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Sulfapyridine and Serum in Experimental Type III Lobar Pneumonia.

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Previous experiments[1] have demonstrated that sulfapyridine and sulfanilamide were about equally effective in reducing mortality in Type III lobar pneumonia of rats. Up to the time of publication of those results, the samples of specific antiserum that we had tested had shown no decisive effects in protecting against Type III infections in rats. Within the last year accurately standardized, highly concentrated Type III serums* have been available and in our experiments, when used in large doses, they have exhibited a protective value approaching that of type specific serum in Type I pneumococcic pneumonia.[2]

In these experiments serum and sulfapyridine† were used together and separately in doses which had been found to afford the greatest degree of protection. The optimal quantity of serum was found to be between 1,000 and 2,000 units per rat when the total was distributed over a period of 7 days and that for sulfapyridine between 850 and 1250 mg when given in divided doses over the same period.

One hundred and sixty young adult rats weighing between 140 and 280 g were infected in groups of 40 by the intrabronchial method previously described by Nungester and Jourdonais.[3] In each group there were 10 untreated controls, 10 treated with serum by intraperitoneal injection, 10 treated with sulfapyridine, administered by stomach tube, and 10 treated with both serum and sulfapyridine.

The strain of Type III pneumococcus was that used in previous experiments.[1] The dose used in the first 2 groups of 40 rats was 0.1 cc of a 16-hour bouillon culture, diluted to 10^{-5}. This produced in the untreated controls a mortality of 63%. In the third and fourth groups the dose was increased 10 times (10^{-4} dilution) and the initial mortality was 100%.

Treatment was begun in all cases about 4 hours after injection.

* Donated by Lederle Laboratories, Inc., New York, N. Y.

† Donated by Merck and Company, Rahway, N. J.

1 Kepl, M., and Gunn, F. D., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 457.

2 Kepl, M., and Gunn, F. D., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 529.

3 Nungester, W. J., and Jourdonais, L. F., *J. Bact.*, 1935, **29**, 34.

TABLE I.
Sulfapyridine and Serum in Experimental Type III Lobar Pneumonia.

Total No. of rats	No. survivors	No. fatalities	% mortality	Therapy	Dilution of organisms
19*	7	12	63	None	1:100,000
20	13	7	35	Serum	1:100,000
19*	14	5	26	Sulfapyr.	1:100,000
19*	14	5	26	Serum and Sulfapyr.	1:100,000
20	0	20	100	None	1:10,000
20	4	16	80	Serum	1:10,000
18*	11	7	39	Sulfapyr.	1:10,000
16*	10	6	37	Serum and Sulfapyr.	1:10,000

*In each group 20 animals were originally injected. However, those killed by trauma incurred by the injection of the drug, or those which did not show the ink spot tracer in the lung on post-mortem examination, were deleted from the experiment.

The initial dose of sulfapyridine was 250 mg, emulsified in 2 cc of 1.5% mucin. This was followed by a twice daily dose of 125 mg for 2 days and then 125 mg daily for 4 more days. In the first 2 experiments the initial dose of serum was 250 units in 1 or 2 cc of saline and the maintenance dose was 125 units given twice daily on the second and third days and once a day for the next 4 days. In the third and fourth experiments the method differed only in that the initial dose was 500 units instead of 125 units.

In the table, the first and second groups and the third and fourth groups are combined. Serum therapy alone resulted in a reduction of mortality from 63% to 35% in the 80 rats which were infected with the smaller dose of pneumococci. Under the same conditions, animals receiving sulfapyridine alone showed a mortality of 26%. The same figure is shown for the group receiving both serum and sulfapyridine.

In the 80 rats which were infected with the larger dose (10^{-4} dilution) serum therapy reduced the mortality from 100% to 80%; sulfapyridine therapy reduced it to 39%. A combination of sulfapyridine and serum showed no significant improvement over sulfapyridine therapy alone, giving a mortality of 37%. Under the second group of conditions, where the most important factor which has been changed is the dose of pneumococci (increased from a dilution of 10^{-5} to 10^{-4}) sulfapyridine appears to be about 3 times as effective as serum (survival rate of about 60% for sulfapyridine and about 20% for serum). In unpublished experiments we have found that a further increase of the dose of serum, especially in the first 2 days, does not further reduce the mortality when the infecting dose is large.

Summary. Under the conditions of our experiments the protective value of highly concentrated type specific serum in optimal doses and that of sulfapyridine in optimal doses are approximately equal when the infecting dose of Type III pneumococci is relatively small, resulting in a mortality of 63% in untreated animals. When the infecting dose is sufficiently large to produce an initial mortality of 100%, the mortality after sulfapyridine therapy is significantly less than after serum therapy. Combining serum and sulfapyridine, each in optimal dose, does not reduce mortality below that of sulfapyridine therapy alone in Type III pneumococcic pneumonia, differing in this respect from results previously obtained from similar experiments with Type I pneumococcic pneumonia.

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Effect of Sulfanilamide, Sulfapyridine, and Sulfathiazole on Staphylococcus Toxins.*

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Conflicting reports have appeared in the literature on the neutralization of staphylococcus toxins by sulfanilamide and allied compounds. Levaditi and Vaisman[1] were unable to demonstrate any effect of prontosil, neoprontosil, and other azo-sulfonamide derivatives against staphylococcal hemolysin, although they claimed these compounds neutralized the effect of streptococcal leucocidin and hemolysin. Later Levaditi, Vaisman, and Reinie[2] reported that none of the compounds tested was effective against staphylococcus lethal toxin. Osgood and Powell[3] found that sulfanilamide in concentrations of 1:1000 or less did not inactivate significant amounts of staphylococcal hemolysin. Recently Carpenter and his co-

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1 Levaditi, C., and Vaisman, A., *Compt. Rend. Soc. de Biol.*, 1935, **120**, 1077.

2 Levaditi, C., Vaisman, A., and Reinie, L., *Compt. Rend. Soc. de Biol.*, 1937, **126**, 1937.

3 Osgood, E. E., and Powell, H. M., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 37.