Deniges'[3] method. Other sections were analyzed for potassium by the Brech and Gaebler[4] method, for calcium by Halverson and Bergeim's[5] method, for total creatinine by Folin's method, using the Jaffe reaction. The water content or percentage of solids was determined by drying oven at 110°C. for 24 to 36 hours.[6]

The results as tabulated indicate that the ischemia and anoxemia resulting from ligation of the smaller branches of the anterior descending branch of the left coronary artery produce significant chemical changes. The losses of creatine are accompanied by losses in the total, acid soluble and lipoid phosphates but not of inorganic phosphates or potassium. The creatine losses are less striking than those recorded previously when the main anterior descending branches of the left coronary arteries were ligated[2] due to the smaller and the less definitely demarcated area of infarcted myocardium and almost inevitable inclusion of some normal tissue with the asphyxiated muscle.

9730

Bacteriostatic Action of Sulfanilamide upon Meningococcus in Spinal Fluid.

ERWIN NETER. (Introduced by Ernest Witebsky.)

From the Laboratories of the Children's Hospital and the Department of Pathology and Bacteriology, University of Buffalo, School of Medicine, Buffalo, N. Y.

It is generally agreed that sulfanilamide and related compounds have a curative effect in natural and experimental infections of man and animals by the hemolytic streptococcus. One of the most interesting features of sulfanilamide as a chemotherapeutic agent is its property to be more or less effective against a wide variety of microörganisms, including the pneumococcus, gonococcus, meningococcus and *Cl. welchii.* The mechanism of the action of sulfanilamide in bacterial infections is not fully understood. There can be no doubt, however, that sulfanilamide exerts a certain degree of

3 Deniges, G., *Compt. rend. Acad. Sci.*, 1927, **184**, 330.

4 Brech, F., and Gaebler, Oliver H., *J. B. C.*, 1930, **87**, 81.

5 Halverson, J. O., and Bergeim, O., *J. B. C.*, 1917, **32**, 159.

6 Shohl's modification of Stolte's dry ashing method, Peters, John P., Van Slyke, Donald D., *Quantitative Clinical Chemistry*, Williams & Wilkens Co., Baltimore, 1932, **2**, 70.

bacteriostatic activity *in vitro,* as shown by Bliss and Long[1] Colebrook, Buttle and O'Meara[2]; Colebrook and Kenny[3]; Long and Bliss[4]; Rosenthal,[5] Wengatz, Boak and Carpenter.[6]* This bacteriostasis may be sufficient to protect leucocytes and to allow the natural defensive macrophages to accumulate (Gay and Clark[7]). Therefore, phagocytosis may be enhanced under treatment with sulfanilamide. It should be kept in mind, however, that no parallelism exists between the effectiveness of sulfanilamide *in vitro* and *in vivo;* Rosenthal[5] could show that sulfanilamide may be more than 100 times as bacteriostatic against pneumococci than against hemolytic streptococci *in vitro,* although this drug is more effective toward the hemolytic streptococcus in animal experiments.

Recently it was reported by Branham and Rosenthal[8]; Buttle, Gray and Stephenson[9]; Long and Bliss[10]; McPherson Brown[11]; Proom[12]; Rosenthal, Bauer and Branham,[13] that sulfanilamide has a curative action in experimental meningococcal infections in mice. Clinical observations concerning the treatment of meningococcal meningitis in man were reported by Schwentker, Gelman and Long.[14] In preliminary experiments, Branham[5, 8] demonstrated a bacteriostatic action of sulfanilamide toward the meningococcus *in vitro.* The experiments to be reported here were performed in an endeavor to determine directly the action of sulfanilamide upon the meningococcus present in spinal fluid obtained from patients with meningococcal meningitis. The procedure is based upon the fact that incubation of spinal fluid, which contains only a relatively small number of meningococci, may result in a

1 Bliss, E. A., and Long, P. H., *J. Am. Med. Assn.,* 1937, **109**, 1524.

2 Colebrook, L., Buttle, G. A. H., and O'Meara, F. A. Q., *Lancet,* 1936, 1323.

3 Colebrook, L., and Kenny, M., *Lancet,* 1936, 1297.

4 Long, P. H., and Bliss, E. A., *J. Am. Med. Assn.,* 1937, **108**, 32.

5 Rosenthal, S. M., *Publ. Health Reports,* 1937, **52**, 192.

6 Wengatz, H. F., Boak, R. A., and Carpenter, Ch. M., *J. Bact.,* 1938, **35**, 36.

* Mellon and Bambas (Mellon, R. R., and Bambas, L. L., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 682) showed that spinal fluid of patients treated with sulfanilamide is bacteriostatic toward the streptococcus.

