

2. A fixed caudad ileac diameter of 0 (complete obstruction) is followed by a contraction of a mean duodenum of 14 c.c. to a mean of 6.25 c.c. in five days. A similar result was noted after acute gangrenous typhlitis and incomplete obstruction of the cephalad colon.

*B. Colon.*

Six experiments have been performed on the colon. Incomplete obstruction of the extreme caudad colon for a mean of 10.75 days was followed by a dilatation of a cecum of a mean volume of 18 c.c. to a cecum of 29.5 c.c.

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**Nephelometric study of the proteins of cerebro spinal fluids.**

**I. RELATION OF EUGLOBULIN, TOTAL-GLOBULIN AND TOTAL-PROTEIN TO WASSERMANN REACTION.**

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**INTRODUCTION.**

In syphilitic diseases of the nervous system the composition of the cerebrospinal fluid has become of increasing importance. On the exact chemical picture of the fluid, especially from a quantitative standpoint nothing has been done. It is true, the proteins and to some extent the phosphorus have been roughly estimated and in some cases correlated to the Wassermann reaction.

For this deficiency of quantitative data the reason is found in the lack of material; the present chemical methods used heretofore having been too crude for the low concentration of substances in the very small amounts of fluid.

Since the development of nephelometry the quantitative

estimation of many of the substances occurring in minute amounts in the body is a comparatively simple matter.

In the hope of getting useful information, we have studied quantitatively the proteins of cerebrospinal fluids with nephelometric methods, and have correlated our findings with the Wassermann reaction and other tests.

#### TECHNIC.

The spinal fluid was accurately measured in a small graduated cylinder or centrifuge tube, and an equal volume of .2 per cent. tricresol added as a preservative.<sup>1</sup> This preserved the fluids for a week or longer.

For the *total-protein* estimation 2 c.c. of diluted fluid (corresponding to 1 c.c. of original) were diluted with 8 c.c. of distilled water, and then precipitated with 20 c.c. of 3 per cent. sulphosalicylic acid. If the amounts of fluid were small, one half or one third these amounts were used.

This suspension was then matched in the nephelometer<sup>2</sup> with a standard made by adding 20 c.c. of 3 per cent. sulphosalicylic acid to 10 c.c. of a .01 per cent. solution of casein. The readings gave at once, upon calculation, the milligrams of total protein in 1 c.c. of spinal fluid. If the standard was much stronger than the "unknowns" a weaker casein solution was used, *e. g.*, .005 per cent., .0025 per cent., .00125 per cent.

For the *total globulin* estimation 2 c.c. of diluted fluid (1 c.c. of original) were diluted with 3 c.c. .1*N* acetic acid and 5 c.c. of saturated ammonium sulphate solution. This was also matched to a casein standard as in the total-protein estimation. Theoretically the standard should be of the same substance as the one to be determined, yet here it seemed best to refer all the estimations to an arbitrary standard for the sake of uniformity, speed and convenience, as pure samples of these proteins are very difficult to obtain.

The *euglobulin content* in spinal fluid has been determined heretofore by one third saturation of ammonium sulphate, but

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<sup>1</sup> S. S. Graves and P. A. Kober, *Journal of Amer. Chem. Soc.*, XXXVI, 751 (1914).

<sup>2</sup> Kober, *Journal of Biolog. Chem.*, 13, 485 (1913); *Journal of Amer. Chem. Soc.*, 35, 290 (1913); *ibid.*, 1585.

recent results by Harriet Chick and others have shown that this is not a sharp method for separating euglobulin from the other globulins. Its most characteristic property is its insolubility at its isoelectric point, but owing to its low concentration (.001 to .020 per cent.) in spinal fluids the estimation in this way has never been attempted heretofore.

From the diluted spinal fluid the euglobulin is precipitated by adding a trace of acid to help free it from its alkaline salt, and diluting. The diluting not only tends to hydrolyze any unneutralized salt of euglobulin but decreases any solvent action due to electrolytes.

To 2 c.c. of diluted spinal fluid were added 0.50 c.c. .01*N* acetic acid and 10.00 c.c. of distilled water, and after waiting a few minutes the suspension was matched with a known casein solution (see total-protein estimation).

It may have occasionally happened that the amount of .01*N* acetic acid was either too much or too little, in which case a slight error resulted, but all the figures given here were obtained in that way, using 0.50 c.c. .01*N* acetic acid.

The Wassermann reactions were performed as described by Field in the *Archives for Internal Medicine*, 13, 790 (1914) and the *Jour. Amer. Med. Assoc.*, 62, 1620 (1914).

The chemical and Wassermann tests were made independently, without duplicates, in separate institutions, and the figures were not compared until the end of the series.

The results with *total protein* estimations show, assuming that figures above .050 per cent. indicated pathological increase, that 34 cases out of 51 agreed with positive Wassermann reactions, while 48 out of 54 agreed with negative Wassermann reactions.

