fourth left intercostal space, the heart rotated to fully expose the anterior aspect of the right ventricle and the pericardium resected over this area. The arch was attached to the anterior surface of the right ventricle by cotton thread sutures, one set near the A-V sulcus and the other near the septum. Two or 3 sutures were laid at each point, threaded through the drilled holes in the feet of the arch and tied. Lead wires were brought out through the operative wound, the chest closed and aspirated. Chief complications in order of occurrence were adhesions, tearing out of sutures and breaking of lead wires. These complications were ordinarily diagnosed readily from the character of the tracing. The diagnosis was facilitated by the administration of epinephrine "test doses" of 0.5 to 1.0 γ/kg intravenously.

Results. The method has been used to measure heart force produced in the intact animal by cardiac glycosides(7), by hyperthermic agents(8), and by sympathomimetic amines(9). It is peculiarly suited to measure changes in heart force during the transitions of general(10) and spinal anesthesia(11), since it smoothly records the force of each contraction during the normal, conscious state as well as during anesthesia. Fig. 2 illustrates changes during induction and recovery from anesthesia with ether and, later in the same animal, with chloroform.

Summary. A strain gauge arch has been described which measures heart force changes in fully conscious, chronically operated dogs. Enclosure of the electrical component in a metal casing prevents insulation breakdown in body fluids.

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Effect of Antibiotic Dosage on Mortality from Whole Body X-Irradiation.* (20613)

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A large amount of data has accumulated on the effect of antibiotics on radiation injury. In general these drugs have been found to be slightly or moderately effective in reducing mortality. Varying amounts of antibiotics have been given at different intervals prior to and following radiation. This report is concerned with the effect of antibiotic dosage on the mortality from whole body x-irradiation.

Exp. 1. One hundred white male rats of the Wistar strain having a mean weight of 221 g, were separated randomly into 5 groups of 20 each. One untreated group served as a control while the 4 remaining groups received terramycin hydrochloride daily in amounts of 0.2 mg, 2.0 mg, 20 mg, or 200 mg, respectively. The antibiotic was given by stomach tube in a 2 cc aqueous solution beginning 72 hours and ending one to 4 hours prior to

* This work performed under contract between the U. S. Atomic Energy Commission and Western Reserve University. Terramycin furnished by courtesy of Chas. Pfizer and Co., Brooklyn, N. Y.

TABLE I. Mortality and Survival Time in Control and Treated Animals. 5 groups, 20 rats in each group.

Dose of terramycin, HCl/rat/day	No. of 30-day survivors	% mortality	Mean survival time in days	s*	S.E.†
(mg)					
None	5	75	8.7	3.5	.9
.2	4	80	9.8	5.6	1.4
2	8	60	11.2	3.6	1.1
20	7	65	11.7	9.8	2.4
200	11	45	13.3	4.9	1.6

* s = Stand. dev. † S.E. = Stand. error.

x-irradiation, a total of 4 doses. No antibiotic was administered after radiation. Each rat received 660 r of whole body radiation. The housing of the animals and the method of administering the terramycin were similar to that previously described(1). The animals were weighed at intervals, 5 times during a 2-week period prior to the experimental period, and any rat whose weight gain was not satisfactory was discarded. The animals were observed daily for 30 days following x-irradiation. The physical factors of x-irradiation were as follows: 220 KV; 15 MA; mean target distance 32.1 cm; filters of 1 mm Al. and ½ mm Cu; output in air 124 r/min.; half-value layer 1.35 mm Cu.

