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Hyperproteinemia with Reversal of the Albumin:Globulin Ratio in Lymphogranuloma Inguinale.

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In the course of an inquiry into the significance of the proteinuria observed in a case of lymphogranuloma inguinale, the protein content of the serum was determined. An unanticipated hyperproteinemia was found, confirmed by 2 subsequent examinations. Further investigation in 12 cases of lymphogranuloma inguinale revealed high serum protein values in all but 2 cases. The hyperproteinemia was more marked in the advanced stages of the disease (cases 1-7, Table I), particularly in females with rectal stricture, than in those patients presenting suppurating inguinal buboes or proctitis. We had no opportunity to study patients with initial lesions.

There was a relative and absolute increase in serum globulin in 11 cases, shown to be due to an increase in euglobulin in 2 cases, with reversal of the albumin:globulin ratio in 9 instances (Table I).^{*} Serum albumin was less than 3.7% in only 2 cases. The fibrinogen content of the plasma and the non-protein nitrogen content of the serum were within normal limits. The serum calcium was 9.1, 10.2, 11.3 and 10.3 mg. % in cases 1, 4, 6, and 11 respectively. The osmotic pressure of the serum in case 1, against normal saline solution buffered at pH 7.4, was within normal limits.

The erythrocytic sedimentation rate^{1, 2} was increased in all but 2 of the cases examined, but was within normal limits in defibrinated blood (5, 2, 6, 5 mm. in 1 hour in cases 8, 9, 10, and 11 respectively). The Takata-Ara test was found to be positive in the 3 cases examined. The Ray globulin flocculation test, carried out as with kala-azar serum, was negative. The urine contained traces of protein in 5 of the 10 cases examined. Precipitin tests were carried

^{*} The occurrence of hyperproteinemia with reversal of the albumin:globulin ratio in lymphogranuloma inguinale appears not to have been recorded in the literature. Nicolau¹ noted an increase in the refractive index and in the viscosity of the serum in this disease and considered that these changes might be due to an increase in serum albumin. Our analyses fail to confirm Nicolau's inference.

¹ Nicolau, C. T., *Bull. et mém. Soc. méd. hôp. Bucarest*, 1933, **13**, 45.

² Bloom, D., *Arch. Derm. and Syphil.*, 1933, **28**, 810.

TABLE I.

No.	Age	Sex	Race	Frei	Wassermann	Dmeleos	Serum			Fibrinogen	Erythrocytic Sedimentation Rate mm. 1st hour
							Total Protein %	Albumin %	Globulin %		
1	48	♀	Negro	+	—	—	11.2	3.3	6.8	0.49	128
2	41	♀	"	+	Anti-comp.	—	10.1	2.9	7.8	0.37	
3	50	♀	"	+	—	—	10.7	3.7	5.6	0.66	79
							9.3	3.4	5.8	0.59	70
4	48	♀	"	+	—	—	9.2	4.0	5.1	0.79	72
							8.8*				
5	31	♀	"	+	—	—	9.1	3.7	5.0	0.76	56
							8.7				
6	55	♂	White	+	—	—	8.5*	4.0	4.6	0.87	64
7	30	♀	Negro	+	—	—	8.6	3.8	4.3	0.83	45
8	44	♂	"	+	—	—	8.4*	4.3	4.1	1.05	19
9	40	♂	White	+	—	—	8.4	3.9	4.3	0.91	20
10	28	♂	Negro	+	—	—	8.2	3.7	4.4	0.84	37
11	35	♂	White	+	—	—	8.1	4.3	3.6	1.19	87
12	35	♂	"	+	—	—	7.9	4.6	2.2	2.10	35
							6.8				

*Total plasma protein in oxalated blood (Some dilution due to shrinkage).

out in 1 instance (Dr. F. E. Kendall) to determine the nature of the protein excreted and revealed globulin as well as albumin. None of the 10 urines tested contained Bence Jones protein.