Similarly, the figures of the *total globulin* estimation showed, assuming .020 per cent. or less as normal, that 24 cases out of 31 agreed with positive Wassermann reaction, while 44 out of 54 cases agreed with negative Wassermann reactions.

The *euglobulin* content seemed to show remarkably close agreement to the Wassermann test: those above .004 per cent. agreed with positive Wassermann test in 14 out of 16 cases, and those below .004 per cent. agreed with a negative Wassermann reaction in 33 out of 35 cases. Of these 4 discrepancies we have good reasons to doubt the figures obtained in at least 2 of them.

## RESULTS.

TABLE I.

No.	Hospital No.	Total Protein, Per Cent.	Total Globulin, Per Cent.	Euglobulin, Per Cent.	Wassermann Reaction.		Diagnosis.
					Fluid.	Blood.	
74	2662	.087		.011	+		Cerebrospinal syphilis
75	2661	.013		.0	-		Questionable.
76	2660	.027		.0	-		Thrombosis.
77	2754	.069		.011	+		General paresis.
78	2752	.072		.014	+	+	" "
79	2746	.051		0	-		G. P.?
80	2691	.029		.002	-	-	G. P.
81	2677	.124		0	-	-	G. P.
82	2930	.041		.005	+	+	Cerebrospinal syphilis.
83	2922	.036		0	-		" "
84	2920	.044		.002	-		G. P.?
85	2919	.043		0	-		Comitose.
86	2912	.040		0	-		G. P.
87	2909	.203	.053	.010	+		G. P. alcoholic.
88	2850	.054		.008	+	+	G. P.
89	2829	.042		.001	-		G. P.
90	2800	.030		0	-	+	G. P.
91	2792	.026		0	-	-	G. P.
92	3401	.016	.008	0	-	-	G. P.?
93	3463	.033	.008	0	-	-	G. P.?
94	3510	.012	.006	0	-	-	Rachitic bronchitis.
95	3610	.029	.006	0	-	-	Uræmia.
96	3628	.023	.007	0	-	-	Hysteria.
97	3584			.006	-	-	G. P.?
98	3586	.024	.008	0	-	-	G. P.?
99	3588			0	-	-	G. P.?
100	3590	.023	.010	0	-	-	G. P.?
101	3595			.008	-	+	G. P.?
102	3939	.049	.002	(.004)	-	-	G. P.
103	3942	.048	.015	.003	+	+	G. P.
104	3944	.044	.003	.001	-	-	G. P.?
105	3945	.097	(.020)	.020	+	+	G. P.
106	3947	.101	.032	.020	+	+	G. P.
107	3950	.044	.001	0	-	-	G. P.?
108	3952			.001	-	-	G. P.?
109	3953	.040	.008	.002	-	-	G. P.?
110	4129	.091	.024	.011	+	+	G. P.
111	4120	.022	.009	0	-	-	Gas poisoning.
112	4113	.047	.010	.005	+	+	Cerebrospinal syphilis.
113	4110	.105	.032	.029	+	+	G. P.
114	4108	.014		0	+(5)	-	Syphilis.
115	4063	.107	.032	.025	+	+	G. P.
116	4065	.033	.011	0	-	-	G. P.?
117	4071	.033	.012	0	-	-	G. P.?
118	4083	.026	.009	0	-	-	G. P.?
119	4087	.027	.010	0	-	-	G. P.?
120	3985	.020	.012	0	-	-	G. P.?
121	3975	.058	.022	.010	+	+	G. P.?
122	3968	.063	.019	.003	-	-	G. P.?
123	3961	.051	.021	.016	+	+	G. P.

## SUMMARY.

In this series an increase in the euglobulin fraction appears to run parallel with a positive Wassermann reaction and vice versa. But what the exact normal limits of the euglobulin content are cannot be determined with certainty from this small series of cases. Not until results from a much larger number of cases are obtained can any positive statement be made. We can only claim that the findings are most suggestive. We are continuing the work along these lines on blood as well as on spinal fluids.

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**The blastophthoric effect of chronic lead poisoning: Breeding experiments. Preliminary report.**

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There have been frequent clinical observations of the apparent deleterious effect upon the germ plasm exerted by chronic lead poisoning. A majority of these cases have been found in female lead workers and in these it might be supposed that abortions, stillbirths and early deaths of infants were due as much to the toxic effect of lead during intra-uterine development as to an actual injury to the germ plasm. In the smaller number of instances in which the male parent alone was poisoned, the resulting sterility without impotency, the stillbirths and the early deaths of offspring are difficult to explain unless they are due to blastophthoria. The work of Stockard and of Cole and Davis has shown that alcohol has a similar effect. In a recent report which appeared as the present series of experiments was being concluded Cole and Bachhuber have demonstrated that the offspring of male rabbits poisoned by lead as well as of male fowls similarly poisoned are of distinctly lower vitality than the offspring of normal males.

In attempting to determine experimentally whether blastophthoria occurs in chronic lead poisoning, guinea pigs were given repeated weighed doses of commercial white lead in capsules by