Results. Mortality. In the control group 15 of 20 rats died during the 30-day experimental period (Table I). In the groups receiving 0.2; 2.0; and 200 mg/day of terramycin the number of deaths was 16, 12, 13, and 9, respectively, with mortalities of 80, 60, 65 and 45%, respectively. The χ^2 value for the difference between the 0.2 and 200 mg/day groups is 5.01 which is significant statistically. The χ^2 value for the difference between the control and the 200 mg/day terramycin group is 3.75. This approaches statistical significance (3.845) at the 5% level. The differences in mortality between the 2.0, 20 and 200 mg/day groups are not sufficient to reach statistical significance. However, there is a tendency for the mortality to decrease with increasing dosage of terramycin. *Survival.* The mean survival time for the control group was 8.7 days and for the groups receiving 0.2, 2, 20, and 200 mg/day of terramycin hydrochloride it was 9.8, 11.2, 11.7, and 13.3 days, respectively. Thus there appears to be a progressive increase in survival time with increasing dosage of terramycin. *Morbidity.* This was greater in the control group from the 4th to the 12th day and in the group receiving 200 mg terramycin from the 12th to the 30th day. In general, in the remaining groups the morbidity paralleled the mortality. Diarrhea was most marked in the group receiving the largest dose of terramycin. With decreasing amounts of terramycin the diarrhea was less marked but in none was it less than in the control group.

Exp. 2. Seventy-five white male rats of the C. F. Wistar strain with a mean weight of 211 g were divided randomly into 3 groups of 25 each. One untreated group served as a control while the 2 remaining groups received terramycin hydrochloride daily in amount of 20 and 200 mg per rat respectively. The schedule and mode of administration of the antibiotic were the same as for Exp. 1. No terramycin was administered after radiation. Each animal received 660 r of whole body radiation.

Results. Survival time and mortality for the 3 groups are given in Table II. In contrast to Exp. 1, there was no increase in survival time for the 20 mg/day group as compared to the control and only a slight increase for the 200 mg/day group. The difference in

TABLE II. Mortality and Survival Time in Control and Treated Animals. 3 groups, 25 rats in each.

Dose of terramycin, HCl/rat/day	No. of 30-day survivors	% mortality	Mean survival time in days
(mg)			
0	5	80	12.8
20	7	72	10.0
200	18	28	14.4

mortality rate between the control and the 20 mg/day treated groups was not significant. However, the differences between the control and the 200 mg/day groups and between the 20 and 200 mg/day groups were highly significant, *i.e.*, statistically at the 0.02 and 0.2% levels respectively. The highest dosage level of terramycin (200 mg/day) appears to have been definitely effective in lowering mortality. In this experiment diarrhea was only slightly more marked in the group receiving the largest dose of antibiotic than in the 20 mg/day and control groups.

Discussion. Koletsky and Christie(2) obtained a 31% reduction in mortality in rats given 120 mg/kg/day of streptomycin and 50,000 units/kg/day of penicillin intramuscularly, beginning as early as 10 days prior to and discontinuing 3 weeks after injection of lethal doses of P^{32}. Miller, Hammond, Tompkins, and Shorter(3) gave mice streptomycin subcutaneously from the 4th to the 28th day following 450 r whole body x-irradiation. Although the mice were not randomly distributed to study the effect of dosage, a review of their figures indicates that relatively large amounts of streptomycin were required for beneficial results. Thus 50 to 100 mg/kg/day of the antibiotic were ineffectual whereas 150 to 350 mg/kg/day reduced mortality from 37 to 55% in various groups.

Additional data pertinent to antibiotic dosage are available in the literature. In mice which received approximately 250 to 350 mg/kg/day of streptomycin subcutaneously, usually from the 4th to the 28th post-radiation day but in some instances from the day of x-radiation until the 24th post-radiation day, the mortality differences between control and treated groups ranged from 43 to 65%(4,5). The use of 40,000 units/kg/day of penicillin in conjunction with the streptomycin gave a reduction in mortality of from 30 to 41%, while subcutaneously administered chloramphenicol (about 100 mg/kg/day) reduced mortality by 24 and 25% in 2 groups of mice, respectively. Sodium salts of terramycin(5) and aureomycin (6) have also been effective in mice; when given subcutaneously in amounts of 25 and 50 mg/kg/day, respectively, mortality was lowered by 25 and 30%. However, Miller *et al.*(3) have concluded that chloramphenicol, aureomycin and terramycin are too irritating to be administered daily by subcutaneous injections, since necrosis of the skin occurred in many of the mice. These drugs were also given with the diet but dosage in these instances is difficult to evaluate.

