

changes, manner of death, congestion and degeneration of the kidneys, age of patient, etc.

The above factors may be minimized by studying renal extracts of dogs with hypertension produced experimentally by means of unilateral renal ischemia.⁹ Fourteen such experiments were performed. After hypertension had been established, the ischemic kidney and the opposite unoperated kidney were removed, extracted and their pressor effects compared. In 11 out of 14 instances, the extract of the ischemic kidney had a significantly greater pressor effect than that of the normal kidney of the same animal, the average difference in maximum pressor effect being 23 mm. of mercury and the range 10 to 41 mm. of mercury. In 2 cases the differences were less than 10 mm. of mercury, and in one no difference was observed. In general the extracts made from ischemic kidneys appeared to have less pronounced preliminary depressor and more prolonged pressor effects than those prepared from normal kidneys. Harrison, Blalock and Mason¹⁰ have obtained similar results in dogs in which hypertension was produced by means of unilateral and bilateral renal ischemia, and by unilateral and bilateral ureteral obstruction.

The data are not sufficient to establish an etiologic relationship between the pressor substance in the kidneys and the elevation in blood pressure. The observations are compatible with the hypothesis that hypertension, both in the experimental animal and in man (whether "essential" or "secondary") may be due to an excess amount of a pressor substance present normally in the kidney.

8882 C

Positive Formol-Gel Reaction Associated with Hyperglobulinemia in Lymphogranuloma Inguinale, Multiple Myeloma and Hepatic Cirrhosis.

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It has been shown recently^{1, 2} that many cases of lymphogranuloma inguinale develop hyperproteinemia, comparable in degree, in-

⁹ Goldblatt, H., Lynch, J., Hanzel, R. F., and Summerville, W. W., *J. Exp. Med.*, 1934, **59**, 346.

¹⁰ Harrison, T. R., Blalock, A., and Mason, M. F. Personal communication.

¹ Williams, R. D., and Gutman, A. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 91.

² Gutman, A. B., Gutman, E. B., Jillson, R., and Williams, R. D., *J. Clin. Invest.*, 1936, **15**, 475.

cidence and fractional distribution to that long known to occur in kala-azar. This observation, it has been pointed out, affords an explanation for certain peculiarities of the serum in lymphogranuloma inguinale—peculiarities which appear to be common to most sera with definite hyperglobulinemia, irrespective of etiology: 1. increased erythrocytic sedimentation rate¹; 2. anticomplementary properties of the serum in a significant proportion of cases³; 3. apparent discrepancy in acid-base equivalence of the blood in that the sum of the determined acid-equivalents appears to exceed the total base.² A further property of the serum in lymphogranuloma inguinale, likewise ascribable to hyperglobulinemia, is described in the present study. It was found that the formol-gel test, used extensively for the diagnosis of kala-azar, is positive in cases of lymphogranuloma inguinale presenting hyperproteinemia.

The total protein of the serum was determined by difference on 1 cc. samples, the macro-Kjeldahl technic being employed for total N and Folin's method with Nesslerization for non-protein N. Partitions were carried out in duplicate on 0.5 cc. samples by Howe's method. The formol-gel test was performed as follows: to 1 cc. of serum in a test tube (8 mm. bore is a convenient size) add 2 drops of 30-40% formaldehyde solution, mix, and allow to stand at room temperature. Normal control sera showed no change in viscosity or transparency in 24 hours.

Results. The formol-gel test was carried out on the sera of 13 cases of lymphogranuloma inguinale, all Negroes with positive Frei reactions, of whom 12 were under treatment for rectal stricture. The Wassermann reaction was positive in Cases 4, 6, 8, and 11, was persistently anticomplementary in Case 5 and negative in the remaining patients. The results are recorded in Table I. In Cases 1 and 2, with total serum proteins of 10.7 and 9.9% respectively, a semi-opaque gel formed within 5 minutes after the addition of formol. In 7 cases with less marked hyperproteinemia, a definitely positive response was obtained within 2 hours in most instances, and within 24 hours in all instances. In 4 cases of lymphogranuloma inguinale with serum proteins within normal limits, the sera were unchanged 24 hours after addition of the formol, or showed questionable slight increase in viscosity or opalescence.

