Influence of Post-Irradiation Medication with Antibiotic JM-57h on Survival Time in Mice.* (21048)

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Investigations have shown that post-irradiation medication with various antibiotics has increased survival through reduction of the infection which follows acute whole body exposure to ionizing radiation(1-9). Miller *et al.*(9) have pointed out that not all antibiotics are effective because they could not control infections with Pseudomonas, Proteus or Salmonella. Recently Stavely(10) stated that the broad spectrum antibiotic JM-57h was effective against the above organisms so we have used it in an attempt to increase survival time in irradiated mice.

Experimental. Male CF-1 strain mice, weighing an average of 24 g each, were arranged in groups of 20 animals each. Except during irradiation, the animals were maintained in an air-conditioned room at 72 ± 5°F and fed a diet of Rockland pellets supplemented weekly with additional vit. A and D. The animals received daily intramuscular injections of 0.36 mg of antibiotic JM-57h† or saline in a total volume of 0.1 ml following the dosage schedules given in Table I and continuing until 90-100% mortality had been attained. An additional non-irradiated antibiotic control group was medicated for 18 days. The 550 r radiation dose was administered from above and below the mice with two 250 KVP Picker Industrial Units operating simultaneously. The technical factors were: 250 KVP; 15 MA; FOD 100 cm; filters, 0.21 mm Cu inherent, 0.5 mm Cu parabolic, and 1.0 mm AL; HVL 2.02; size of field—total body; r/min. measured in air 17.19. Both units were calibrated prior to each experiment with a Victoreen thimble r-meter. The animals were restrained in a plastic cage similar to the one previously described for guinea pigs(11). The results obtained were analyzed statistically by the method of Litchfield(12).

Results. Upon the basis of the data in Table I, it is evident that, in general, antibiotic JM-57h did not significantly increase the total number of survivors although it had some effect on survival time. Medication throughout the experimental period (Group 6) resulted in a significant increase in the ST_{50} compared to the saline controls (Group 5). It is also apparent that the animals must be medicated during the first post-irradiation week if any benefit whatsoever is to be obtained (compare Groups 2 and 6 with the balance of the medicated groups). From the infection viewpoint, the first post-irradiation week is critical because the leukocytes are disappearing at a rapid rate while a bacteremia is developing. Vincent and Veomett (13) found that a massive bacteremia from Proteus and Pseudomonas organisms begins during this time interval and Miller *et al.*(9) made similar observations in the CF-1 mouse. Thus it would appear that after irradiation injury, antibiotic medication with an agent which has a more specific effect on Proteus and Pseudomonas organisms, must be started on the first post-irradiation day and continued for at least 15 days or until the natural body defense mechanisms have recovered their function.

The deaths in the antibiotic treated animals cannot be ascribed to the drug, although the dose used was 0.1 of its LD_{50} (highest dose tolerated chronicly), because there were no deaths or untoward reactions in Group 9. Furthermore, these animals gained an average of 2 g during the experimental period.

Summary. Antibiotic JM-57h, a wide spectrum agent, has been used to combat post-irradiation infection without significantly increasing the total number of survivors. In

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TABLE I. Survival Time in Antibiotic-Treated Irradiated Mice. 9 groups.

Treatment	Days	ST_{50},* range in days	Slope, range	Total mortality %	Total mortality Day
Saline	1– 7	11.4 (10.8–12.0)	1.12 (1.08–1.16)	95	13
Antibiotic	1– 7	12.2 (11.4–13.1)	1.18 (1.12–1.24)	90	16
Saline	8–15	12.0 (11.0–13.1)	1.22 (1.15–1.3)	90	17
Antibiotic	8–15	11.7 (11.2–12.2)	1.11 (1.07–1.14)	100	18
Saline	1–18	10.7 (10.3–11.1)	1.08 (1.06–1.11)	100	13
Antibiotic	1–18	12.2 (11.7–12.8)	1.11 (1.07–1.15)	95	16
Saline	8–18	11.0 (10.3–11.8)	1.16 (1.11–1.22)	100	15
Antibiotic	8–18	10.0 (9.1–10.9)	1.23 (1.15–1.31)	100	14
Non-irradiated controls, antibiotic	1–18	0	0	0	18

* ST_{50} = day on which 50% of animals were still alive. All values at odds of 19/20.

the group medicated daily an increase in the ST_{50} day was noted. The results obtained indicate that medication must be started during the first post-irradiation week before massive bacteremia occurs, otherwise such therapy will not be beneficial. At a dose of 0.1 of its LD_{50}, antibiotic JM-57h was well tolerated and produced no fatalities or untoward reactions in CF-1 strain mice.

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