

Summary. A group of castrated male albino mice and an uncastrated control group were equally infected with *Schistosoma mansoni*. Nine weeks later the animals were sacrificed and the adult parasites collected, separated according to sex and counted. The mean adult parasite count per mouse, for each group, showed a significant reduction in the male schistosomes of the castrated animals. This difference indicates a relationship between male sex hormones and the male parasite.

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Effect of Somatotrophic Hormone and Streptomycin on Mice Exposed to Total Body X-Irradiation.* (20273)

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Selye, Salgado and Procopio(1) have reported that rats subjected to whole body x-radiation (671 r total dose in 2 exposures 6 days apart) and treated twice daily with subcutaneous injections of 1.5 mg of somatotrophic hormone (STH) gained weight, whereas untreated controls lost weight during the 2nd and 3rd weeks post-irradiation. This treatment did not, however, reduce the mortality. Since loss of weight is a well recognized effect of radiation injury(2,3), their observation suggested that treatment with

STH might have exerted some beneficial effect which was not reflected in the survival rates because of the occurrence of post-irradiation infection. In fact, they noted that some of the STH treated rats at autopsy showed lesions suggestive of infection.

Infection has been shown to play a significant role in the death of mice exposed to moderate doses of x-radiation(4). It seemed possible, therefore, that any therapeutic effect of STH in the treatment of radiation injury might be more clearly demonstrable in animals protected against infection by concomitant treatment with streptomycin. Accordingly, the following experiments were made to

* This investigation was carried out under a contract between the U. S. Atomic Energy Commission and The University of Chicago.

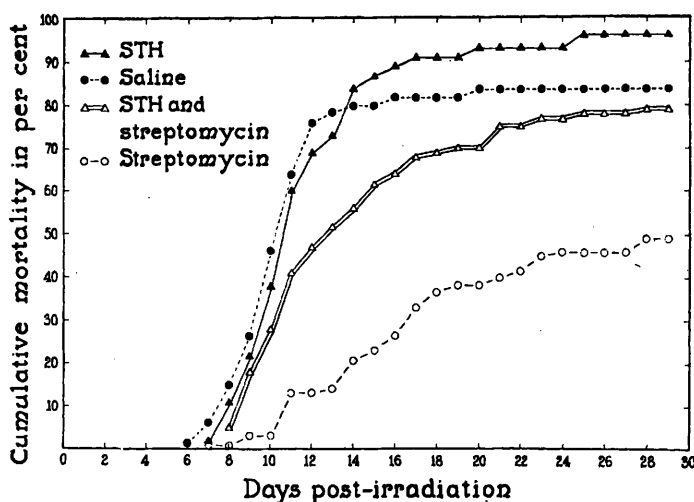


FIG. 1. Mortality curves of x-irradiated mice treated with STH and streptomycin, STH alone, streptomycin alone, or saline.

explore this possibility. Irradiated mice were treated with both STH and streptomycin. Streptomycin was chosen because it had been found, by Miller, Hammond and Tompkins (5), to be the most effective of the antibiotics studied in controlling post-irradiation infection.

Methods. The mice were Rockland, female, RAP mice, 11 weeks old, weighing 20-25 g. They were housed in groups of about 20, in metal cages, the floors of which were covered with wood shavings. Rockland mouse pellets and water were available to them at all times. They were exposed to a single dose of 550 r total body x-radiation, delivered at 250 kv, 15 ma at a distance of 51.0 cms, with 0.25 mm of copper and 1.0 mm of aluminum filtration at a rate of approximately 30 r/min.[†] The mice were divided into 4 groups which were treated as follows: 81 mice were given somatotrophic hormone and streptomycin; 45 mice, somatotrophic hormone alone; 106 mice, streptomycin alone; and 45 controls, sterile saline. All injections were made subcutaneously. The first dose of 0.6 mg somatotrophic hormone[‡] was given within

one hour after irradiation and repeated daily for 20 days. It was prepared fresh each day. This dose of hormone was found to produce good gains in body weight of normal mice. No evidence of toxicity appeared when this dose or more than twice this amount was given to normal mice for 5 days. Streptomycin[§] (6 mg a day) was begun on the third day post-irradiation and continued for 20 days.

