iron, leaving zinc sulphate as the most effective protective agent of all the substances investigated. This high efficiency of zinc sulphate is in agreement with recent observations of Schultz and Gebhardt.[2] With this very potent test dose of virus zinc sulphate protected 16 of 17 monkeys tested at 2 days, all of 4 at 30 days and 2 of 5 at 49 days after the last chemical treatment.

9299

P-Aminobenzenesulfonamide and Antipneumococcal Serum Therapy in Type I Pneumococcal Infections of Rats.

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Although Hörlein[1] claimed that Prontosil was effective against Type III pneumococcal infections, experimental proof for this assertion was lacking until Rosenthal[2] and Cooper, Gross, and Mellon[3] independently investigated this problem.

They demonstrated that *p*-aminobenzenesulfonamide gave mice a certain degree of protection against lethal doses of the particular strains of Type III pneumococcus employed. Buttle, Parish, McLeod, and Stephenson,[4] however, were unable to demonstrate any significant protection in mice infected with Types I and II pneumococci, whereas Rosenthal[2] obtained protection against all 3 fixed types.

The lack of parallelism between pneumococcal septicemia in mice and pneumonia in man led to the choice of the experimental pneumococcal pneumonia in the rat[5, 6] as a closer approximation to human pneumonia. The encouraging results obtained by treating such experimental Type III pneumonia with *p*-aminobenzenesulfonamide[7, 8]

[2] Schultz, E. W., and Gebhardt, L. P., PROC. SOC. EXP. BIOL. AND MED., 1937, **35**, 524.

[1] Hörlein, H., *Proc. Royal Soc. Med.*, 1936, **29**, 321.

[2] Rosenthal, S. M., *Public Health Reports*, 1937, **52**, 48.

[3] Cooper, F. B., Gross, P., and Mellon, R. R., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 148.

[4] Buttle, G. A. H., Parish, H. J., McLeod, M., and Stephenson, D., *Lancet*, 1937, **1**, 681.

[5] Nungester, W. J., and Jourdonais, L. F., *J. Bact.*, 1935, **29**, 34.

[6] Gunn, F. D., and Nungester, W. J., *Arch. Path.*, 1936, **21**, 813.

[7] Gross, P., and Cooper, F. B., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 225.

[8] Cooper, F. B., and Gross, P., to be published.

have been duplicated in the treatment of human Type III pneumococcal pneumonia as reported by Heintzelman, Hadley and Mellon.[9]

The relative therapeutic efficacy of *p*-aminobenzenesulfonamide and of potent specific antipneumococcal serum was investigated in rats infected intrabronchially with the Type I (Neufeld) strain. The inoculum, 0.1 cc. of which was injected, consisted of an 18-hour broth culture diluted 1000 times with broth, and sufficient mucin (Armour) added to give a viscous solution.

Fifty-six rats, infected in this manner, were divided into 4 groups of 14 each: Group A—Untreated controls. Group B—Given 250 units of Type I antipneumococcal serum intraäbdominally 6 hours after infection, followed by 2 similar daily doses. Group C—Given

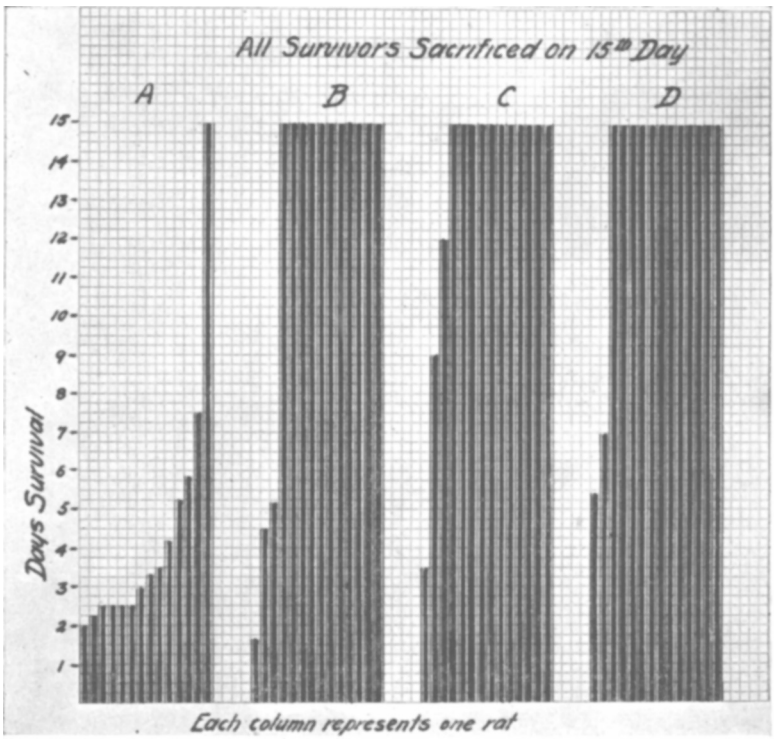

FIG. 1.

