

Guanidine-like Substances in the Blood of Normal and Hypertensive Dogs.

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Guanidine and methylguanidine when administered to dogs and cats cause the arterial blood pressure to rise probably chiefly by constricting peripheral blood vessels. It was suggested by Major and Weber^{1, 2} that they might be associated with the genesis of essential hypertension because of these properties and because they found guanidine-like substances elevated in the blood of many patients suffering from this disease. The observation of hyperguanidemia has not been generally confirmed in such cases without demonstrable renal damage.³⁻⁶ However, several investigators noted a correlation between the degree of azotemia and hyperguanidemia when retention of waste products occurred in the blood.^{8, 9} Observations of Andes, Andes, and Myers,¹⁰ and Stander¹¹ have demonstrated increased amounts of guanidine-like substances in severe toxemias of pregnancy. Minot and her associates¹² appear to have established guanidine-like substances as responsible in part for certain of the clinical manifestations of extensive tissue necrosis as in hepatic intoxication or during the morbid withdrawal of interstitial fluid into the blood stream as in diarrhea. Dodd and Minot¹³ found hyperguanidemia in several cases of tetany which exhibited insufficient changes in the inorganic constituents of the blood to account for the tetany.

¹ Major, R. H., *Am. J. Med. Sci.*, 1935, **170**, 228.

² Major, R. H., and Weber, C. J., *Bull. Johns Hopkins Hosp.*, 1927, **40**, 85; *Arch. Int. Med.*, 1927, **40**, 891.

³ Marcolongo, F., *Minerva med.*, 1933, **2**, 501.

⁴ Marcolongo, F., and Bernabo-Silorata, A., *Clin. med. ital.*, 1924, **65**, 23.

⁵ Kleeberg, P., and Schlapp, W., *Z. f. physiol. Chem.*, 1930, **188**, 81.

⁶ Bohn, H., and Schlapp, W., *Zentralbl. f. inn. Med.*, 1932, **53**, 571.

⁷ De Weselow, O. L. V. S., and Griffith, W. J., *Brit. J. Exp. Path.*, 1932, **13**, 428.

⁸ Turries, J., *Compt. rend. Soc. biol.*, 1933, **112**, 658.

⁹ Andes, J. E., Linegar, C. R., and Myers, V. C., *J. Lab. Clin. Med.*, 1937, **22**, 1209.

¹⁰ Andes, J. E., Andes, E. J., and Myers, V. C., *J. Lab. Clin. Med.*, 1937, **23**, 9.

¹¹ Stander, H. J., *Am. J. Obs. and Gyn.*, 1932, **23**, 373.

¹² Minot, A. S., and Dodd, K., *Am. J. Dis. Children*, 1933, **46**, 522.

¹³ Dodd, K., and Minot, A. S., *Am. J. Dis. Children*, 1934, **47**, 958.

No association has been conclusively demonstrated in human beings between occurrence of increased amounts of guanidine-like substances and the appearance of hypertension. In spite of this the physiological properties of guanidine are such as to fulfill the requirements of an effector substance which has been postulated to explain the genesis of experimental hypertension in dogs.^{14, 15} For this reason the amount of these guanidine-like substances was determined in the whole blood of normal dogs and dogs made hypertensive by constricting the renal arteries by Goldblatt's clamp.¹⁶

The method of Andes and Myers¹⁷ which is a modification of those of Major and Weber² and Pfiffner and Myers¹⁸ was employed. Urea nitrogen was ascertained by the gasometric hypobromite method of Van Slyke and Kugel.¹⁹

The guanidine-like substance in the blood of 5 normal dogs varied from 0.35 mg./100 cc. to 0.74 mg./100 cc.

Unilateral nephrectomy did not alter this nor did it cause rise in

TABLE I.
Results of Determination of Guanidine-like Substances in Whole Blood of Normal and Hypertensive Dogs.

Dog No.	Blood Pressure mm. Hg.	Operation	Urea nitrogen, mg. in 100 cc.	Guanidine-like substance, mg. in 100 cc.
213	136	None	—	.42
212	140	"	—	.65
222	112	"	—	.56
223	122	"	—	.35
214	130/80	"	13.5	.74
214	136/82	Nephrectomy	—	.63
212	140/90	"	14.9	.63
209	160/100	"	28.6	.43
210	152	"	19.7	.62
216	250	1 clamp	—	.56
216	280	1 "	—	.65
189	160/100	1 "	—	.57
167	150/90	1 "	—	.56
204	242	1 "	8.8	.57
204	240	1 "	—	.79
193	252	2 "	15.1	.63
193	268	2 "	—	.57
43	286	2 "	12.6	.79
43	244	2 "	—	.72
40	224	2 "	17.8	.56
40	210	2 "	—	.65

¹⁴ Goldblatt, H., *Ann. Int. Med.*, 1937, **11**, 69.

¹⁵ Page, I. H., *Bull. N. Y. Acad. Med.*, 1937, **13**, 645.

¹⁶ Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W., *J. Exp. Med.*, 1934, **59**, 347.

¹⁷ Andes, J. E., and Myers, V. C., *J. Lab. Clin. Med.*, 1937, **22**, 1147.

¹⁸ Pfiffner, J. J., and Myers, V. C., *J. Biol. Chem.*, 1930, **87**, 345.

¹⁹ Van Slyke, D. D., and Kugel, V., *J. Biol. Chem.*, 1933, **102**, 489.

blood urea nitrogen or arterial blood pressure. Constriction of either one (6 examples) or both (7 examples) renal arteries caused rise in arterial pressure to as high as 286 mm. of Hg., but neither procedure elevated the guanidine-like substances or the urea nitrogen. It is noteworthy that the blood of dogs appears to contain slightly more (0.60 mg./100 cc.) of the guanidine-like substances than human blood (average 0.24 mg./100 cc.).¹⁰

Conclusions. Guanidine-like substances exhibit physiological properties similar to those that might be expected of an effector substance liberated from the kidneys when the renal arteries are constricted by Goldblatt's clamp. Despite this, no significant increase was found in the whole blood of dogs made severely hypertensive by this method when no rise in the urea nitrogen occurred.

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A Heavily Encapsulated Form of *B. typhosus*.

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It has been reported by the authors¹ that if certain strains of *B. coli* are incubated within a range of temperature of 4 to 17°C., a mucoid growth will appear.

We have utilized similar technic in examining 9 strains of *B. typhosus*. All of these have been isolated recently from feces or from blood. Petri dishes containing beef-extract agar plus 1% glucose were inoculated by streaking and then were incubated at 14°C. Two of these 9 strains developed growth definitely mucoid in character but the mucilaginous consistency was less marked than that observed with the colon organism in earlier experiments.

Preparations made by Gins' India-ink method revealed long rods surrounded by heavy capsules, although parallel cultures incubated at 37°C. for 48 hours yielded the usual form of the organism which was much shorter and which was provided with much less capsular structure.

It is suggested that this form described by us may be the mucoid type of *B. typhosus*.

¹ Beckwith, T. D., and Morgan, H. R., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 606.