13078

Inhibition of Sulfapyridine by the Procaine in Chest Fluids after Procaine Anesthesia.*

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Wood[1] reported the inhibition of bacteriostasis of hemolytic streptococci by sulfanilamide induced by yeast extract. He showed by chemical analysis that the active fraction of the yeast extract was probably identical with p-aminobenzoic acid. He also tested the anti-sulfanilamide action of various compounds related to p-aminobenzoic acid. One of these was an ester derivative, procaine (novocaine). The inhibiting action of procaine was of the same order as p-aminobenzoic acid, though its action was delayed.

Procaine is widely used as a local anesthetic for pleural aspirations and it is possible to demonstrate its presence in the fluids removed, so that a study was undertaken to determine the amount of procaine present, and the inhibitory effect of these amounts on sulfapyridine.

To determine the amount of procaine in pleural fluids, Marshall's test[2] for sulfapyridine was employed, because procaine couples with N (1 naphthyl) ethylene diamine dihydrochloride to give the characteristic red color. With known concentrations of procaine, using a photoelectric colorimeter, a standard curve was drawn.

Pleural fluid‡ was aspirated from 10 tuberculosis patients under procaine§ anesthesia using a syringe and needle uncontaminated by procaine; they had received no chemotherapy. The average concentration of procaine in these fluids was 0.0002%. To test the inhibiting effect of these concentrations, sulfonamide inhibitor-free liver media (MacLeod)[3] was employed in all experiments. Tubes containing 5 ml of medium were seeded to contain 1,000 organisms

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1 Wood, D. D., *Brit. J. Exp. Path.*, 1940, **21**, 74.

2 Bratton, A. C., and Marshall, E. K., Jr., *J. Biol. Chem.*, 1939, **128**, 537.

‡ Obtained through the courtesy of Dr. Barnet P. Stivelman.

§ 2% (about 1½ cc).

3 MacLeod, C. M., *J. Exp. Med.*, 1940, **72**, 217.

4 Bukantz, S. C., Cooper, A., and Bullowa, J. G. M., accepted for publication in *J. Bact.*

TABLE I.
Inhibitory Effect of Procaine on Bacteriostatic Action of Sulfapyridine Against Pneumococcus III (T3-1).*

Conc. of Sulfapyridine	Concentration of procaine				
	0	.02%	.002%	.0002%	.00002%
%					
0	++++	++++	++++	++++	++++
.003	—	++++	++++	++++	—
.004	—	++++	++++	++++	+
.005	—	++++	++++	++++	—

— no growth.
+ slight growth.
++++ abundant growth.
*Growth observed at 18 hours after incubation at 37°C.

per ml of a standardized strain of Pneumococcus III (T3-1).[4] A series of concentrations of procaine were tested with varying amounts of sulfapyridine. Table I shows that 0.0002% of procaine, which is the average amount found in plural fluids of patients thus anesthetized, is sufficient to inhibit the action of 0.003, 0.004, and 0.005% of sulfapyridine.

It is possible that after procaine anesthesia sufficient procaine may be present in the remaining chest fluid to at least temporarily inhibit the action of sulfapyridine and permit bacterial growth. The effect of urethane on sulfapyridine was studied because it does not couple in the Marshall test. It was found that in concentrations as high as 0.05% urethane did not inhibit sulfapyridine.

Summary. 1. The average concentration of procaine in pleural fluids removed with this anesthetic was 0.0002%. 2. Sulfapyridine in concentrations as high as 0.005% was inhibited by procaine *in vitro*. 3. Concentrations of urethane as high as 0.05% do not inhibit the action of sulfapyridine *in vitro*.

13079

Influence of Prolonged Electrolyte Deprivation and Final Restoration on Fluid Intake, Balance and Distribution.

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Gilman[1] found that the intravenous injection of an hypertonic salt solution, which increased the volume of the plasma and interstitial

[1] Gilman, A., *Am. J. Physiol.*, 1937, **120**, 323.