Included in Table I are the results of the formol-gel test applied to sera obtained from patients with multiple myeloma and with cirrho-

³ Gutman, A. B., and Williams, R. D., *J. Clin. Invest. (Proc.)*, 1936, **15**, 458.

TABLE I.
Formol-gel reaction in 13 cases of lymphogranuloma inguinale (L.I.), 6 cases of multiple myeloma (M.M.), and 3 cases of cirrhosis of the liver (C.L.); with representative results on 2 control sera (N.S.).

Case	Diagnosis	Serum Proteins			Formol-gel reaction of serum					
		Total Prot. %	Glob. %	Englob. %	1/12 hr.	2 hrs.	24 hrs.	1 1/2 hr.	8 hrs.	24 hrs.
1	L.I.	10.7	7.8	4.0	++	++	++	++	++	++
2	L.I.	9.9	6.1	2.3	++	++	++	++	++	++
3	L.I.	9.7	6.2	2.4	++	++	++	++	++	++
4	L.I.	9.5	6.1	2.3	++	++	++	++	++	++
5	L.I.	9.1	5.6	2.9	++	++	++	++	++	++
6	L.I.	8.7	5.3	1.7	++	++	++	++	++	++
7	L.I.	8.6	5.0	1.7	++	++	++	++	++	++
8	L.I.	8.6	4.7	1.7	++	++	++	++	++	++
9	L.I.	8.5	4.8	0.9	++	++	++	++	++	++
10	L.I.	7.7	3.9	0.9	++	++	++	++	++	++
11	L.I.	7.5	3.4	0.9	++	++	++	++	++	++
12	L.I.	7.3	3.1	0.7	++	++	++	++	++	++
13	L.I.	7.0	3.3	1.1	++	++	++	++	++	++
14	M.M.	11.1	8.8	0.4	++	++	++	++	++	++
15	M.M.	9.5	7.1	5.4	++	++	++	++	++	++
16	M.M.	9.2	6.1	2.3	++	++	++	++	++	++
17	M.M.	8.6	4.8	1.8	++	++	++	++	++	++
18	M.M.	7.7	2.3	0.4	++	++	++	++	++	++
19	M.M.	6.3	3.2	0.6	++	++	++	++	++	++
20	C.L.	8.4	6.0	2.1	++	++	++	++	++	++
21	C.L.	7.4	5.6	2.2	++	++	++	++	++	++
22	C.L.	7.2	5.0	1.7	++	++	++	++	++	++
23	N.S.	7.3	2.4	0.4	++	++	++	++	++	++
24	N.S.	7.4	2.4	0.3	++	++	++	++	++	++

*Gelation — = no increase in viscosity
 — = questionable increase in viscosity
 + = increased viscosity
 ++ = very viscous flow
 +++ = semi-solid
 ++++ = solid
 †Opacity — = no change
 — = questionable slight opalescence
 + = opalescent
 ++ = translucent
 +++ = semi-opaque
 ++++ = opaque

sis of the liver. As reported by Sweigert⁴ and by Bing,⁵ an opaque gel forms rapidly in cases of multiple myeloma with marked hyperglobulinemia (Cases 14-17). A questionable slight opalescence after 24 hours was the only change noted in 2 additional instances with serum-proteins within normal limits.

Some patients with cirrhosis of the liver develop definite hyperglobulinemia. The serum of such patients gives a positive formol-gel reaction (Cases 20-22), the gel having a muddy-yellow appearance where jaundice is present (Cases 21 and 22). No change was noted within 24 hours in jaundiced sera without hyperglobulinemia.