Graph of survival-time of rats infected intrabronchially with Type I pneumococcus.
A. Untreated controls.
B. Treated with Type I antipneumococcal serum.
C. Treated with *p*-aminobenzenesulfonamide by mouth.
D. Treated with both serum and *p*-aminobenzenesulfonamide.

[9] Heintzelman, J. H. L., Hadley, P., and Mellon, R. R., *Am. J. Med. Sci.*, in press.

125 mg. of *p*-aminobenzenesulfonamide* by mouth 6 hours after infection, followed by 10 daily similar doses. Group D—Treated 6 hours after infection by a combination of the treatments used in Groups B and C.

Animals surviving to the 15th day were killed with ether. All animals of each group were necropsied and smears from the blood (femoral vein), peritoneum, and pleura, were stained by Gram's method. Sections were made from all lobes of the lungs of each rat.

The effect of the various types of treatment on the survival-time and rate is shown graphically in Fig. 1. The gross and microscopic anatomic changes in the lungs, as well as the bacteriologic findings, are tabulated in Table I. A summary of the findings is given in Table II.

Contrary to the results reported by Gunn and Nungester[6] and by us,[7, 8] a lobar type of pneumonia developed in only a few rats. Curiously enough, the most extensive and fully developed lobar type was seen in the non-survivors of the treated groups.

Inflammatory changes were found in the lungs of every animal. Grossly, the changes were often minimal and not recognized. Bilateral empyema was frequently the outstanding postmortem finding. The most constant change was the interstitial pneumonia, more severe in the survivors than in the rats which died early. These interstitial changes represented, no doubt, the residues of subsiding pneumonias.

The reduction in the mortality-rate from 93% in the control group to 21% in the groups treated with serum or the drug, and to 14% in the group treated with both, clearly indicates that *p*-aminobenzenesulfonamide may have a definite place in the treatment of human Type I pneumococcal pneumonia in conjunction with specific antiserum; and particularly where antiserum is not available for economic or other reasons. Concomitant with the drop in mortality-rate there was a reduction in bacteremia, peritonitis (determined by the smears), and empyema (Table II).

The deaths in the drug-treated Group C occurred later than those of the serum-treated Group B, although they were numerically equal. Also, in the drug-treated group, 64% of the rats had no broncho- or lobar pneumonia, whereas only 50% of the rats in the serum-treated group were so spared. A rough approximation of the degree of microscopic involvement indicates less impairment in the group treated with *p*-aminobenzenesulfonamide than in the group treated with serum.

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

TABLE I.

Tabulation of necropsy findings. All animals which survived to the 15th day were sacrificed.

Treatment	No. Rat	Days Survival	Gross Pneumonia		Microscopic Pneumonia			Empyema	Peritonitis	Pneumococci in Smears of Blood Pleura Peritoneum		
			Right Lung	Left Lung	Lobar	Broncho	Interstitial					
None	1	2	—	—	—	+	++	—	—	+	+	—
	2	2	—	+	—	+	++	—	+	++	++	++
	3	2½	—	+	++	—	+	—	+	++	++	++
	4	2½	++	++	—	++++	—	+	+	++	++	++
	5	2½	—	+	+	+++	+++	—	+	++	++	++
	6	2½	++	—	++	+	+++	—	+	++	++	++
	7	3	++	—	—	++	+	+	+	+	++	++
	8	3	—	—	—	+	+	+	+	—	++	++
	9	3½	—	+	—	+++	++	+	+	+	++	++
	10	4	—	+	—	+++	+	+	+	++	++	++
	11	5	—	—	++	++	++	+	+	—	++	++
	12	6	—	+	—	+	++++	+	+	—	++	++
	13	7½	—	+	—	++	—	—	+	—	++	+
	14	15	—	—	—	—	+	—	—	—	++	—
250 units serum, 3 successive days	1	1½	++++	+	++++	—	+	—	—	+	++	—
	2	4½	+	+	++	++	+	+	—	—	++	—
	3	5	—	++++	++++	—	++++	+	—	—	++	—
	4	15	—	—	—	—	++	—	—	—	—	—
	5	15	—	—	—	+	+++	—	—	—	—	—
	6	15	—	—	—	—	+++	—	—	—	—	—
	7	15	—	—	—	—	++	—	—	—	—	—
	8	15	++	+	—	++	+++	—	—	—	—	—
	9	15	++	+	—	+	+++	—	—	—	—	—
	10	15	—	—	—	—	+	—	—	—	—	—
	11	15	—	—	—	—	++	—	—	—	—	—
	12	15	—	+++	—	+++	+++	—	—	—	—	—
	13	15	—	—	—	—	+	—	—	—	—	—
	14	15	—	—	—	—	++	—	—	—	—	—

