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Research Article

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## THE PROTEIN CONTENT OF THE CEREBROSPINAL FLUID IN MYXEDEMA

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Measurements have been made of the concentration of protein in the spinal fluid<sup>3</sup> in myxedema, before and after the administration of thyroid extract. These measurements are summarized in table 1. They show two things:

1. In most of the cases, the protein concentration was high during the period of myxedema.

2. In all but two cases, a well marked drop in the concentration occurred as the basal metabolism approached normal (fig. 1), following the administration of thyroid extract. In the two that showed no decrease, the protein content was normal to begin with.

It may be seen from table 1 and figure 1 that there were marked variations in the concentration from patient to patient, during the period of myxedema. These variations bore no relation either to the severity of the disease or to the degree of depression of the basal metabolism. There were also definite but less marked differences in the levels to which thyroid feeding depressed the protein content. These levels, in all but the first two patients, were within normal limits (20 to 45 mgm. per 100 cc.).

The change in protein concentration occurs gradually and may not be complete until some time after the basal metabolism has reached a

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<sup>3</sup> The method of Denis and Ayer (1) was used. This is the best quantitative method known, the error being not greater than 5 per cent.

The spinal fluid was always removed under basal conditions.

normal level. In this respect, it is similar to a slow change in the myxedematous condition of the tissues.

The change appears to persist as long as the metabolism is held at a normal level by the administration of thyroid extract.

TABLE 1

Case number	Name	Age	Laboratory number	Before administration of thyroid extract		After administration of thyroid extract	
				Basal metabolic rate	Concentration of protein* in spinal fluid	Basal metabolic rate	Concentration of protein* in spinal fluid
				<i>per cent of normal</i>	<i>mgm. per 100 cc.</i>	<i>per cent of normal</i>	<i>mgm. per 100 cc.</i>
1	Mr. J. G.	53	4236	-26	221	-3	49
2	Mrs. J. W.	50	4224	-21	129	+2	58
3	Mr. H. L.	21	4302	-34	111	+19	30
4	Mrs. M. V. L.	47	3984	-17	93	+23	32
5	Mrs. M. B.	30	4533	-40	80	-12	43
6	Mrs. L. C.	53	4532	-46	73	-10	32
7	Mrs. E. G.	48	4671	-43	72	-9	36
8	Miss E. MacD.	43	4423	-24	72	±0	44
9	Mrs. G. M.	33	4434	-27	65	+7	27
10	Mrs. A. J.	33	4681	-28	61	-11	34
11	Mrs. M. LeB.	43	3532	-24	58	+15	41
12	Mrs. M. B.	57	1836	-24	48	-5	24
13	Mrs. A. H.	48	1807	-22	46	+16	27
14	Mrs. M. H.	35	4179	-28	38	+8	44
15	Mrs. D. B.	51	4339	-25	34	+17	21
16	Mrs. M. M.	53	4651	-29	34	+6	22
17	Miss J. W.	47	2680	-22	28	±0	31

The cell count was normal throughout.

In most of the cases each figure represents the average of two or more determinations made on different days.

\*The determinations were made on the first 2 to 3 cc. of fluid removed from the lumbar region.

The protein content of the fluid obtained after withdrawing large quantities from the lumbar region (60 to 90 cc.), was much greater than is found normally under these conditions, and was sometimes only slightly less than that of the first 2 cc. removed. This finding indicated that the protein content of cerebral fluid was greater than normal, a supposition that was supported by obtaining cistern

fluid<sup>4</sup> on case 1, the protein concentration of which was 130 mgm. per 100 cc.