7 Gay, F. P., and Clark, A. R., *J. Exp. Med.,* 1937, **66**, 535.

8 Branham, S. E., and Rosenthal, S. M., *Publ. Health Reports,* 1937, **52**, 685.

9 Buttle, G. A., Gray, W. R., and Stephenson, D., *Lancet,* 1936, 1286.

10 Long, P. H., and Bliss, E. A., *J. Bact.,* 1938, **35**, 35.

11 McPherson Brown, Th., *Bull. Johns Hopkins Hosp.,* 1937, **61**, 272.

12 Proom, H., *Lancet,* 1937, 16.

13 Rosenthal, S. M., Bauer, H., and Branham, S. E., *Publ. Health Rep.,* 1937, **52**, 662.

14 Schwentker, F. F., Gelman, S., and Long, P. H., *J. Am. Med. Assn.,* 1937, **108**, 1407.

marked increase in the number of microörganisms. Therefore, the influence of sulfanilamide upon the growth of meningococci in the spinal fluid itself can be examined.

The following protocol represents a typical experiment: Four drops of cloudy spinal fluid obtained from a patient with meningococcal meningitis prior to treatment, were mixed with 10 drops of each of the following dilutions of 0.8% sulfanilamide dissolved in physiological saline solution: 1:1; 1:10; 1:100; 1:1000, and 1:10,000 (tubes a-e respectively). The preparation used was *p*-aminophenylsulphonamide, repurified for injection. To the control tube (f) 10 drops of physiological saline solution were added. The experiments were carried out under sterile precautions. The tubes were well shaken and incubated at 37°C. for 48 hours. Films were made at various intervals from all tubes. The result of this experiment is given in Table I.

TABLE I.

Action of P-aminophenylsulphonamide on Growth of Meningococci in Spinal Fluid. 4 drops of spinal fluid of patient with meningococcal meningitis mixed with

	10 drops 0.8% Prontylin diluted with saline solution					10 drops saline solution
	1:1	1:10	1:100	1:1000	1:10,000	
Tubes	a	b	c	d	e	f
Growth after				Growth		
18 hr. at 37°C.	No	No	No	No	Marked	Marked
48 hr. at 37°C.	"	"	"	Some	"	"

It may be seen that sulfanilamide markedly inhibits the growth of meningococcus in spinal fluid. Dilutions of 1:1 (800 mg. %) up to 1:100 (8 mg. %) completely prevented the augmentation of meningococci during 24 to 48 hours; a dilution of 1:1,000 (0.8 mg. %) caused only a partial inhibition. The control tube of spinal fluid mixed with physiological saline solution instead of sulfanilamide showed a very marked increase in the number of meningococci within 24 hours. Similar results were obtained with spinal fluids of 4 more patients.

In order to determine the influence of sulfanilamide upon the viability of meningococci present in spinal fluid, subcultures were made from the spinal fluid-drug mixtures on chocolate ascitic agar plates. These plates were incubated at 37°C. in a jar containing about 10% CO_2. The experiments revealed that no growth or a markedly diminished growth occurred in the spinal fluids previously incubated with sulfanilamide in dilutions of 1:1 (800 mg. %) or 1:10 (80 mg. %) in comparison with spinal fluid mixed with physiological saline solution. Smaller amounts were ineffective in this

particular case. In another experiment, spinal fluid incubated with the drug in dilutions up to 1:1,000 (0.8 mg. %) for 24 hours failed to show growth; the same specimen incubated with sulfanilamide in a dilution of 1:10,000 (0.08 mg. %) showed some growth of meningococci while the control tube of spinal fluid mixed with saline solution grew out profusely. Similar experiments revealed that large numbers of meningococci present in incubated spinal fluid, when treated with sulfanilamide, may fail to grow or may grow less profusely than in spinal fluid mixed with physiological saline solution. Notwithstanding this result, no conclusion should be drawn concerning a true bactericidal action of sulfanilamide upon the meningococcus present in spinal fluids.

In summary, sulfanilamide exerts a bacteriostatic effect upon the meningococcus present in spinal fluid obtained from patients with meningococcal meningitis. Clinical observations may show whether this kind of experiment can give an indication of the effectiveness of this drug in the treatment of meningococcal meningitis.

9731 P

Experimental Street Virus Rabies in White Mice. Studies on Passive Immunization. II.*

ANSON HOYT AND M. KATHERINE GURLEY.

From the Department of Bacteriology, School of Medicine, University of Southern California, and the Los Angeles County Hospital, Los Angeles.

In a recent publication[1] from our department it was reported that white mice could be afforded a certain degree of passive protection against intracerebral inoculations of rabies street virus if large amounts of antirabic serum were injected intraäbdominally before the administration of virus. One experiment indicated that rabbit antirabic serum gave better protection than had previously been demonstrated for goat antiserum. The present report covers further evidence of the value of rabbit antirabic serum.

Rabbits were immunized by weekly intramuscular injections of 5 cc. of a 5% fixed virus suspension in saline solution. Phenolized virus (½% phenol) was used for the first few injections; fresh

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[1] Hoyt, Anson, and Gurley, M. Katherine, PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 454.