
| Carbon dioxide | 0.00110 | | 0.00124 |
| Potassium | 0.00011 | | 0.00020 |
| Other inorganic substances | 0.00008 | | 0.00023 |
| Glucose | 0.00050 | | 0.00090 |
| Albumin | 0.00012 | | 0.00036 |
| Globulin | 0.00002 | | 0.00006 |
| Urea | 0.00013 | | 0.00041 |
| Lactic acid | 0.00008 | | 0.00015 |
| Other organic substances | 0.00006 | | 0.00014 |
| Total (Gm./cc.) | 0.99207 | to | 1.00866 |

* Temperatures unknown.

specific gravities and protein concentrations of plasma do (5). Thus in cerebrospinal fluid the role of protein is obscured by other constituents.

The theory has been suggested that the lumbar cerebrospinal fluid is denser than the cisternal or ventricular fluids because the lumbar fluid contains more albumin than the latter two (7, 8, 9). However, the other constituents, especially glucose, were neglected, and lumbar fluid has been quantitatively reported to four significant figures to have the same specific gravity as ventricular fluid (10). More sensitive determinations might alter this precise equality without effecting a statistical difference.

In determining the density of cerebrospinal fluid of man at 37 C. two methods are used; one involves the determination of a thermal coefficient of density for cerebrospinal fluid and applying it to densities at 25 C.; the other involves direct measurements at 37 C.

## REVIEW OF LITERATURE

In published reports, specific gravities range from 1.001 to 1.010 (2c), but very few articles contain the two required temperature reports. The few that we could find were converted, when necessary, to density, and are reviewed in table 3.

TABLE 2

EFFECT OF TEMPERATURE ON THE DENSITY OF WATER

| Degrees, C. | Density (6), Gm./ml. | Difference, Gm./ml. |
|---|---|---|
| 4 | 1.0000 | |
| | | 0.0009 |
| 15 | 0.9991 | |
| | | 0.0020 |
| 25 | 0.9971 | |
| | | 0.0037 |
| 37 | 0.9934 | |

Stanford (4), cited by Macintosh (12), measured densities of cerebrospinal fluid to six significant figures with his 5 milliliter pyknometer (13). Unfortunately his results cannot be regarded as "normal" because most of his subjects were in institutions for chronic neurological disorders, and a significant number died while under study. A distribution curve of his results is skewed and does not lend itself to statistical analysis.

Using specific gravity beads in 2 ml. of cerebrospinal fluid, Etherington-Wilson (11) reported that the specific gravity at normal body temperature was constant between 1.003 and 1.004, closer to 1.003, and was identical within the age range of 2 to 90 years. Except for elevation of the sugar content, other pathologic changes, including involvement of the nervous system, did not consistently alter the values. These values, but not the conclusions, were immediately contested (7, 14),

TABLE 3

REVIEW OF DENSITIES OF CEREBROSPINAL FLUID OF HUMAN BEINGS

| | Density, 25 C., Gm./ml. | Density, 37 C., Gm./ml. | Difference, Gm./ml. |
|---|---|---|---|
| Stanford (4): 61 cases<br>All severe disorders of the nervous system | Mean: 1.00473<br>Range: 1.00432 to 1.00663 | | |
| Etherington-Wilson (11): 314 cases*<br>62% healthy, 38% ill | 1.005 | 1.002 | 0.003 |
| Wolman *et al.* (9): 150 cases*<br>All healthy | 1.0040<br>±0.0004** | | |
| Authors (cf. table 5): 8 cases<br>All mild disorders of the nervous system | 1.0040<br>±0.0004** | 1.0010<br>±0.0003** | 0.0031<br>±0.0003** |

* Converted from published specific gravities.
** Standard deviation of the mean.
"Healthy" denotes neither metabolic nor nervous system disorders.

without rebuttal, and Hewer (7) offered the information that the beads were designed to operate in a medium of 15 C. The values in table 3 are derived by conversion from the specific gravities T/15 C. and by linear interpolation necessitated by Etherington-Wilson's use of the Fahrenheit scale. At present the tabulated values for 25 and 37 C. are not considered reliable because of the aforementioned controversy; however, the tabulated difference in densities can be mathematically demonstrated to be reliable regardless of this controversy. Computations of the density difference, using either Etherington-Wilson's original data or Hewer's correction factor, yield the identical value.

