

ments the tissues may be graded in order of decreasing reactivity (weight changes) as: thymus, cervical lymph nodes, mesenteric lymph nodes and spleen.

To determine whether changes in the thymus were positively correlated with similar changes in the lymph nodes, a correlation ratio was obtained between the thymus and the cervical lymph node weights employing the above and comparable data. A positive coefficient of correlation of  $0.591 \pm 0.080$  was obtained. This would indicate that when changes occur in the one tissue, similar changes in the same direction are apt to occur in the other.

*Summary.* 1. Evidence is presented that there is a relationship in the reactions of the thymus, spleen, and lymph nodes to the effects of castration, thyroidectomy, and treatment with thyroxin or testosterone propionate, or combinations of these in the male rat. 2. Castration and thyroxin cause comparable increases in the weights of thymus, lymph nodes and spleen. Thyroidectomy and treatment with testosterone propionate tend to decrease the weights of these tissues. Thyroidectomy and testosterone propionate prevent the increase in the weights of thymus, spleen and lymph nodes which follow castration. The order of decreasing sensitivity to the stimuli employed is as follows: thymus, cervical lymph nodes, mesenteric lymph nodes and spleen. 3. A positive coefficient of correlation of  $0.591 \pm 0.080$  was calculated from the data derived from the above experiments for the thymus and the cervical lymph nodes. This is further evidence of a similarity in reaction of these tissues.

### 13534

#### **Electrophoretic Patterns of Concentrated Cerebrospinal Fluid.\***

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(Introduced by Michael Heidelberger.)

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The protein content of cerebrospinal fluid is of significance in the diagnosis of neurological disorders such as brain and spinal cord tumors, neurosyphilis, peripheral neuritis, etc. Very little is known, however, about the origin or composition of spinal fluid proteins, or

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\* Aided in part by a grant from the William J. Matheson Commission.

of the variations in composition which accompany disease states. The Tiselius electrophoresis apparatus<sup>1</sup> has proven a valuable tool in the study of proteins, and has disclosed the presence in serum of 3 globulin fractions of different mobility. Variations in the electrophoretic patterns of human sera have been described in diseases such as lymphopathia venereum, multiple myeloma, etc.<sup>2, 3, 4</sup> It seemed possible that this method might be used in the study of the spinal fluid protein.

Large volumes of cerebrospinal fluid obtained at encephalography and ventriculography were concentrated to a volume of about 2 ml by dialysis under pressure against saline in the icebox at 5°C to avoid denaturation. Concentrations of protein of from 0.4 to 1.5% or more could thus be obtained. These solutions were then dialyzed against 0.02 M phosphate buffer containing 0.15 M NaCl and studied in the Tiselius electrophoresis apparatus with a micro cell. Photographs of the migrating boundaries were taken by the Longsworth<sup>5</sup> method. Concentrations of protein and electrophoretic mobilities were calculated from the descending boundaries. Typical results are shown in Table I. Multiplying the total protein content of the original spinal fluid by the percent composition of any fraction gave approximate values for the amount of each component in mg per 100 ml.

Cerebrospinal fluid proteins show a pattern similar to that of the plasma proteins. When the total protein of the cerebrospinal fluid is elevated, all of the plasma components may be found (Fig. 1 A. No. 3). In those with normal levels of total protein, alpha globulin and fibrinogen may not be detected (Fig. 1 B. No. 2). The ratio of albumin to globulin is frequently somewhat higher than that found in serum; when the total protein of the spinal fluid is increased, the greater part of this increase is generally due to albumin. Alterations in the pattern of the serum proteins are, however, reflected in the cerebrospinal fluid; thus, in the 2 cases of lymphopathia venereum (4 and 5) it will be seen that the percentage of gamma globulin is high both in the serum and in the spinal fluid. Similarly, the albumin-globulin ratio is lowered in both, although this reduction in ratio is less marked in the spinal fluid.

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<sup>1</sup> Tiselius, A., *Faraday Soc.*, 1937, **33**, 524.

<sup>2</sup> Longsworth, L. G., Shedlovsky, T., and MacInnes, D. A., *J. Exp. Med.*, 1939, **70**, 309.

<sup>3</sup> Luetscher, J. A., Jr., *J. Clin. Invest.*, 1940, **19**, 313; 1941, **20**, 99.

<sup>4</sup> Gutman, A. B., Moore, D. H., Gutman, E. B., McClellan, V., and Kabat, E. A., *J. Clin. Invest.*, 1941, **20**, 765.