A high concentration of protein in spinal fluid is found in so many conditions that, in itself, it is of little diagnostic significance. Chronic nephritis not infrequently, and brain tumor rarely, may be confused with myxedema. In both myxedema and chronic nephritis one may

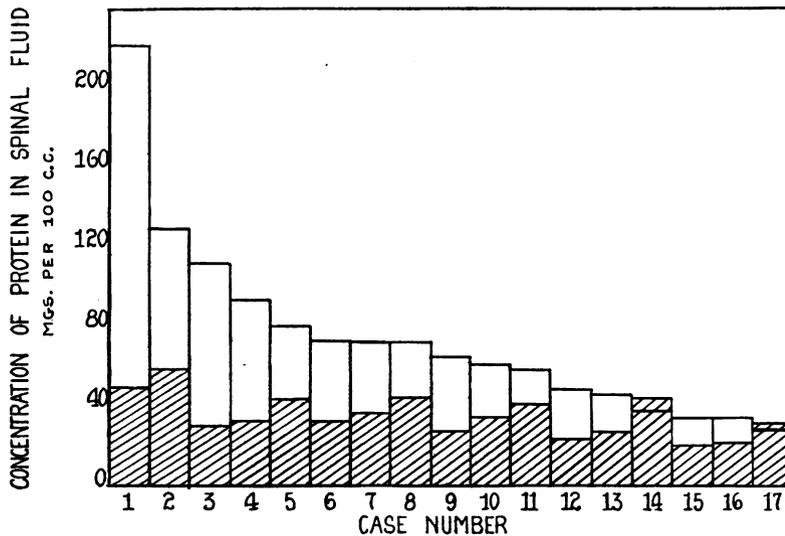


FIG. 1. THE CONCENTRATION OF PROTEIN IN THE SPINAL FLUID IN 17 CASES OF MYXEDEMA, BEFORE (TOTAL HEIGHT OF COLUMNS) AND AFTER (CROSS-HATCHED AREAS) THE ADMINISTRATION OF THYROID EXTRACT

In cases 14 and 17 no decrease occurred and the lower horizontal line represents the concentration during the period of myxedema.

find a high blood pressure, a well marked secondary anemia, albuminuria, and a high concentration of protein in the spinal fluid. In fact, nephritis is the disease most commonly mistaken for myxedema by those not very familiar with the latter. The appearance, history and basal metabolic rate are usually sufficient to differentiate the two diseases, however. For several months, because of the presence of headaches and ataxia, there was some uncertainty as to whether

<sup>4</sup> The cistern puncture was done by Dr. James B. Ayer.

J. G. (case 1) had myxedema or a brain tumor. The latter diagnosis was seemingly corroborated by the finding of a high pressure as well as a high concentration of protein in the spinal fluid. His appearance was not characteristic of the full blown picture of myxedema. While the diagnosis was in doubt, similar spinal fluid findings were obtained for the first time in several cases of typical myxedema. Thyroid extract was, therefore, administered to J. G. and produced a well marked reduction in the concentration of protein, as well as a clinical cure.

The cause of the high protein concentration in the spinal fluid is uncertain. It is possibly related in some way to the storage of nitrogenous substances in myxedema (2) (3). It is of interest that an albuminuria is frequently present in this disease (2) (4) (5). This usually disappears or decreases markedly when thyroid is administered (5). The albuminuria and the high spinal fluid protein content may be, in part, manifestations of the same pathological condition, viz., an altered permeability of cell membranes throughout the body.

#### SUMMARY AND CONCLUSIONS

The concentration of protein in the spinal fluid is high in most cases of myxedema, and usually drops to within normal limits when thyroid extract is administered.

The high protein content both of cistern fluid and of fluid obtained after withdrawing large quantities from the lumbar region, indicates that the protein content of cerebral fluid is also high during the period of myxedema. This finding suggests that the fluid which comes through the choroid plexus may have a greater protein concentration than normal.

The knowledge that the concentration of protein in the spinal fluid is usually high in myxedema is of diagnostic value in rare instances in which this disease may be confused with brain tumor and chronic nephritis.

We wish to thank Drs. James B. Ayer and Frank Fremont-Smith, whose interest in this and related problems made it possible to combine the research facilities of the metabolism and neurological labora-

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