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Chemotherapeutic Evaluation of Sulfanilamide and 2-(Sulfanilamido)-Pyridine in Type II Pneumococcal Infections in Mice and Rats.

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The single report by Whitby[1] of the superiority of 2-(sulfanilamido)-pyridine (sulfapyridine) to sulfanilamide in treating pneumococcal infections of the magnitude of 10,000 fatal doses in mice still lacks confirmation. Since Whitby's results were expressed by a figure representing the average survival time for a 7-day period, there is no indication of the actual number of survivors, except in experiments in which no deaths occurred.

In the following experiments, the 2 drugs were assayed against Type II pneumococcal septicemia in mice and also against Type II pneumococcal meningitis in rats; and the results expressed in terms of actual survivals over a considerably longer period of observation.

In the mouse experiments reported below, all animals were inoculated subcutaneously (for reasons previously mentioned[2, 3]) with between 10 and 100 fatal doses of pneumococci and treated, after infection was established, as shown in Table I. It is evident from the 21-day survival values that 2-(sulfanilamido)-pyridine is somewhat more efficacious than sulfanilamide.

TABLE I.
Therapeutic Efficacy of 2-(Sulfanilamido)-Pyridine and Sulfanilamide Against Type II Pneumococcal Infection of Mice.

Treatment	No. of deaths (of 20 mice) daily during 21 days									% Survival
	1	2	3	4	5	6	7	8	9-15	
None	4	11	5							0
Sulfanilamide*		1	3	5		4	1	1		25
2-(Sulfanilamido)-pyridine†	1			2	3	2	2	1		45

Infection: 0.5 cc of an 10^{-6} broth dilution of an 18-hour Type II (X 2B) broth culture subcutaneously. (Between 10 and 100 fatal doses.)

Treatment: Control group: None. Treated groups: 20 mg of drug suspended in 0.2 cc of 15% gum acacia orally 3, 23, 47 and 72 hours after infection.

*Synthesized and donated to us by the Monsanto Chemical Co., St. Louis, Mo.

†Kindly supplied by Merck and Co., Rahway, N. J.

1 Whitby, L. E. H., *Lancet*, 1938, **1**, 1210.

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

3 Cooper, F. B., Gross, P., and Lewis, M., *Am. J. M. Sc.*, 1938, **196**, 343.

Previous studies[3, 4] indicate that a higher percentage of survivals, but a less accurate evaluation of the drugs would doubtless have resulted from a more prolonged course of treatment.

A more critical evaluation of the efficacy of the drugs was obtained by treating rats suffering from well-developed Type II pneumococcal meningitis.[5, 6, 7] The results given in Table II also point to a slight superiority of the new drug over sulfanilamide.

TABLE II.

Therapeutic Efficacy of 2-(Sulfanilamido)-Pyridine and Sulfanilamide Against Type II Pneumococcal Meningitis of Rats.

Treatment	No. of Rats	No. of deaths daily during 21 days											% Survival
		1	2	3	4	5	6	7	8	9	10	11-15	
None	16	7	7	1	1								0
Sulfanilamide	32	2	3	4	3		2					2	50
2-(Sulfanilamido)-pyridine	30	2	2		3		1	1	1	1		2	57

Infection: 0.1 cc of a 10^{-4} broth dilution of an 18-hour Type II (X 2B) broth culture intracranially. (Less than 100 fatal doses.)

Treatment: Control group: None. Treated groups: 100 mg of drug suspended in 0.5 cc of 15% gum acacia orally 6, 13 and 23 hours after infection, then once daily for 8 additional days.

Conclusions. The above experiments, more rigorous than those previously reported[1] because treatment was purposely withheld until infection was established and then conducted with equal doses of the 2 drugs, show 2-(sulfanilamido)-pyridine slightly superior to sulfanilamide in combatting Type II pneumococcal infections of less than 100 fatal doses in mice and rats.* These conclusions are based on survival values only.

4 Cooper, F. B., Gross, P., and Lewis, M., *J. Chemotherapy*, 1938, **15**, 31.

5 Cooper, F. B., Gross, P., and Lewis, M., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 835.

6 Gross, P., Cooper, F. B., and Lewis, M., *Am. J. M. Sc.*, in press.

7 Gross, P., Cooper, F. B., and Lewis, M., *Am. J. M. Sc.*, in press.

* More recent work, to be published, has shown sulfanilamide superior to 2-(sulfanilamido)-pyridine in combatting experimental Type III pneumococcal pneumonia and meningitis of rats.