<sup>5</sup> Longsworth, L. G., *J. Am. Chem. Soc.*, 1939, **61**, 529.

TABLE I.  
Electrophoretic Mobilities and Concentrations of the Protein Components in Cerebrospinal Fluid.

Case No.	Diagnosis	Cerebral fluid used	pH	Mobilities $\times 10^{-5}$					% composition					Total protein found	A/G found	Calc. individual components					Colloidal gold curve	
				A	$\alpha$	$\beta$	$\phi$	$\gamma$	A	$\alpha$	$\beta$	$\phi$	$\gamma$			A	$\alpha$	$\beta$	$\phi$	$\gamma$		
1	Chromophobe Pituitary Adenoma	46	7.4	6.0	3.0	0.5	58.4	23.4	18.2	1.4	31	18	7	6	1100000000							
2	Idiopathic grand mal	60.0	7.3	5.9	2.9	0.7	62.4	6.7	13.4	17.4	1.7	31	19	2	4	6	"					
3	Polynneuritis	16.5	7.4	5.8	3.9	2.8	1.9	0.7	65.9	8.5	11.4	3.8	10.4	2.2	198	130	17	23	3	21	"	
4	Lymphopathia (Serum) Venereum		7.5	5.0	3.2	2.3	0.6	39.6	8.4	17.7	34.3	0.65										
4	Lymphopathia Venereum	16.0	7.4	5.9	3.1	1.0	56.3	12.0	31.8	1.3	90	51	11	29	1111223100							
5	Lymphopathia (Serum) Venereum		7.3	4.8	3.3	2.4	1.6*	0.5	34.0	3.6	12.3	11.7*	38.4	0.5								
5	Lymphopathia Venereum	25	7.3	5.5	4.1	2.7	1.9	0.4	42.4	9.4	21.9	26.5	0.7	27	12	3	6	7	1100000000			
6	Neurosyphilis (Serum)		7.3	5.4	3.6	2.5	0.8	60.7	12.3	16.1	11.0	1.6										
6	Neurosyphilis	34.0	7.3	5.4	3.9	2.5	4.7	0.2	49.6	5.0	7.2	38.2	1.0	55	27	3	4	21	4334421100			
7	Neurosyphilis	10.0	7.3	5.8			0.8	43.8	56.2	0.8	92	40	52	5555544210								

\*Not fibrinogen, but an unknown component.

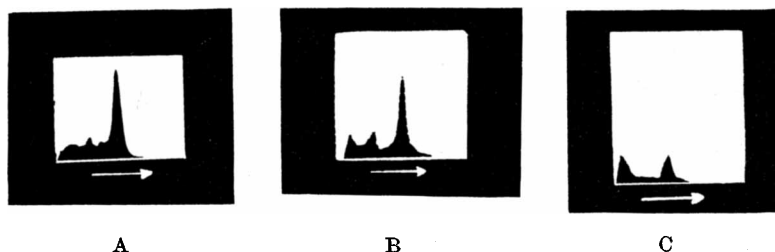


FIG. 1.

Electrophoretic patterns for cerebrospinal fluid (A) with high total protein content (case 3), (B) with normal total protein content (case 2), and (C) with abnormal colloidal gold curve (case 7).

Two cases of neurosyphilis whose spinal fluids showed abnormal colloidal gold curves, had a marked increase in the gamma globulin fraction. When the gamma globulin of case 7 (Fig. 1 C) was separated from the albumin electrophoretically, all of the colloidal gold reactivity was found in the gamma fraction and none in the albumin fraction. Although the colloidal gold reacting material is found in the gamma fraction, it may differ from the normal gamma component of spinal fluid since other fluids which contain equally large amounts of gamma globulin yield normal colloidal gold curves.

*Summary.* The electrophoretic pattern of the cerebrospinal fluid proteins resembles that of the plasma. Alterations in the composition of the serum proteins produce similar changes in the spinal fluid patterns. Colloidal gold activity in pathological fluids is associated with the gamma globulin.

## 13535

**Inactivation of Sulfonamide Inhibitor by Azochloramid.**

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The bactericidal effect *in vitro* of sulfonamide derivatives has been extensively investigated. Recently Neter<sup>1</sup> has reported that of a variety of bactericidal compounds which he studied only Azochloramid when used jointly with sulfonamides showed more than a mere additive effect upon the test organism.

<sup>1</sup> Neter, E., PROC. SOC. EXP. BIOL. AND MED., 1941, 47, 303.