Comment. 1. Opaque gel-formation has been described in few diseases other than kala-azar, chiefly in occasional cases of malaria, leprosy and tuberculosis,⁶ in all of which hyperglobulinemia may be marked. The formation of a *clear* gel, however, is said to occur sporadically in a variety of diseases,⁷ notably in syphilis.⁸ Opacity without gelation has been noted in early cases of kala-azar.⁶

The occurrence of gelation without opacity and opacity without gelation suggests that these two phenomena may be due to different factors. There is some experimental evidence that the formation of an *opaque* gel depends upon qualitative as well as quantitative changes in the serum-globulin fractions.^{9, 10} In accord with this view, we have found that *normal* serum, if it is sufficiently dehydrated, will gel after treatment with formol, but will not become opaque or opalescent. Normal serum concentrated *in vacuo* until the protein content was 18% congealed within 5 minutes; normal serum concentrated until the protein content was 12% formed a gel in 24 hours.* No opalescence developed after 48 hours. On the other hand, pathological serum of high protein content, which formed an opaque gel in 5 minutes, did not gel when the protein concentration was reduced to normal values by dilution with physiological saline solution. Opalescence, however, persisted even when the concentration of protein was reduced far below the normal level. Thus, the serum of Case 15 did not gel if diluted beyond 1:1½ with saline, but opalescence developed in all dilutions up to 1:10.

⁴ Sweigert, C. F., *Am. J. Med. Sc.*, 1935, **190**, 245.

⁵ Bing, J., *Acta med. Scand.*, 1936, **88**, 478.

⁶ Manson-Bahr, P. H., *Manson's Tropical Diseases*, London, 1935, 10th edition, p. 157.

⁷ Giraud, P., Montus, and Audier, *Bull. Soc. de Péd. Paris*, 1933, **31**, 115.

⁸ Gaté and Papacostas, *Compt. rend. Soc. de Biol.*, 1920, **83**, 1432.

⁹ Lloyd, R. B., and Paul, S. N., *Indian J. Med. Research*, 1928, **16**, 203.

¹⁰ Chopra, R. N., and Chaudhury, S. G., *Indian J. Med. Research*, 1929, **16**, 925.

* Gelation was not due to irreversible denaturation because after redilution to normal protein values, neither gelation nor opalescence occurred in 24 hours.

2. Case 14 is of exceptional interest in that the increase in serum-globulin consistently involved only the pseudoglobulin I fraction as determined by Howe's method (*Cf.* Gros¹¹). The fact that this serum formed an opaque gel within 5 minutes after treatment with formol is contrary to the view that the formation of an opaque gel is dependent solely upon hypereuglobulinemia. Our data would suggest that a positive formol-gel reaction is obtained in the presence of "abnormal" globulins irrespective of whether their solubility characteristics with respect to sodium sulfate correspond with those of euglobulin or pseudoglobulin.

3. We find the formol-gel reaction a convenient preliminary test for the detection of gross hyperglobulinemia in lymphogranuloma inguinale. Its reliability for this purpose in other conditions is being investigated further.

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Experimental Production of Exophthalmos Resembling that Found in Graves Disease.

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Experimental production of exophthalmos has been accomplished repeatedly by stimulating the sympathetic innervation of the eye. MacCallum and Cornell,¹ Code² produced, by electrical stimulation of the cervical sympathetic ganglion of dogs and cats, a contraction of the smooth muscle elements in the orbit which caused exophthalmos. Schockaert,³ Loeb,⁴ Friedgood,⁵ and Marine^{6, 7} have reported exophthalmos resulting from the injection of thyrotropic anterior pituitary extracts into ducks, normal and thyroidectomized guinea pigs, and by the injection of methylcyanide into normal and thyroidectomized rabbits. Loeb and Schockaert noted that the exophthalmos

¹¹ Gros, W., *Deutsches Arch. f. klin. Med.*, 1935, **177**, 461.

¹ MacCallum, W. G., and Cornell, W. B., *Med. News*, 1904, **85**, 732.

² Code, C. F., and Essex, H. E., *Am. J. Oph.*, 1935, **18**, 1123.

³ Schockaert, J. A., *Am. J. Anat.*, 1932, **49**, 379.

⁴ Loeb, L., and Friedman, H., *PROC. SOC. EXP. BIOL. AND MED.*, 1932, **29**, 648.

⁵ Friedgood, H. B., *Bull. Johns Hopkins Hosp.*, 1934, **54**, 48.

⁶ Marine, D., and Rosen, S. H., *PROC. SOC. EXP. BIOL. AND MED.*, 1933, **30**, 901.

⁷ Marine, D., and Rosen, S. H., *Am. J. Med. Sci.*, 1934, **188**, 565.