The cause of the hyperproteinemia described above is not clear. It is not the result of dehydration, of which there was no clinical evidence, since this would not account for the alteration in the A/G ratio. Moreover, hematocrit determination of blood cell volume, carried out in 3 instances, gave normal values. Unlike the changes in plasma proteins described in acute infections such as pneumonia,^{3, 4} the fibrinogen content is not increased and the ratio fibrinogen:total plasma protein is decreased. The hyperglobulinemia observed in lymphogranuloma inguinale appears to be similar to that described in kala-azar,⁵ leprosy,⁶ and other chronic infections, perhaps also to that seen in neoplasia such as multiple myeloma.⁷

Hyperproteinemia is neither as constant nor as specific a manifestation of lymphogranuloma inguinale as is the Frei reaction. It is apparent, however, that the possibility of lymphogranuloma inguinale should be considered in cases presenting unexplained hyperproteinemia, particularly in negroes, and that this possibility should be ruled out by means of the Frei test. Lymphogranuloma inguinale is not uncommon in the United States; 54 cases have been seen at the Presbyterian Hospital in the past 2 years.

The hyperglobulinemia observed in lymphogranuloma inguinale may account, in part, for several interesting phenomena associated with the disease: the high sedimentation rate, often greatly in excess of the level consistent with the degree of obviously active infection; and the falsely positive and repeatedly anti-complementary Wassermann reactions reported in the literature,⁸ and encountered in several of our cases.

Serum protein, non-protein nitrogen, fibrinogen and calcium were determined⁹ by the macro-Kjeldahl, micro-Folin-Wu, a modified Cullen and Van Slyke and the Clark-Collip modification of the Kramer-Tisdall methods respectively. Albumin, globulin and the euglobulin fraction were determined by Howe's method. Bloods

³ Gram, H. C., *Acta med. Scand.*, 1922, **56**, 107.

⁴ Foster, D. P., *Arch. Int. Med.*, 1924, **34**, 301.

⁵ Sia, R. H. P., and Wu, H., *China Med. J.*, 1921, **35**, 527.

⁶ Frazier, C. N., and Wu, H., *Am. J. Trop. Med.*, 1925, **5**, 297.

⁷ Perlzweig, W. A., Delrue, G., and Geschickter, C., *J. Am. Med. Assn.*, 1928, **90**, 755.

⁸ Sulzberger, M. B., and Wise, F., *J. Am. Med. Assn.*, 1932, **99**, 1407.

⁹ Peters, J., and Van Slyke, D. D., *Quantitative Clinical Chemistry*, **2**, Williams and Wilkins, Baltimore, 1931.

were collected with minimal stasis. The erythrocytic sedimentation rate was estimated by Westergren's modification.

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Effect of Oestrus and Certain Gonadotropic Hormones on Life-Span of Adrenalectomized Animals.

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A. *Effect of oestrus on the life-span of the adrenalectomized dog not receiving adrenal cortical hormone.* Rogoff and Stewart¹ first demonstrated that the bitch, if adrenalectomized when in heat, could survive in normal health and without treatment of any kind, for as long as 65 days. This observation has been repeatedly confirmed in this laboratory by withholding hormone from the animal in heat.²

During the past 2 years we have studied 5 dogs in heat. The span of normal health varied, but in all cases it was greatly in excess of the longest time interval we have observed to intervene between cortical extract withdrawal and onset of adrenal insufficiency. The dogs were maintained without cortical hormone as follows: One dog 60 days; one 57 days; one 47 days; one 45 days; and one 40 days. At the end of these intervals adrenal insufficiency symptoms were evident and cortical hormone was injected. The arterial pressure, serum sodium, chloride, blood urea nitrogen, hemoglobin and glucose remained within normal limits throughout the period of good health.

Oestrus was experimentally induced in one adrenalectomized bitch by injections of extracts of menopause urine containing follicle-stimulating hormone of the anterior pituitary, followed by Follutein (pregnancy urine extract, E. R. Squibb & Sons). The animal

¹ Rogoff, J. M., and Stewart, G. N., *Am. J. Physiol.*, 1928, **86**, 20.

² Piffner, J. J., Swingle, W. W., and Vars, Harry M., *J. Biol. Chem.*, 1934, **104**, 701.