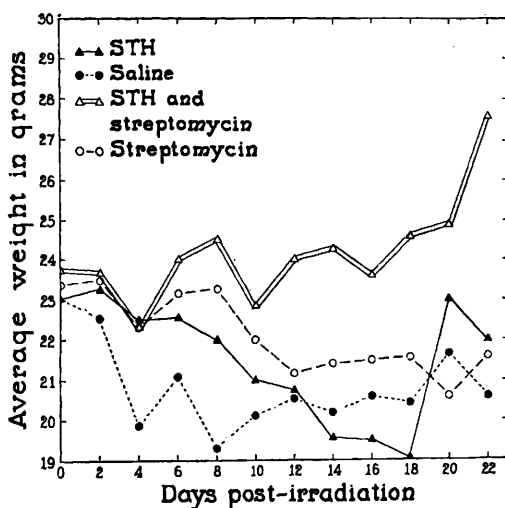


FIG. 2. Average weights of x-irradiated mice treated with STH and streptomycin, STH alone, streptomycin alone, or saline.

[†] The authors are indebted to the U. S. Air Force Radiation Laboratory, University of Chicago, for use of their x-ray facilities.

[‡] Lot No. R491024 generously supplied by Dr. Irby Bunding of The Armour Laboratories, Chicago, Ill.

[§] Kindly furnished by Charles Pfizer & Co., Brooklyn, N. Y., through the courtesy of Dr. Gladys L. Hobby.

TABLE I. Incidence of Positive Blood Cultures in Autopsied Mice.

	STH and streptomycin	Streptomycin	STH	Saline
No. of mice treated	81	106	45	45
" " deaths	64	52	43	38
" autopsied and cultured	43	27	43	38
" positive blood cultures	12	5	37	38
% of blood cultures positive	28	18	86	100

TABLE II. Microorganisms Recovered from Blood Cultures of Autopsied Mice.

	Mice treated with—			
	STH and streptomycin	Streptomycin	STH	Saline
<i>Proteus</i>	—	—	15	11
<i>Escherichia coli</i>	1	—	3	5
<i>Alcaligenes fecalis</i>	6	—	2	—
<i>Aerobacter aerogenes</i>	—	—	—	1
<i>Salmonella</i>	3	2	4	10
<i>Enterococcus</i>	2	3	—	3
<i>Paracolobactrum</i>	—	—	10	8
Beta hemolytic streptococcus	—	—	—	1

The mice were weighed in groups every other day. All mice which died were autopsied, except those which were badly mutilated when found in the morning. Heart's blood was cultured in brain-heart infusion broth (Difco) which was subcultured after 24 hours incubation onto blood agar and Eosin Methylene blue agar.

Results. Fig. 1, which plots the cumulative mortality curves, shows that the combination of STH and streptomycin did not significantly reduce the mortality (30 days) below that of the saline treated controls. The only group showing a significant reduction in mortality was that treated with streptomycin alone.

The weight curves, presented in Fig. 2, show that the saline controls lost weight most rapidly and those treated with somatotrophic hormone alone lost weight at almost the same rate. Those treated with streptomycin alone lost weight still less rapidly. Only one group—that treated with both STH and streptomycin—maintained body weight and began to gain weight by the end of the 2nd week post-irradiation.

Table I shows the incidence of positive cultures of heart's blood in the four groups of mice. The smallest number of positive cultures was found in the two groups treated with streptomycin, alone or in combination with STH (18% and 28%, respectively, of the

animals autopsied and cultured).

Table II lists the microorganisms recovered from the positive blood cultures. All of them, with the exception of one Beta hemolytic streptococcus, belong to the normal microflora of the lower gastrointestinal tract of this strain of mice and are essentially the same as those found by Miller, Hammond and Tompkins(4,6) to be responsible for the post-irradiation bacteremias of mice.

