

Treatment with all compounds was carried out at the following time intervals: 1½, 7, 24 and 32 hours after inoculation and once each day thereafter until death occurred, or up to and including the 15th day. The preparations were administered as suspension in ¼ to ½ cc of milk (per single dose) by means of the stomach tube.

In the first experiment, all surviving mice were killed and necropsied on the 20th day. The results of this study, based on the pathological findings, are shown in Table I.

A second experiment was carried out in similar manner except that on the 20th day one kidney was removed and cultured. The results of this study, based on pathologic and bacteriologic findings, are shown in Table II.

At necropsy there was a striking contrast in the gross appearance of the tissues of mice treated with sulfathiazol and sulfamethylthiazol as compared with mice which had received sulfapyridine or minimal doses of sulfanilyl sulfanilamide. In a significant number of animals treated with these two thiazol compounds the kidneys, prostate, liver and spleen were essentially normal except for a few scars from healed abscesses. In several mice to which sulfathiazol and sulfamethylthiazol had been administered no *Staphylococcus* infection could be demonstrated by pathological or bacteriological methods.

Conclusions. Sulfathiazol and sulfamethylthiazol prolong the life of mice infected experimentally with a highly mouse virulent strain of *Staphylococcus aureus* and prevent the development and allow healing of abscesses in kidneys and other organs in a significant number of animals.

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Effectiveness of Neoarsphenamine, Sulfanilamide, Sulfapyridine in Marrow Cultures with *Staphylococci* and *Alpha Streptococci*.

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Edward and John LeCocq¹ have reported beneficial effects of therapy with neoarsphenamine in patients with osteomyelitis and bacteriemia due to the hemolytic *Staphylococcus aureus*. Using the

¹ LeCocq, E., *West. J. Surg.*, 1936, 44, 655; LeCocq, John, personal communication.

TABLE I.
Effect of Neoarsphenamine on Hemolytic *Staphylococcus aureus* Infections of Marrow Cultures.

Initial colonies per cc	Arsenic per cc in mg	Neoarsphenamine, mg per cc	No. of colonies per cc			
			4-6 hr	24 hr	48 hr	72 hr
Controls*	0.00	0.0	870	400,000,000		
5	2.06	6.4	0	0	0	
5	.01	.05	5	0	0	
10	.014	.045		0	0	
10	.012	.04		0	0	
10	.010	.03		0	0	
10	.007	.02		0	0	
11	.005	.015	5	0	0	
51	.004	.012	16	0	0	
11	.004	.012	0	0	0	
51	.003	.010	25	4	0	
3	.003	.009	0	0		
11	.003	.008	0	0	0	
13	.003	.008	14	16		
3	.003	.008	0	0		
3	.0025	.008	0	0		
13	.0025	.008	40	160	290	
51	.0025	.008	150	103		5
13	.002	.006	48	400	9,340	
51	.002	.006	40	5		2
3	.002	.006	0	0		
3	.0016	.005	0	0		
5	.0016	.005	15	184,000	199,000,000	
11	.0016	.005	25	25	12	
13	.0016	.005	192	49,000	250,000	
51	.0016	.005	40	25		1
3	.0014	.004	2	0		
13	.0012	.004	304	125,000	500,000	
3	.0011	.003	2	0		
10	.0002	.0006	15	282,000,000		
10	.0001	.0003	120	320,000,000		

* Controls were run for each experiment, but all were similar.

marrow culture technic,² the data given in Table I were obtained on hemolytic *Staphylococcus aureus* infections. Note that in all the controls the colony count reached 400,000,000 per cc in 24 hours. In those cultures containing over 15 parts per million of neoarsphenamine marrow cells were destroyed as well as the staphylococci. In those cultures containing over 9 parts per million of neoarsphenamine sterility uniformly resulted. In those cultures containing 3 to 6 parts per million of neoarsphenamine sterility frequently occurred, and in the others growth of the organism was greatly inhibited. Marrow cells were completely undamaged by 6 parts per million of the drug. In no culture did the presence of 1-10,000 concentrations of sulfanil-

² Osgood, E. E., and Brownlee, Inez E., *J. A. M. A.*, 1937, **108**, 1793; Osgood, E. E., *J. A. M. A.*, 1938, **110**, 349; Osgood, E. E., *Arch. Int. Med.*, 1938, **62**, 181; Osgood, E. E., *J. Lab. and Clin. Med.*, 1939, **24**, 954.

amide or sulfapyridine result in sterility, and the colony counts were usually of the order of 12,000,000 per cc for sulfapyridine and 40,000,000 per cc for sulfanilamide at the time when the colony count in the control reached 100,000,000 per cc.³

Studies of alpha hemolytic streptococcus infections made by the same technic showed an even greater effectiveness of neoarsphenamine and an even lesser effectiveness of sulfanilamide and sulfapyridine.

Since the concentration of the drug must be above 3 parts per million for a period of 6 to 24 hours it would seem that frequent small doses or administration of neoarsphenamine by the method of continuous drip⁴ should be more effective than single larger doses at longer intervals. Studies of the clinical effectiveness of this drug in staphylococcal bacteriemia and in subacute bacterial endocarditis and of the comparative effectiveness in marrow cultures of other arsenicals are in progress.

Summary. In cultures of living human marrow inoculated with hemolytic *Staphylococcus aureus* or alpha streptococci (*Streptococcus viridans*) neoarsphenamine in concentrations of 3 to 9 parts per million was far more effective than 1-10,000 concentrations of either sulfanilamide or sulfapyridine, and did not significantly damage marrow cells.

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Hyaluronic Acid in Pleura Fluid Associated with Malignant Tumor Involving Pleura and Peritoneum.

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Hyaluronic acid, a high molecular weight polysaccharide composed of acetylglucosamine and glucuronic acid in equimolar concentrations, has been obtained from the following sources: vitreous humor of cattle and swine,^{1, 2} human umbilical cord,¹ cattle and human synovial

³ Osgood, E. E., Marrow Cultures, Figures 17-19 and 21, Symposium of the Blood and Blood-Forming Organs, University of Wisconsin Press, pp. 219-241, 1939.

⁴ Hyman, H. T., Chargin, L., Rice, J. L., and Leifer, J. A. M. A., 1939, **113**, 1208.

¹ Meyer, K., and Palmer, J. W., *J. Biol. Chem.*, 1936, **114**, 689.

² Meyer, K., Smyth, E. M., and Gallardo, E., *Am. J. Ophthal.*, 1938, **21**, 1083.