10708 P

Sulfanilamide and Sulfapyridine in Type III Lobar Pneumonia of Rats.

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In testing experimentally the relative therapeutic effects of sulfanilamide and sulfapyridine in Type III pneumococcic pneumonia we have used the same method that was used successfully in previous experiments with Type I infections in rats.[1] The culture used was recently isolated from the lung of a fatal case of lobar pneumonia in a man. The culture was maintained on blood agar and passed through rats at least once a week in order to keep its virulence at a maximum. Eighteen-hour bouillon cultures diluted to 10^{-6} and suspended in mucin have killed rats when introduced into the lung by intrabronchial insufflation in doses of 0.1 cc. Death resulted within 5 days from lobar pneumonia, empyema and pericarditis, characterized by a profuse gelatinous exudate.

Therapy was begun about 4 hours after the time of injection of the infecting dose and consisted of the administration by stomach tube of sulfanilamide or sulfapyridine,* suspended in 5% mucin. The initial dose in each case was 250 mg and the daily maintenance dose was 125 mg, continued for 6 days in the first group and for 10 days in the second group of rats. No claim is made that optimal results are obtained by daily administration of the drugs but it is sufficiently effective for comparative results and involves less frequent handling of the sick animals, which in itself probably influences favorably the number of survivors.

Of the first group of 37 rats, weighing on the average about 185 g, 12 were used as untreated controls. All of these died from infection within 4 days. Of the 12 receiving sulfanilamide, 2 survived indefinitely, the others dying at intervals up to 14 days. Of the 13 rats receiving sulfapyridine, 5 lived indefinitely and the others died at various intervals up to 24 days after inoculation.

In an attempt to ascertain whether or not the survival rate could be improved by prolonging the period of treatment, a second group of 35 rats was infected in the same manner and by the same dose that was used in the first group. The treatment also was the same with

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

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

the exception that the daily maintenance dose was continued for 10 days instead of 6 days. One of the 11 untreated controls survived and was sacrificed on the 20th day. There was no evidence of persistent infection but a black spot (India ink tracer) was found in the base of the left lung, indicating that the lung had been properly injected. The others died from infection within 5 days, all except 2 showing lobar consolidation of the lungs. These 2 showed empyema and evidence of septicemia. Of the 12 rats receiving sulfanilamide, 4 survived and 8 died in 7 to 9 days. Of the 12 receiving sulfapyridine, only one survived indefinitely, the rest dying in 5 to 19 days with lesions differing from those of the controls in that they showed

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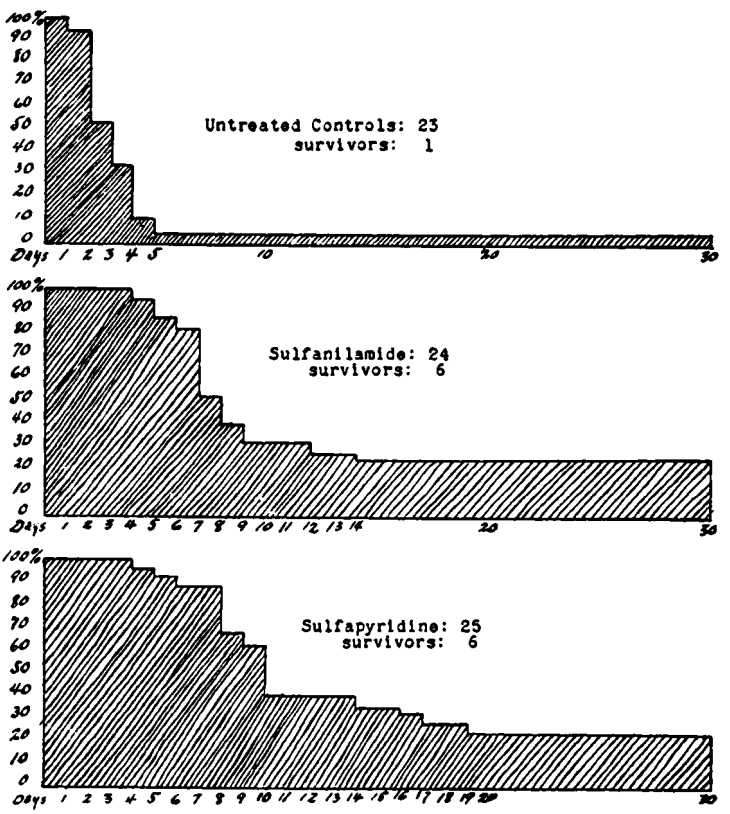

Infecting dose: 0.5 cc. of 10^{-6} dilution; 18 hour bouillon culture.

Number of animals surviving at various intervals expressed in %.

FIG. 1.

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.