Wolman *et al.* (9), measured the specific gravities of men aged 17 to 25 years with neither metabolic nor nervous system disorders, but who were to undergo surgical procedures. Their gradient, or falling-drop, method required less than 1 ml. of cerebrospinal fluid and yielded results to five significant figures. Since the distribution was normal, their results were analyzed statistically (15) and converted to density.

## METHOD

The technique is that previously described (1) with the addition of a 25 C. water bath accurate to plus or minus 0.5 C. The float of the Westphal balance reposes in the cerebrospinal fluid which is contained in a 25 by 100 mm. culture tube (4.9 sq. cm. surface area). This balance has the advantage of being easily calibrated for any temperature and was, indeed, recalibrated for every change of temperature, but it has the disadvantage of requiring 33 ml. of cerebrospinal fluid. Such large specimens were obtained from patients undergoing pneumoencephalography.‖ The maximal amount of cerebrospinal fluid was withdrawn

TABLE 4

CERTAIN EFFECTS OF EXPOSURE UPON CEREBROSPINAL FLUID OF HUMAN BEINGS

| Exposure Time, hours | Total Increase in pH (2) | Carbon Dioxide Content (2), mg. % | Total Increase in Density (25 C.), Gm./ml. |
|---|---|---|---|
| 0.0 | — | 110 to 124 | — |
| 0.5 | 0.1 | — | 0.0001 |
| 1 | 0.2 | — | 0.0002 |
| 2 | 0.5 | — | 0.0002 |
| 5 to 6 | — | 98 to 106 | 0.0000 |
| 12 | 0.8 to 1.1 | — | — |
| 24 | No further change | — | 0.0002 |

under mineral oil (liquid petrolatum, U.S.P.), and after gentle agitation, aliquots were withdrawn for measurement. The chemical determinations were begun two to four hours after collection.

## PRELIMINARY STUDY

It is recognized that upon exposure to air the carbon dioxide of cerebrospinal fluid will volatilize, representing a decrease in acidity, mass and density (table 4). In addition, water evaporates, representing a decrease in volume and an increase in density. The net density change on exposure is primarily the resultant of the rates of these two opposing reactions.

A 35 ml. aliquot of one specimen, collected under mineral oil, was routinely arranged and exposed for twenty-four hours at 24 to 25 C. with density variations reported in table 4. Approximately 5 ml. of water, 14 per cent, evaporated during this time. Another aliquot from the same specimen was retained under mineral oil for twenty-four hours and was found to have undergone no change in density.

‖ We thank Drs. M. E. Jones, E. J. Morrissey, W. A. Newsom, and H. V. Petzold for collecting the specimens.

Hence, in our primary study all specimens were maintained under mineral oil until measured within three hours of collection.

## RESULTS

Our measurements are recorded in table 5 and summarized in table 3. All subjects were outpatients referred for diagnosis or follow-up, suffered relatively mild neurological disorders, and were engaged in normal activities. The only metabolic disturbance occurred in case 4, a diabetic not included in the statistics, whose densities were the highest.

Our value at 25 C., 1.0040 ± 0.0004 Gm. per milliliter confirms that derived from Wolman *et al.*, and our thermal coefficient of density, 0.0031 gm. per milliliter, is compatible with that derived from Etherington-Wilson's data. Hence, our measured density at 37 C., 1.0010 ± 0.0003 Gm. per milliliter seems substantiated, although a larger series might yield a standard deviation of the mean approximating that at 25 C., namely, 0.0004 Gm. per milliliter.