125 mg. *P*-aminobenzenesulfonamide for 11 consecutive days	1	3½	++	+	—	+	++	+	—	—	+	—
	2	9	—	+++	++++	++	+++	+	+	—	+	+
	3	12	—	++++	++++	—	—	+	—	+	+	—
	4	15	—	—	—	—	+	—	—	—	—	—
	5	15	—	—	—	—	++	—	—	—	—	—
	6	15	—	—	—	—	++	—	—	—	—	—
	7	15	—	—	—	—	+	—	—	—	—	—
	8	15	—	—	—	—	++	—	—	—	—	—
	9	15	—	—	—	—	+	—	—	—	—	—
	10	15	+	+	—	+++	++	—	—	—	—	—
	11	15	—	—	—	—	+++	—	—	—	—	—
	12	15	+	—	—	—	++	—	—	—	—	—
	13	15	+	—	—	—	++	—	—	—	—	—
	14	15	++	+	—	+	+++	—	—	—	—	—
Treated with both serum and drug as above	1	5½	—	—	—	++	+++	—	—	—	—	—
	2	7	++++	+	++++	—	—	—	—	—	+	—
	3	15	—	—	—	—	+	—	—	—	—	—
	4	15	—	—	—	—	++	—	—	—	—	—
	5	15	—	—	—	—	+	—	—	—	—	—
	6	15	—	—	—	—	++	—	—	—	—	—
	7	15	—	+	—	—	+++	—	—	—	—	—
	8	15	—	—	—	—	++	—	—	—	—	—
	9	15	—	—	—	+	+++	—	—	—	—	—
	10	15	—	—	—	—	++	—	—	—	—	—
	11	15	—	—	—	—	++	—	—	—	—	—
	12	15	—	—	—	—	++	—	—	—	—	—
	13	15	—	—	—	—	+	—	—	—	—	—
	14	15	—	—	—	—	+	—	—	—	—	—

TABLE II.
Summary of Results Listed in Table I.

	Group A Control	Group B Serum Treated	Group C *P*-amino-benzenesul-fonamide Treated	Group D Combination Drug and Serum Treated
	%	%	%	%
Mortality rate	93	21	21	14
Bacteremia	64	7	7	0
Peritonitis	86	0	7	0
Empyema	50	14	21	0
Absence of lobar or broncho-pneumonia microscopically	7	50	64	79
Degree* of microscopic pulmonary involvement	3.9	3.6	2.9	2.3

* These values represent the group-average of the number of plus signs found in the columns "Microscopic Pneumonia" of Table I.

It appears, therefore, that in the relative dosages employed in this experiment, the efficacy of the drug is as great as, if not greater than, that of the specific serum. The data also show that the best therapeutic results were obtained by a combination of serum and drug, indicating that the two methods of treatment are synergistic. On the basis of the excellent therapeutic results here obtained, it is suggested that this drug be tried in human Type I pneumonia in conjunction with the specific antiserum and particularly in cases where the antiserum is not available. This suggestion is supported by the parallelism which has been demonstrated with *p*-aminobenzenesulfonamide therapeusis of both rat and human Type III pneumococcal pneumonia and also by the fact that at times hemolytic streptococci are known to complicate pneumococcal pneumonias.

9300

Effect of Hypophysectomy on Blood Lactic Acid of *Rhesus* Monkeys.

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Work on blood sugars in normal and hypophysectomized monkeys has been recently reported (Smith, *et al.*[1]). Blood lactic acid was simultaneously determined in many of these samples.

1 Smith, P. E., Dotti, L., Tyndale, H. H., and Engle, E. T., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 247.