

Toxicity and Influence of Streptomycin in Breeding of Mice.

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Since preliminary observations¹ in this laboratory indicate that streptomycin* may be a practical means of controlling *Salmonella* infections in colonies of mice, it was thought desirable to determine what influence streptomycin may have on breeding of mice, weight gains of young mice, and on the general condition of the animals. In addition to observing any obvious toxic effects of this antibiotic when given orally over considerable periods of time, studies of such indirect effects as changes in the intestinal flora were also planned.

Experimental. Young adult Swiss albino mice were obtained for the breeding phase of the work from Rockland Farms.[†] Fecal samples from each mouse were tested for presence of *Salmonella* organisms and any giving a positive test were eliminated. Females in good condition which had produced

at least one litter of mice were selected and mated in metal cages, one male to 2 females. When the mice were obviously pregnant, they were placed in separate cages. Litters and parent stock were weighed at weekly intervals over a period of 4 weeks. The young males and females of the litters, were weighed individually at 3 and 4 weeks of age. The young were weaned when 3 weeks old. During the entire experiment the basal ration was Rockland Mouse Diet. Streptomycin was incorporated in the diet so that the daily intake of each mouse of 5 groups consisting of 20 females and 10 males each was approximately 1000, 400, 200, 100, and 50 μ g respectively. Three additional groups were given 200, 100, and 50 μ g per mouse daily in drinking water. The young mice were kept on the same diet as their parents after weaning, until the end of the weighing

TABLE I.
Influence of Streptomycin on Breeding, Number of Mice Per Litter at Birth and at Weaning.

μ g basal diet	No. of litters born	Sterile females	Avg No. of mice per litter	
			At birth	Weaned
First Litters.				
1000	14	6	7	6.0
400	16	4	7	6.0
200	15	5	8	8.0
100	18	2	8	7.6
50	17	3	6	5.9
Controls	15	5	6	5.6
Second Litters.				
1000	4	1	6	6.0
400	4	0	9	9.0
200	10	3	8	7.0
100	10	3	5	4.5
50	10	3	9	8.0
Controls	14	2	7	7.0
First Litters.				
200 units H ₂ O	17	3	9	7.9
100 " "	16	4	7	6.2
50 " "	19	1	7	5.8

¹ Slanetz, C. A., PROC. SOC. EXP. BIOL. AND MED., 1946, **62**, 248.

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TABLE II.
Influence of Streptomycin on Weight Increase in Mice.

Litter No.		7	14	21	21	28	28	Age in days
First Litters.								
1000 μ g daily basal ration	1	3.1	6.1	♀ 8.5	♂ 9.5	♀ 14.0	♂ 15.1	
	1A	2.3	4.0	8.0	7.0	9.5	11.0	
	2A	1.8	4.5	7.5	7.5	12.0	12.5	
	3	3.1	4.8	9.5	6.5	11.8	11.9	
	3A	3.0	4.1	4.8	5.0	9.4	11.0	
	4A	2.3	5.3	7.5	8.5	12.0	12.5	
	5	3.3	4.2	7.3	7.1	11.3	13.8	
	5A	2.3	4.6	4.5	5.9	9.5	12.3	
	8A	2.8	5.5	9.0	8.5	11.8	14.5	
	9	3.7	5.9	7.5	7.0	8.5	8.5	
	9A	4.5	5.3	9.8	10.5	17.5	13.5	
	10A	2.1	3.6	5.5	4.0	10.3	9.0	
	Avg	2.9	4.8	7.5	7.3	11.4	12.1	
Second Litters.								
Controls	85A	1.9	4.8	7.1	7.1	11.1	12.0	
	86A	2.3	3.7	7.3	5.5	11.5	8.5	
	87	1.3	3.5	4.0	4.3	8.5	9.0	
	88	3.1	4.0	6.1	6.1	11.5	10.7	
	88A	2.5	3.9	6.0	6.0	9.7	11.7	
	89	3.0	4.2	7.0	6.5	11.3	9.0	
	89A	5.2	6.8	10.5	10.5	16.5	15.5	
	90	3.1	5.0	7.8	7.5	13.2	13.5	
	Avg	2.8	4.5	7.1	6.7	11.4	11.2	

TABLE III.
Averages of Weight Increases in First and Second Litters of Mice Fed Various Levels of Streptomycin in Basal Ration.