Discussion. These results fail to demonstrate any reduction in mortality in irradiated mice from treatment with somatotrophic hormone even when it is combined with streptomycin. In fact, the mortality among the mice treated with both STH and streptomycin was significantly higher than in those treated with streptomycin alone, even though the incidence of bacteremia was markedly reduced. It is interesting to note that the animals that had received both STH and streptomycin maintained better body weights. In spite of this finding and positive evidence of control of bacteremia, these animals died more rapidly than did those receiving streptomycin alone.

Summary. 1. Treatment with somatotrophic hormone failed to reduce the mortality of mice exposed to 550 r total body x-radiation, even when it was combined with streptomycin to control the development of post-irradiation infection. 2. The mice which received both

drugs maintained body weight, but those which received either drug alone lost weight.

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Effect of Feeding Several Sulfonamides and Related Compounds on Growth of Chicks.* (20274)

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Stimulation of animal growth has been observed when certain non-absorbable sulfonamides, such as sulfasuxidine or sulfathalidine are fed continuously in the diet in substantial concentrations(1-6). However, the feeding of similar concentrations of absorbable sulfonamides has been found to have a deleterious or growth depressing effect(7). It was of interest, therefore, to ascertain the growth effect brought about by feeding high dietary concentrations of Gantrisin®,† (sulfisoxazole), a soluble, readily absorbable sulfonamide of low toxicity(8-10) and the sparingly soluble, non-absorbable γ -keto sulfones of the intestinal antiseptic type, Ro 2-0201‡ and Ro 2-0404 (11).§ Sulfamethazine, sulfadiazine, sulfaguanidine, sulfanilamide and sulfaquinoxaline were included for comparison. Because of its sensitivity to the neuropathological effects of sulfonamides(12) and its suitability for growth studies, the chick was chosen as the test animal.

Procedure. Day-old straight run sexed single comb White Leghorn chicks|| were placed on raised wire floors in electrically heated brooders and were maintained on the

basal ration for 3 days. The basal ration used was an antibiotic-free¶ commercial chick starting mash. After 3 days acclimatization on the basic diet, all runts and giants were discarded, the birds were wing banded and grouped into equally weighted groups of 20, containing equal numbers of males and females. The groups of birds were then placed on the experimental rations and maintained so in the brooders to the age of 4 weeks, after which time they were transferred to growing cages where they remained until the termination of the experiment. All birds were weighed weekly. Water and feed were provided *ad libitum*. The lights were controlled to keep the room well illuminated between the hours of 5 a.m.

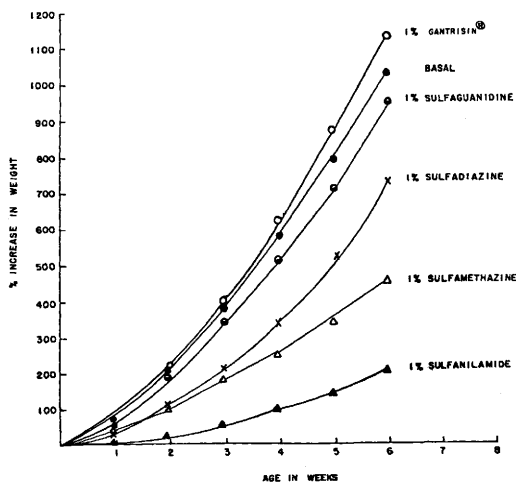


FIG. 1. Rate of increase in growth of chicks fed diets containing 1% sulfonamide.

* Roche Publication No. 344.

† 3,4-Dimethyl-5-sulfanilamido isoxazole.

‡ 4-Phenyl-4-sulfanilyl-2-butanone

§ β -Phenyl- β -sulfanilyl-propionophenone.

|| Obtained from Kerr Chickeries, Frenchtown, N. J.

¶ "Start and Grow" chick mash, manufactured by GLF Feed Co-Op Mills.