fewer instances of purulent pleuritis and pericarditis. Eight, however, showed fully developed lobar pneumonia and the others evidence of septicemia (splenitis, pyemic abscesses, etc.) at the time of death.

Since the number of survivors was not increased in significant degree by prolongation of the period of therapy (actually decreased in the case of sulfapyridine) we have combined the figures from the 2 groups for comparative purposes and they are illustrated in percentage values in the block graph (Fig. 1).

Summary. When treatment was begun 4 hours after the time of inoculation with the infecting dose, both sulfanilamide and sulfapyridine were partly effective in protecting rats against Type III pneumococcal pneumonia. There was no significant difference under the conditions stated between the effects of the 2 drugs in preserving life but the survival time of animals dying of infection was on the average 2 days longer in the group treated with sulfapyridine. Prolongation of the period of treatment from 6 to 10 days did not appear to reduce the mortality but the number of animals used was insufficient to permit definite conclusions on this point. The complications of empyema and purulent pericarditis were less frequent in animals treated with sulfapyridine even though the period of survival was longer in the treated animals.

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Sulfapyridine in Experimental Lobar Pneumonia in the Dog.

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The reported mortality of pneumococcic pneumonia in patients treated with sulfapyridine has been remarkably low. Yet, in controlled experiments with the drug in pneumococcus-infected mice and rats, the results obtained by different investigators have not been uniformly so striking. Animals used in those studies are species highly susceptible to the pneumococcus. Man, conversely, is relatively resistant and is in that regard, resembled by the dog. O. H. Robertson and coworkers[1] have shown that lobar pneumonia

[1] Robertson, O. H., *J. Am. Med. Assn.*, 1938, **111**, 1432.

TABLE I.
Mortality and Duration of Fever in Controls and in Dogs Treated with Sulfapyridine.

Sulfapyridine			Duration of Fever* Number of dogs showing drop of temperature to normal					
				between hours				
Begun at intervals after infection, hr	Total amt given, g	No. of dogs	within 24 hr	24-48	48-72	72-96	after 96 hr	Total Mortality
3	5 to 7	10	0	5	3	1	1	
12	5 to 6	5	0	3	2	—	—	0
18-24	3.7 to 6	9	1‡	2	5	1	—	
Control dogs								
Surviving		16	1‡	4	9	1	1	
Dying†		16	1	4	4	4	3	50%

Dosage of drug: initial dose 2 or 3 g, followed in 6-8 hours with ⅓ g three times a day for 2 to 5 days.
* Temperatures (rectal) above 102.9°F considered to indicate fever.
† Figures in columns 4-7 indicate time of death.
‡ Temperature not taken until 24 hr.

TABLE II.
Production of Lobar Pneumonia in Dogs Receiving Sulfapyridine Prior to Infection.
Dogs sacrificed 24 hours after infection.

Dog No.	Infecting dose of culture cc	Concentration of drug in the blood		Extent of lung involvement at autopsy, lobes	Lung puncture at autopsy		Rectal temperature when sacrificed, degrees F.
		when infected mg%	when sacrificed mg%		Gram-pos. diplococci	Neufeld reaction	
251 T	1.0	10.0	2.8	>1	+†	+	104.0
281 T	1.0	4.9	3.7	>1	+†	+	104.0
271 T	0.02*	3.3	3.6	⅓	0†	—	103.8
272 T	0.02*	18.0	2.8	1	0	—	102.5
273 T	0.02*	12.0	5.1	<1	+†	+	104.3
280 T	0.02*	12.8	5.0	>1	+†	+	102.4

* Suspended in 1 cc of starch-broth medium.
† Pneumococci present on culture.
> = more than.
< = less than.
Quantity of drug before infection: 3 to 5 g; after infection: 2 to 4 g.

can be produced in the dog, which is in all essential respects comparable to the human disease.

In the present investigation dogs weighing 8 to 15 kg were infected intrabronchially by the method of Robertson and Fox[2] with 1 cc of Type I pneumococcus culture followed by 3 cc of mucin, resulting in a disease 50% fatal in the controls. Sulfapyridine* was given orally in capsules or compressed tablets.

Of 24 dogs receiving the first dose of drug 3 to 24 hours after infection, none died (Table I). In 9 instances where serial blood-determinations were made, the content of free sulfapyridine was generally 2 to 6 mg %.

In the group not treated until 18 or 24 hours after infection, one had a bacteremia of 26 colonies per cc of blood at the time of treatment and another had 230. Of the 5 control dogs whose blood at 24 hours contained on culture more than 20 colonies per cc, none survived.

Four additional bacteremic dogs, all but one having a colony count of more than 1,000 per cc of blood were selected for treatment. A total of 5.7 or 6 g of sulfapyridine was given to each, beginning 29 to 72 hours after infection. All died, one with empyema and another with purulent pericarditis. In the other 2, the blood culture became sterile within 48 hours, but several days later severe anemia and jaundice appeared. Post-mortem cultures from the latter 2 yielded no pneumococci. Profound anemia with jaundice has been observed in this laboratory otherwise but once in over 1,000 dogs with experimental pneumonia.

Table II shows that with the method here employed for its production, a lobar pneumonia can evolve despite the administration of large doses of sulfapyridine before and after infection, and despite its presence in the blood in concentrations equal to or greater than those obtaining under conditions when the drug is regularly curative.

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[2] Robertson, O. H., and Fox, J. P., *J. Exp. Med.*, 1938, **69**, 229.

* We are indebted to Merck and Company for supplying us with sulfapyridine.