μ g daily	Litter	7	14	21	21	28	28	Age in days
				♀	♂	♀	♂	
1000	1st	2.9	4.8	7.5	7.3	11.4	12.1	
1000	2nd	3.7	6.0	8.6	8.6	13.8	14.2	
400	1st	2.5	4.5	6.4	6.8	9.9	10.1	
400	2nd	3.2	4.4	5.6	6.2	10.1	12.3	
200	1st	2.2	4.5	5.7	6.1	8.9	9.6	
200	2nd	2.8	5.3	7.0	7.4	12.0	12.8	
100	1st	2.2	4.6	6.8	7.4	9.5	11.2	
100	2nd	3.0	5.8	8.2	8.6	10.2	13.5	
50	1st	2.3	4.9	6.0	7.7	9.7	10.5	
50	2nd	2.7	4.9	6.5	6.5	9.7	10.9	
Controls	1st	3.2	5.1	6.8	7.3	10.4	12.5	
"	2nd	2.8	4.5	7.1	6.7	11.4	11.2	

period.

Records were kept as to the number of mice in each litter at birth and at weaning. Table I presents the results obtained at the several levels of streptomycin feeding. Table II shows average weight gains of litters in 2 representative groups of mice at 1, 2, 3, and 4 weeks of age. One week after weaning of their first litters, a number of mice were selected from each group and again mated. The litters of mice obtained from

these females are referred to as second litters and weight gains on these litters are given in Table III along with average weight gains of the first litters. At weekly intervals the streptomycin-fed mice were carefully examined as to condition of hair, eyes, tails, and feet, and compared with the control mice fed only the stock mouse diet.

Discussion. The general condition of the streptomycin-fed mice was similar to that of the control mice kept on the stock mouse diet.

There was no evidence of toxicity even in the mice fed 1000 μg of streptomycin daily for 4 to 6 months. No significant difference was apparent between the streptomycin-fed mice and controls in regard to percentage fertility; size of litters and number of mice weaned. The first litters of mice fed various levels of streptomycin showed no significant differences in weight gains but the second litters at the higher levels made greater gains as a rule than controls and those at low level intakes.

First Litters. Weight gains of first litters from mice fed streptomycin were similar to those of control mice fed stock diet.

Second Litters. The mice fed at a daily level of 1000 μg of streptomycin made greater gains than control mice and those given 50 μg daily. At the 400, 200, and 100 μg levels, the trend toward greater weight gains is evident (Table III). A possible explanation for the greater gain in weight of second litters may be that the mothers had obviously been on the streptomycin-containing diet longer, at the time of their birth than when the first litters were produced. Work is now in progress to check the influence of the 1000 μg

level as well as 3000, and 6000 μg daily intake of streptomycin on weight gains of young litters of mice.

No gross pathology was evident in several mice sacrificed and autopsied from each group. Histological examination[‡] of tissues from mice fed 1000 μg of streptomycin daily revealed no significant changes.

A study of the intestinal bacterial flora of mice receiving 1000 μg of streptomycin daily and of control mice is in progress.

Summary. No toxic effects were observed in albino mice fed streptomycin at daily levels of 1000, 400, 200, 100, and 50 μg for periods of one to 6 months. These levels had no significant influence on percentage fertility, litter size, number of young mice weaned, and general condition of the animals. Although no influence was evident at the various levels of streptomycin in the weight gains of first litters of mice, a greater increase in weight occurred in second litters at higher levels compared to second litters of the control and 50 μg groups.

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Histamine and Anaphylactic Shock in the Mouse.*

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Anaphylaxis may be defined as an acute and frequently damaging reaction of a sensitized animal to the specific antigen used in sensitization. This phenomenon has been studied in many animals but only recently has it been described adequately in mice.¹ The experiments cited below not only confirm that mice are susceptible to anaphylactic shock but also indicate that they are re-

fractory to histamine shock.

White mice of an inbred *Olitsky* strain varying in age from 2 to 6 months were sensitized by intraperitoneal injection of 1 ml of egg white (diluted 1:4 with normal saline) every second day to a total of 4 ml, following the procedure of Weiser, Golub and Hamre.¹ Twelve days after the last sensitizing injection anaphylactic shock was produced by injection of 1 ml of the antigen into the tail vein.

The anaphylactic shock syndrome in the mouse was characterized by sluggishness, wobbling gait, dyspnea, cyanosis, paralysis of extremities, loss of sphincter control,

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¹ Weiser, R. S., Golub, O. J., and Hamre, D. M., *J. Inf. Dis.*, 1941, **68**, 97.