TABLE 5

AUTHORS' DENSITIES OF CEREBROSPINAL FLUID OF HUMAN BEINGS

| Case | Age, Years and Sex | Diagnosis | Cerebrospinal Fluid, Gm. per ml. | | | Sp. Gr., 25/25 C. | Density, 25 C., Gm./ml. | Sp. Gr., 37/37 C. | Density, 37 C., Gm./ml. | Difference in Gm./ml. |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Protein | Glucose | Chlorine | | | | | |
| 1 | Adult M | Posttraumatic convulsions | 0.00031 | | | 1.0063 | 1.0034 | 1.0072 | 1.0006 | 0.0028 |
| 2 | 3 M | Erythroblastotic cerebral spastic | 0.00018 | | | 1.0068 | 1.0039 | 1.0079 | 1.0012 | 0.0027 |
| 3 | 42 M | Mild cerebral spastic | 0.00042 | | | 1.0076 | 1.0047 | 1.0080 | 1.0013 | 0.0034 |
| 4* | 9 F | Diabetes mellitus with convulsions | 0.00050 | 0.00156 | 0.00462 | 1.0080 | 1.0050 | 1.0080 | 1.0013 | 0.0037 |
| 5 | 36 M | Convulsive disorder | 0.00022 | 0.00071 | 0.00447 | 1.0071 | 1.0042 | 1.0070 | 1.0012 | 0.0030 |
| 6 | 56 M | Convulsive disorder | 0.00033 | 0.00074 | 0.00437 | 1.0073 | 1.0044 | 1.0077 | 1.0010 | 0.0034 |
| 7 | 20 F | Focal cortical atrophy | 0.00038 | 0.00065 | 0.00437 | 1.0071 | 1.0042 | 1.0079 | 1.0012 | 0.0030 |
| 8 | 32 M | Convulsive disorder | 0.00024 | 0.00088 | 0.00430 | 1.0068 | 1.0039 | 1.0073 | 1.0007 | 0.0032 |
| 9 | 32 M | Convulsive disorder | 0.00024 | 0.00077 | 0.00422 | 1.0065 | 1.0036 | 1.0073 | 1.0007 | 0.0029 |
| | | Mean ± standard deviation of small samples (15) | | | | | $1.0040_4$ ±$.0004_3$ | | $1.0009_8$ ±$.0002_8$ | $0.0030_1$ ±$.0002_4$ |

* Not included in statistics.

## COMMENT

Since 99.73 per cent of all values for cerebrospinal fluid lies within plus or minus three standard deviations, we believe that those anesthesiologists who desire to utilize the effects of baricity upon normal patients can safely administer hyperbaric solutions whose densities at 37 C. are above 1.0022 Gm. per milliliter and hypobaric solutions below 0.9998 Gm. per milliliter.

Two possible criticisms of our method have been thoroughly considered: our technique required large volumes of cerebrospinal fluid, and our subjects were not strictly normal. Reference has already been made to the facts that the densities of lumbar and ventricular fluids do not vary significantly (10) and that even severe disease of the nervous system does not consistently alter the fourth significant figure (11). Representing the sum of a series of chemical quantities, density is affected only when the total is altered. Homeostatic variations and pathological conditions which do not affect the total composition of the cerebrospinal fluid will not produce an abnormal density.

The normal laboratory examinations of cerebrospinal fluid (table 5) and apparently normal activity of our subjects, combined with the foregoing evidence, seem sufficient to establish our results as normal.

The specific gravities of the same sample of cerebrospinal fluid may range from 1.0013 37/4 C. to 1.0076 25/25 C. (table 5); yet very few

TABLE 6

BARIC GRAVITIES AND DENSITIES OF PREVIOUSLY TESTED SOLUTIONS

| Solution | Baric Gravity, 37/37 C. | Density, Gm./ml., 37 C. |
|---|---|---|
| Tetracaine hydrochloride (pontocaine), 0.1% in 0.09% saline | 0.9943 | 0.9953 |
| Dibucaine hydrochloride (nupercaine), 0.066% in 0.5% saline | 0.9957 | 0.9967 |
| Procaine hydrochloride, 2.5% in water | 0.9976 | 0.9986 |
| Procaine hydrochloride, 5% in 0.05% epinephrine and 0.2% sodium bisulfite | 0.9985 | 0.9995 |
| Human cerebrospinal fluid (mean) | 1.0000 | 1.0010 |
| Piperocaine hydrochloride (metycaine), 1.5% in Ringer's solution | 1.0013 | 1.0023 |
| Piperocaine hydrochloride (metycaine), 5% in Ringer's solution | 1.0036 | 1.0046 |
| Dibucaine hydrochloride (nupercaine), 0.25% in 5% dextrose | 1.0101 | 1.0111 |
| Tetracaine hydrochloride (pontocaine), 0.5% in 0.45% saline and 5% dextrose | 1.0127 | 1.0137 |
| Diethoxin (intracaine), 2.5% in 0.45% saline and 5% dextrose | 1.0157 | 1.0167 |

