might be one of the main activities of the sulfonamide compounds, and that more potent antitoxic compounds might prove even more useful in the treatment of bacterial infections. These experiments, however, lead one to believe that the only manner in which the toxicity of staphylococci is affected is by an inhibition of growth of the organism with a consequent decreased production of toxin.

Summary. Toxic manifestations of staphylococci are not inactivated *in vitro* by sulfanilamide, sulfapyridine, or sulfathiazole. The lethal toxin, dermo-necrotic toxin, coagulase, and enterotoxin are not neutralized by solutions of the sulfonamides tested at 37°C. α- and β-hemolysins are slightly diminished in activity at concentrations approaching the saturation point of the sulfonamides, but are unaffected at concentrations of less than .01%. These compounds appeared to decrease hemolysin production by decreasing the growth rate of the organism.

11516 P

Response of Plasma Volume to Diuretics.

D. B. CALVIN, GEORGE DECHERD AND GEORGE HERRMANN.

From the Departments of Biological Chemistry and Medicine, University of Texas, School of Medicine, Galveston, Texas.

Previous work[1] has led us to conclude that mercurial diuretics act by diminishing tubular reabsorption, while administration of aminophyllin produces an increase in the volume of the glomerular filtrate. Earlier work[2] suggested a high circulating blood volume in congestive heart failure, but there was no complete agreement as to the change following diuresis. Recent determinations[3] by a more satisfactory method[4] demonstrate a marked elevation of blood and plasma volume in patients with failure, and a decrease towards normal with the development of circulatory compensation. A similar decrease has been noted after the use of mercurial diuretics.[5]

We have followed over 12 to 24 hours the changes in plasma volume, determined by the method of Gibson and Evelyn,[4] after the

1 Herrmann, G., and Decherd, G., *J. Lab. and Clin. Med.*, 1937, **22**, 767.

2 Goldhammer, S., Leiner, G., and Scherf, D., *Klin. Woch.*, 1935, **14**, 1109.

3 Gibson, J. G., and Evans, W. A., *J. Clin. Invest.*, 1937, **16**, 851.

4 Gibson, J. G., and Evelyn, K., *J. Clin. Invest.*, 1938, **17**, 153.

5 Harris, Alfred W., personal communication.

TABLE I.
Plasma Volume After Injection of Diuretics.

Hr after drug inj.	Plasma vol, cc	Urine flow, cc/min	Plasma vol, cc	Urine flow, cc/min	Plasma vol, cc	Urine flow, cc/min
			Salyrgan.			
	LH		ET		V	
0	4634	0.86	5260	0.47	5140	0.53
½	4486	1.17	5520	.70	5110	.85
1	4386	8.00	5000	.79	4620	1.78
2	4060	11.33	4894	.48	4620	4.58
3			4394	.56		
5			4916	.99	3280	3.78
7			5088	1.29		
9			4826	1.31		
11			4045	1.33		
			Aminophyllin.			
	A		R		AO	
0	3440	1.00	6240	1.05	6120	1.17
½					6488	3.09
1	3713	1.05	6840	2.87	6383	5.14
2	4170	1.70	6720	3.35	6500	5.02
3	3976	1.92	6660	3.14	6697	4.77
5	3537	1.58	6220	2.04	7202	1.80
7	3732		5220	1.70	6278	1.55
9	3649				4913	1.08
11	3683	.16	5580	1.20	4072	.60
			Digoxin.			
	A		HB		SC	
0	5070	0.37	3890	0.10	4710	.83
1	5190	.56	4130	4.52	4310	3.84
2	5150	.85	3640	2.24	4237	3.67
3	4970	.91	3682	5.20	4273	1.80
5	5170	.90	3800	2.26	4164	6.08
7	5140	1.33	3790	3.43	3982	4.50
9	4830	1.70	3060	3.81	3947	8.20
11	4446	2.29	2505	3.28	3645	10.00
24	3820	2.25				

injection intravenously of one of the 3 types of diuretic drugs, salyrgan, aminophyllin, and digoxin. The urinary output has also been carefully followed, and the plasma volume correlated with the degree of diuresis. Data from typical experiments are recorded in Table I. It is to be emphasized that under the conditions of our experiments the plasma volume is influenced by fluid loss through the kidneys and fluid mobilization from the tissues. These factors exert an opposite effect, and their relative magnitude determines the blood volume.

When digoxin is injected in a dose of 2 mg there is first noted a slight increase in the plasma volume. This has never been great, and the time of its appearance seems to depend on the attainment

of the desired myocardial effect. As the rate of urinary flow accelerates, this increase disappears and is followed by a reduction, the amount of which is determined by the rate of diuresis.

The fluid eliminated during a rapid salyrgan diuresis seems to come largely from the plasma during the first 8 to 12 hours. After this period, as the rate of diuresis drops, the plasma volume is partially restored. In one of our cases there was a delayed diuresis, in one no diuretic response to the drug, and the plasma volume was slightly increased in each, suggesting that in addition to the usually dominant renal action, the mercurial also exerted an accessory effect on tissue fluid mobilization.[5]

The administration of 0.48 g of aminophyllin intravenously results in relatively large rise in the plasma volume, amounting in various individuals to from 400 to 1200 cc. The first rise coincides with the time of maximal diuresis; the plasma volume drops slightly during the period of rapid urine flow, but the rise continues as the degree of diuresis abates, and persists for approximately 6 hours. After this time the volume drops sharply, presumably due to a return of fluid into the tissues, for the rate of urine production has by then dropped back nearly to the control level. In one experiment the usual rise in plasma volume was preceded 20 minutes after injection by a slight drop. The significance of this finding must be further explored. The striking increase in plasma volume after aminophyllin injection cannot be adequately explained by the available data. The possible mechanisms for tissue fluid mobilization, as well as the concomitant shifts in total circulating plasma protein[6] are being further investigated.

[6] Calvin, D. B., *Proc. Am. Physiol. Soc.*, in press.