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Sulfapyridine*: Immunity to Reinfection with Type I Pneumococcus.†

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Whitby[1] found that mice infected with Type I pneumococcus and treated with sulfapyridine were immune, on recovery, to subsequent infection with this pneumococcus. Long[2] stated that he was unable to confirm this observation. The following experiments were performed in order to obtain more information on this disputed point.

One hundred twelve white mice were infected intraperitoneally, with approximately 100 lethal doses of a Type I pneumococcus, this quantity of organisms being contained in 10^{-7} cc of a 12-hour blood-broth culture. Twenty-four of these mice served as untreated controls. The remaining 88 received sulfapyridine; 20 mg of the drug, suspended in a 10% acacia solution, were administered orally 2, 8, 14, and 20 hours after infection and every 24 hours thereafter for 5 successive days. As Table I shows, 75 of the treated mice survived infection. At 7, 14, and 28 days after the initial infection, groups of these survivors were reinfected with 100 lethal doses of the same Type I pneumococcus. Groups of untreated mice served as controls for each of the above groups. Surviving mice were killed 7 days after reinfection. Cultures of heart-blood made at that time were uniformly negative.

The results summarized in Table I show that when mice were reinfected 7 and 14 days after the initial infection, 86% survived. When reinfected at the end of 28 days, only 6% survived.

Before concluding that the mice survived because of immunity to Type I pneumococcus, 2 other possibilities had to be considered: (1) that protection was due to the retention of small but therapeutically effective amount of sulfapyridine by the mouse, and (2) that sulfapyridine *per se* stimulated natural defensive mechanisms.

The first possibility seems unlikely, because experiments have

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

2 Long, P. H., *J. A. M. A.*, 1939, **112**, 538.

TABLE I.
Immunity of Sulfapyridine-treated Mice to Reinfection with Type I Pneumococcus.

Initial Infection-experiments					Reinfection-experiments				
			Survivors				Reinfection-days after initial infection	Survivors	
Group	No. of mice	Treatment	No.	%	Group	No. of mice		No.	%
I	88	Sulfapyridine	75	85	Survivors Group I	15	7	13	86
					Untreated controls	6	—	0	0
Untreated controls	24	None	0	0					
					Survivors Group I	14	14	12	86
					Untreated controls	10	—	0	0
					Survivors Group I	36	28	2	6
					Untreated controls	12	—	0	0

shown[3] that sulfapyridine administered to normal mice, as in the above experiments, was completely eliminated from blood and urine within 72 hours after the last dose of the drug. Yet mice were immune to reinfection as long as 8 days after the last dose of sulfapyridine.

The second possibility was eliminated by the following experiment. Twenty-five normal mice received 20 mg doses of sulfapyridine as described previously; 24 hours after the last dose of the drug, they were infected with 100 lethal doses of Type I pneumococcus. The administration of sulfapyridine did not increase the resistance of these animals for they were all dead within 36 hours, as were 12 untreated controls infected similarly.

These data justify the conclusion that mice that have recovered from infection with Type I pneumococcus, through treatment with sulfapyridine, are immune to reinfection for a limited time. Our experiments have confirmed Whitby's observation. Since Long has not presented his experimental data, it is impossible to explain the apparent discrepancy between his conclusion and that warranted by Whitby's results and our own. The discrepancy could be explained if one assumed that Long reinfected his mice later than 14 days after the initial infection. In this event our data would support his conclusion.

Summary. Mice recovering from a Type I pneumococcal infection, as a result of sulfapyridine therapy, are generally immune to reinfection for at least 14 days after the initial infection. This immunity is lost within 28 days.

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Effect of Artificially Induced Hyperpyrexia on Tooth Structure of the Rabbit.

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The increasing therapeutic importance of artificially induced fever raises the question of its effect on developing tooth structure. Damage to the enamel by infections accompanied by high fever during the

[3] Schmidt, L. H., and Hughes, H. B., results to be published.