investigators make adequate temperature reports. Stanford (4) sought laboratory findings that would correlate with the condition of his deteriorating neurological patients, and he found that density did not correlate well. Etherington-Wilson (11) attempted to establish a normal specific gravity of cerebrospinal fluid at body temperature for anesthetic purposes, but the failure to mention the calibration of his beads has led to an unresolvable controversy. Only the thermal coefficient derived from his data can now be considered reliable. Wolman *et al.* (9) were concerned in establishing a normal specific gravity for cerebrospinal fluid at laboratory temperature for comparison with those of syphilitic patients. We have high regard for their method, and we believe that the confirmation of their data at 25 C. firmly establishes a value for this temperature. Our reported density at 37 C. awaits the necessary confirmation.

For completeness, table 6 records the baric gravities 37/37 C. of certain spinal anesthetic solutions based upon data previously published (1) and the mean density of cerebrospinal fluid at 37 C., 1.0010 Gm. per milliliter.

## SUMMARY

Controlled laboratory evidence indicates that the densities of cerebrospinal fluid of human beings are 1.0040 ± 0.0004 Gm. per milliter at 25 C. and 1.0010 ± 0.0003 Gm. per milliliter at body temperature, 37 C. A quantitative analysis of the normal composition of cerebrospinal fluid aids the presentation that protein is a minor factor and, contrary to its role in blood plasma, protein in cerebrospinal fluid correlates poorly with density. The density is most dependent upon temperature, sodium, chlorine and carbon dioxide. Specimens of cerebrospinal fluid exposed to air lose both carbon dioxide and water. The density can be preserved at least twenty-four hours by collection under mineral oil.

## REFERENCES

1. Davis, H., and King, W. R.: Densities of Common Spinal Anesthetic Solutions at Body Temperature, Anesthesiology 13: 184–188 (March) 1952.
2. Levinson, A.: Cerebrospinal Fluid in Health and in Disease, St. Louis, C. V. Mosby Co., 1929, pp. 111–129; p. 336; p. 90; pp. 97–106 and pp. 116–117.
3. Kolmer, J. A.: Clinical Diagnosis by Laboratory Examination. New York, D. Appleton-Century Co., 1944, pp. 335–337.
4. Stanford, R. V.: Vergleichende Studien ueber Cerebrospinalfluessigkeit bei Geisteskrankheiten, 1. Dichte und 2. Stickstoff, Hoppe-Seyler's Ztschr. f. physiol. Chem. 86: 43–50 (July 1) 1913, and 86: 219–233 (July 15) 1913.
5. Moore, N. S., and Van Slyke, D. D.: Relationships between Plasma Specific Gravity, Plasma Protein Content and Edema in Nephritis, J. Clin. Investigation 8: 337–355 (April) 1930.
6. International Critical Tables, Vol. 3, ed. 1, New York, McGraw-Hill Book Co., 1928, pp. 24–25.
7. Hewer, C. L.: Specific Gravity of Cerebrospinal Fluid, Brit. M. J. 2: 245 (Aug. 21) 1943.
8. Kafka, V.: Die Cerebrospinalfluessigkeit, Ztschr. f.d. ges. Neurologie u. Psychiatrie 6: 321–361 (Heft 4) 1913.
9. Wolman, I. J.; Evans, B., and Lasker, S.: Specific Gravity of Cerebrospinal Fluid, Am. J. Clin. Path. Tech. Sect. 10: 33–39 (March) 1946.
10. Dogliotti, A. M.: Anesthesia, Chicago, S. B. Debour, 1939, p. 568.
11. Etherington-Wilson, W.: Specific Gravity of the Cerebrospinal Fluid, Brit. M. J. 2: 165–167 (Aug. 7) 1943.
12. Macintosh, R. R.: Lumbar Puncture and Spinal Analgesia, Edinburgh, E. and S. Livingstone, Ltd., 1951, p. 125.
13. Stanford, R. V.: A New Form of Pyknometer, Phil. Mag. and J. of Science (London) 10: 269–270 (Aug.) 1905.
14. Hasler, J. K.: Specific Gravity of Cerebrospinal Fluid, Brit. M. J. 2: 314 (Sept. 4) 1943.
15. Hill, A. B.: Principles of Medical Statistics, ed. 5, New York, Oxford University Press, 1950, pp. 70–80.