on the respiratory center. It is planned to test the effects of thebaine and of n-allylnormorphine in this manner, which should furnish further evidence for the role of the respiratory center in protection against radiation toxicity.

Summary. Morphine sulfate, injected intramuscularly into ZBC male mice 30 minutes before exposure to total-body X-radiation, raises the LD_{50} of the radiation from 609 r to 830 r. Possible mechanisms of this effect are discussed.

Received September 14, 1951. P.S.E.B.M., 1951, v78.

Effect of Oral Terramycin Prior to Whole Body X-Radiation.* (19114)

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Severe radiation injury is often complicated by bacteremia(1-3). The intestinal tract probably serves as the main portal of entry for organisms. This study was made to determine whether reduction or alteration in the intestinal flora by antibiotic therapy prior to radiation would be effective in lowering mortality.

Method. Two hundred white male rats of the C. F. Wistar strain having a mean weight of 195 g were separated randomly into 2 groups of 100 each. Animals were kept in cages having dimensions of 22 by 20 by 15 inches in groups not exceeding 10 rats per cage. Terramycin hydrochloride (10% aqueous solution) was administered orally, using a French No. 8 soft rubber catheter, by a modification of the technic described by Levin(4). The antibiotic was given in 5 doses of 100 mg each, at intervals of 10 to 14 hours, beginning 48 hours prior to radiation and ending 1 to 4 hours prior to radiation. No antibiotic was used after radiation. The rats were weighed 9, 3, and 1 day prior to x-radiation, daily for the first 6 days following radiation, and thereafter at 2 or 3 day intervals. The experiment was discontinued at the end of 30 days. X-radiation was carried out with a 250 KV, 15 MA unit at a distance of 44.3 cm using ½ mm copper and 1 mm aluminum filters. The dosage rate was approximately 60 r per minute. The total dose was 660 r.

Results. (1) Mortality. The 30 day mortality for the control group was 72% and for the treated group 48%. Analysis of the data by the method of Chi square gives a value of 4.08. This is statistically significant. (2) Survival. The mean survival time of the rats in the control group was 10.6 days as compared to 15 days for the treated group. The mean difference is 4.4 days and the mean standard error is 1.3 days. Statistically this difference is highly significant. Fig. 1 shows a plot of per cent mortality against days after x-radiation. The control rats began to die earlier than the treated rats and had a higher death rate up to the 12th day. From the 4th to the 12th day the mean death rate for the control group was 6.2% per day and for the treated group 2.6% per day. From the 12th to the 30th day the mean death rate for the control group was 0.9% per day and for the treated group 1.4% per day. However, when the death rate is calculated on the basis of the number of rats alive on the 12th day, the death rate for the control group is 2.3% per day and for the treated group 1.7% per day. (3) Morbidity. In general this paralleled the death rate. Morbidity was greater in the

* This work performed under contract between the U. S. Atomic Energy Commission and Western Reserve University, Contract No. W31-109-eng-78. Terramycin furnished by courtesy of Chas. Pfizer and Co., Brooklyn, N. Y.

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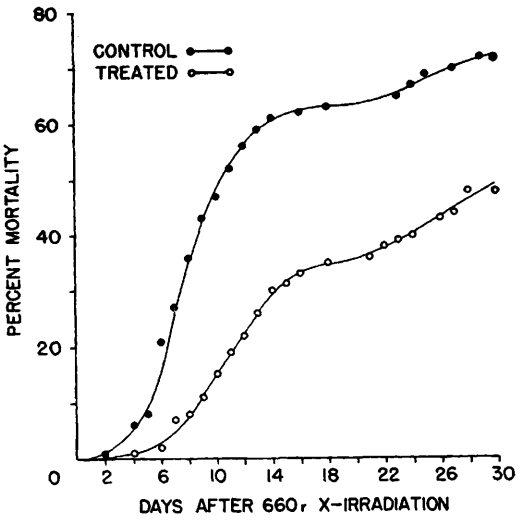

FIG. 1. Mortality in control and treated rats.

control group from the 4th to the 12th day and in the treated group from the 12th to the 30th day. Diarrhea was greater in the treated group than in the control group probably because of the large amount of terramycin which the former received. (4) Weights. The mean weights of the rats in the two groups were virtually identical except from the 5th to the 12th day post-radiation. During this period the terramycin rats gained weight faster than the controls. The maximum difference occurred from the 6th through the 8th day when the mean weight of the rats which received terramycin was 15 g greater than that of the controls. After the 12th day post-radiation there was no significant difference in the mean weights of the two groups.

Discussion. Koletsky and Christie(5) administered streptomycin and penicillin in combination parenterally to rats from 3 to 10 days prior to and for 3 weeks following injection of rats with lethal doses of P^{32}. In another group of animals the use of antibiotics began immediately after the P^{32} was injected and continued for 3 weeks. The treatment was effective in increasing the survival time and decreasing the mortality from internal radiation. Miller and Hammond(6) and Hammond and Miller(7) used several antibiotics effectively in irradiated mice, *i.e.*, streptomycin, streptomycin combined with penicillin, chloromycetin, terramycin and aureomycin. The last three were employed orally and also by parenteral route. Therapy was usually started on the first day post-radiation and continued through the 19th or 24th day, although in two experiments chloromycetin and aureomycin respectively were given orally from the 4th through the 24th day. The best results were apparently obtained with streptomycin alone. Furth, Coulter, and Howland(8) gave antibiotics from the time of x-radiation through the 28th day. They found no significant difference in the 28 day mortality with aureomycin but stated that terramycin appeared to be effective in reducing mortality. The most obvious result of the antibiotics was to decrease the incidence of post-radiation diarrhea.

In this study prophylaxis with oral terramycin for only 48 hours prior to x-radiation proved beneficial. By altering the intestinal flora, the antibiotic presumably reduced the incidence of bacteremia following radiation. Terramycin may be even more effective when used for 72 rather than 48 hours before radiation. In an experiment employing pre-treatment for 72 hours, the 30 day mortality for treated rats given 660 r of whole body x-radiation was 32% as compared to 86% for the control animals(9).

Summary. Terramycin has been shown to be effective in reducing the mortality in rats when administered for a period of only 48 hours prior to 660 r of whole body x-radiation.

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Received September 16, 1951. P.S.E.B.M., 1951, v78.