Furth, Coulter and Howland(7) gave rats approximately 80 to 100 mg/kg/day of aureomycin or terramycin as part of the diet from the time of x-irradiation until the 28th post-radiation day. Aureomycin had no apparent effect on mortality but terramycin gave about an 18% reduction in mortality. A similar procedure in dogs which received 100 mg/kg/day of antibiotic orally, produced mortality reductions of 14 and 42% for aureomycin and terramycin, respectively(8,9). Smith, *et al.* (10) gave mice streptomycin sulfate in amounts of 75 to 1000 mg/kg/day, subcutaneously or orally, with somewhat variable but usually beneficial effect. In these experiments other undetermined factors influenced mortality to such a degree that evaluation of dosage was unsuccessful. Gustafson and Koletsky(1) gave rats approximately 1,000 mg/kg/day of terramycin hydrochloride by gavage for only 48 hours prior to x-irradiation and obtained a 24% reduction in mortality. No antibiotic treatment at all was given after x-irradiation.

In all reports in which antibiotics have been effective in reducing mortality in the x-irradiation syndrome the quantity administered has been relatively large. Amounts from 3 to 7 times the human dose on a comparable weight basis have been effective as against equivocal results for doses equal to or even twice the human dose. In this study amounts of terramycin approximately 30 times the corresponding human dosage were beneficial in reducing mortality. However, smaller doses were less effective and an amount comparable to the dosage required to stimulate growth in chicks and swine was ineffective. In our opinion the beneficial action of the terramycin was probably related to its antibacterial property. It seems likely that in the radiation syndrome the impairment of all normal defense mechanisms against disease makes it necessary to administer large amounts of antibiotic for

maximum beneficial effect. In preliminary experiments a dose of 2000 mg/kg/day of terramycin (10 times the highest level used in this study) was tried but the preparation was so strongly acid that in many instances it caused perforation of the stomach and had to be abandoned(11).

Summary. Rats were given varying doses of terramycin hydrochloride beginning 72 hours and ending 1 to 4 hours prior to x-irradiation. The highest dosage level (200 mg/rat/day) was the most effective in lowering mortality. It is probable that larger doses of antibiotics are required in the x-irradiation syndrome than are required for the treatment of other diseases.

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Interference in Cortisone-Treated Hosts.* (20614)

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Cortisone has been shown to suppress inflammation(1) and antibody formation(2), to induce lymphocytolysis and dissolution of lymphoid tissue(3), to enhance viral multiplication(4), and to increase the severity of infections produced by a wide variety of organisms(5-8). It is evident that a multitude of effects may be attributed to the action of cortisone. The present paper reports the results of studies of the interference phenomenon in cortisone-treated hosts.

Materials and methods. Virus. An egg-adapted strain of influenza A (PR8) virus was used and prepared by allantoic inoculation of 11-day embryos with 0.05 ml of a 10^{-6} dilution of infected allantoic fluid; after incubation of eggs at 36°C for 42-48 hours, the fluids were collected and concentrated by the method of red cell adsorption and elution. A final concentration of 5% chicken red cells was used for adsorption of virus; after 45 minutes in the cold, the supernatant fluid was removed and the agglutinated cells resuspended in a small volume of 0.2 M phosphate buffer, pH 7.4. Elution of virus was carried out in a 37°C water bath for 4 hours. The red cells were sedimented by brief centrifugation and the supernatant fluid used as a source of virus after adjustment of the hemagglutinin titer to 2560.

Preparation of interfering virus. Virus prepared in the above manner was exposed to 5 x 10^{-3} M sulfur mustard, [bis (β-chloroethyl) sulfide], for 3 hours at room temperature. The viral suspension was then centrifuged briefly to remove precipitated material and the supernatant fluid used as an interfering suspension after testing for inactivation of virus. The advantages of a sulfur mustard-inactivated interfering suspension will be described elsewhere(9). *Tests of inactivation of virus.* 11-day embryos were inoculated allantoically with 0.5 or 0.05 ml of undiluted suspension, and 0.05 ml of serial 10-fold dilutions

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