# Vitamin Levels in Normal Cerebrospinal Fluid.* (25675)

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While studying the role of vitamins in various metabolic disorders, we became interested in the vitamin content of cerebrospinal fluid (CSF). We found in the literature only a few scattered data on ascorbic acid in CSF(1). We therefore investigated the content of those water-soluble components of the B-complex for which we had developed microbiological assay methods: folic acid(2), folinic acid (citrovorum factor)(3), pantothenic acid(4), thiamine(5), cyanocobalamin(6), and the Vit. $B_6$-group (to be published).

*Methods.* The microbiological assay methods have been described. They require only small quantities of CSF, such as were available from patients undergoing a spinal tap prior to spinal anesthesia for minor surgical conditions.

*Results.* The ranges for a group of 43 subjects are given in Table I. For comparison the ranges for whole blood are also listed. These data permit evaluation of the quotient of titre in blood over titre in CSF.

*Discussion.* Pantothenic acid appears to be evenly distributed between the 2 liquids as if it had no barrier to contend with. Folic acid likewise gives a ratio near unity for its concentrations in CSF and blood. Thiamine is 3-5 times less concentrated in CSF than in blood. This quotient assumes a much lower value for cyanocobalamin, which rarely reaches in normal CSF a concentration higher than 30 $\mu\mu$g (= 0.03 m$\mu$g), while its titre in blood is 10-30 times higher(5) in CSF than in serum. Its quotient of dilution is of the same range of magnitude as that of the serum proteins of which we find in healthy CSF about 1/250 of their concentration in serum. This would suggest that Vit. $B_6$ crosses the blood/CSF barrier only attached to serum protein.

These wide discrepancies in the blood/CSF quotients of vitamins are in line with analogous variations in the major blood constituents. CSF is evidently not an ultrafiltrate or transudate of the blood serum. It must be the result of a highly selective secretion by the lining of some regions of its anatomical boundaries. The diffusion at this border must be a 2-way process including absorption as well as secretion, and there must exist 3 barriers: a blood/CSF, a CSF/brain and a blood/brain barrier. A contemplation of the protein pattern of the CSF leads to the conclusion that this protein, about 1/250 of the concentration in blood serum, originates in the general circulation. Since CSF is never without it, but normally contains amounts within the range of 20-40 mg/100 ml, the protein in CSF cannot be due to accidental leakage; nor is its origin by diffusion more likely. One would rather assume the existence of a "window" in the blood/CSF barrier through which limited amounts will constantly pass, possibly in the *regio postrema*. The amounts penetrating into the CSF are small compared to the metabolic turnover. Thus, their concentration in CSF never reaches a static equilibrium. The occurrence and quantity of a given vitamin in CSF is subject to highly individual laws, which are determined by the function and the fate of the vitamin in the CSF.

*Summary.* Using our microbiological assay methods, we established normal ranges in CSF for folic acid, folinic acid, thiamine, cyanocobalamin, pantothenic acid and the Vit.

TABLE I. Vitamin Content of Normal CSF and Whole Blood.

| Vitamin | M.W. | CSF (mμg/ml) | Blood (mμg/ml) | Quotient, blood/CSF |
|---|---|---|---|---|
| Pantothenic acid | 219 | 100-1000 | 100-1000 | 1 |
| Folic acid | 441 | 10-30 | 7-40 | 1 |
| Folinic acid | 473 | 1-5 | 0 | |
| Thiamine | 337 | 10-20 | 25-80 | 3-5 |
| Cyanocobalamin | 1387 | 0-0.03 | 0.3-1.0 | 30 |
| $B_6$ group | 206 | 0-0.75 | 100-180 | 250 |

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$B_6$-group. The ratios of CSF levels to blood levels of these vitamins are shown in Table I.

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## Macroglobulinemia in a Transplantable Mouse Leukemia.* (25676)

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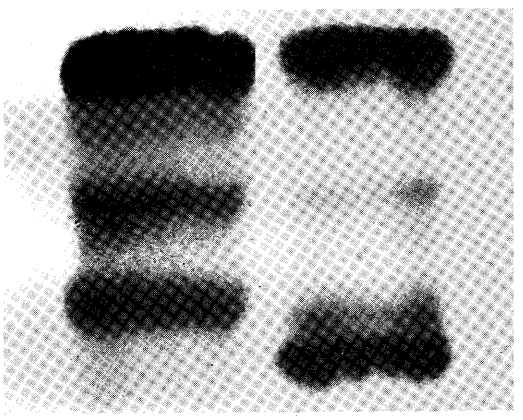
Gamma globulin-like paraproteins have been described in various mouse transplantation lines characterized by myelomatous(1,2) or plasmacellular leukemic(3-7) lesions. The subject of this report is the new observation that the paraprotein of a new transplantation line of leukemia appeared to be a macroglobulin and that the microscopic lesions seen in this line are comparable to those described in Waldenström's macroglobulinemia in man.

*Material and methods.* Methods of total protein estimation, paper- and immunoelectrophoresis, have been described(7). Ultracentrifugation was performed in a Spinco ultracentrifuge (Model E equipped with a rotor temperature indicator and control unit at 59,780 rpm at 20°C) on serum samples, diluted with 2 volumes of 0.9% NaCl. *The transplantation line,* originated in a 28-months old, untreated (CBA x DBA/2) $F_1$ mouse(8) with enlargement of lymph nodes and splenomegaly. Following subcutaneous inoculation of leukemic tissue, percentage of takes through 12 transfer generations was 100, survival time being 6 to 10 weeks, gradually shortening to 4 to 6 weeks.

*Results. Total serum protein* was found reduced to 3-4.5 g% (normal values 6.1-6.7 g %).

*Serum protein pattern* in (a) *paper electrophoresis* (Fig. 1) showed a pathologic globulin fraction of fast gamma mobility, in the first 5 passages constituting up to 40% of total protein; gradually fading, it disappeared in the tenth passage. b) *Immunoelectrophoresis* (Fig. 2) revealed an abnormal precipitation bow in the beta-1-beta-2- area located



| 6.1 g % | Total protein | 5.1 g % |
|---|---|---|
| 60% | Alb. | 29% |
| 5% | $\alpha_1$ | 6% |
| 9% | $\alpha_2$ | 10% |
| 15% | $\beta$ | 15% |
| | Path. fr. | 35% |
| 11% | $\gamma$ | 5% |

FIG. 1. Paper electrophoresis of normal mouse serum (left), and of serum from a mouse No. 2420 of fourth transfer (right) characterized by large, abnormal gamma fraction.

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