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Sulfanilamide, Antipneumococcus Serum and Vitamin C Therapy in Type II Pneumococcal Pneumonia of Rats.

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We have reported the successful therapy of experimental Type III and Type I pneumococcal rat pneumonia by the oral administration of sulfanilamide* (*p*-aminobenzenesulfonamide),[1, 2, 3] and also a comparison of sulfanilamide and serum therapy, as well as the combination of both, in Type I pneumococcal rat pneumonia.[3]

The present report is based on experiments with 2 different strains of the Type II pneumococcus and 162 rats. The efficacy of sulfanilamide was tested against these infections and compared with that of Type II antiserum, vitamin C,† and all possible combinations of these substances.

All animals were infected as previously described[2] and treated as indicated under Figs. 1 and 2. Preliminary titrations showed that while strain II-B caused death consistently in rats in a dilution of 1:500 in 1 to 5 days by empyema, bacteremia, and only a minimal pneumonia, dilutions of 1:5 (which were used in this experiment) were necessary to produce a lobar type of pneumonia. Dilutions of 1:1000 of the "Binda" strain regularly produced the desired lesion.

In Experiment 1 treatment was discontinued on the 4th day because most of the controls were dead and the lack of deaths in Groups D, F, G, and H had failed to show any advantage of combination therapy over sulfanilamide alone. Since the deaths that occurred in the next 5 days were evenly distributed throughout these groups, treatment was resumed as indicated.

All rats, including the 15-day survivors, were necropsied and examined as in the previous experiments.[1, 2, 3] The results are shown graphically in Figures 1 and 2.

Sections from the lungs of the fatalities, with the exceptions noted (Fig. 1), showed a lobar type of pneumonia of variable degree and in different stages of development. In the survivors, the infection

* Kindly supplied by Merck & Co., Inc., Rahway, N. J.

1 Gross, Paul, and Cooper, Frank B., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 225.

2 Cooper, Frank B., and Gross, Paul, PROC. SOC. EXP. BIOL. AND MED., in press.

3 Gross, Paul, and Cooper, Frank B., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 535.

† Kindly supplied by Chas. Pfizer and Co., New York.

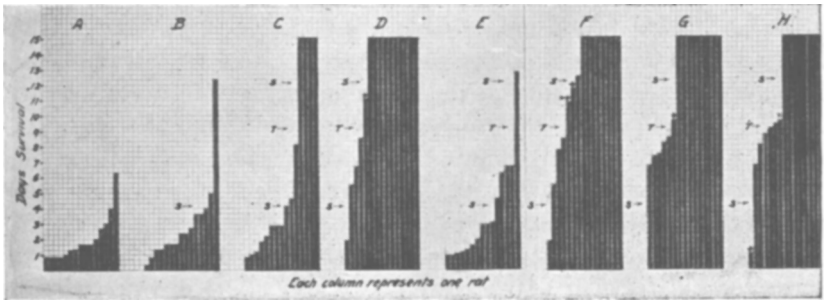

FIG. 1.

Infecting dose: 0.2 cc. of a 1:1000 dilution (in mucin) of an 18-hour broth culture of Strain Binda intrabronchially. A. Untreated control. B. Vitamin C, 10 mg. in water (freshly prepared) twice daily, by mouth. C. 300 units of Type II antiserum intraäbdominally, daily. D. Single dose of 125 mg. sulfanilamide by mouth, daily. E. Combination of B and C. F. Combination of B and D. G. Combination of C and D. H. Combination of B, C and D. All initial treatments given 6 hours after infection. S. Treatments stopped. T. Treatments again started. †No gross evidence of pneumonia. *Enteritis.

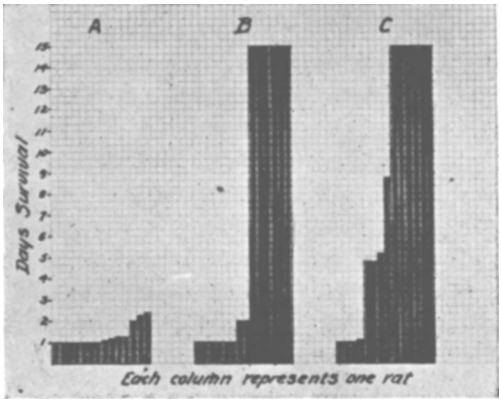

FIG. 2.

Infecting dose: 0.2 cc. of a 1:5 dilution (in mucin) of an 18-hour broth culture of Strain II-B intrabronchially. A. Untreated control. B. 250 units of Type II antiserum, intraäbdominally for 3 consecutive days. C. Single dose of 125 mg. sulfanilamide by mouth, daily, for 9 consecutive days. All initial treatments were given 6 hours after infection.

was represented either by a thickening of the alveolar walls with associated monocytic infiltration, or by a variety of other lesions such as well walled-off abscesses, foci of chronic, organizing pneumonia, and occasionally foci of more recently developed pneumonia.

Experiments with both strains showed that sulfanilamide alone was highly efficacious in reducing the mortality of rats suffering from Type II pneumococcal pneumonia. Compared with the specific antiserum, in the doses employed, the sulfanilamide was at least as

effective against heavy doses of Strain II-B, and twice as effective as the serum against a moderate, but lethal, dose of Strain Binda. The average survival time of the rats that ultimately succumbed was 2 to 3 times greater in the groups in which sulfanilamide was given alone or in combination, than in the groups treated only with serum. The combination of any 2 or of all 3 therapeutic agents gave no better results than sulfanilamide alone.

Vitamin C administration alone or in combination with either the serum or the drug, or both, had no beneficial effect in rats; whereas in rabbits, Locke and Mellon[4] observed a marked reinforcement of the drug's action, apparently through stimulation of the phagocyting mechanism. But in mice the sulfanilamide alone appears to overcome hemolytic streptococcal infections largely by its rapid mobilization of the clasmatocytes.[5]

It should be noted that some of the deaths in Groups D, F, G, and H, were probably due to premature termination of the treatments on the 4th day. Many of the rats that died after this time showed pneumonias which appeared to be no older than 48 to 72 hours. Three of the late fatalities in these groups died of intercurrent enteritis and showed a minimal residual pneumonia.

Bacteremia, as judged from stained blood smears, was reduced 50% to 70% in all groups of both experiments where treatment included sulfanilamide. In this respect, serum was effective against Strain II-B, but not significantly so against the Binda strain.

Conclusions. 1. Sulfanilamide was at least as effective as specific antiserum, in the doses employed, in treating Type II pneumococcal rat pneumonia. A probable clinical application to similar human pneumonia is thereby suggested. 2. The combination of sulfanilamide and serum was no more effective than sulfanilamide alone. 3. Contrary to the observations in rabbits (Locke and Mellon[4]), in rats Vitamin C alone, or in any combination tried, is ineffective.

[4] Locke, A. P., and Mellon, R. R., in press.

[5] Mellon, R. R., and McKinney, R. A., in press.