THE EFFECT OF ORAL NEOMYCIN THERAPY FOLLOWING WHOLE-BODY X-IRRADIATION OF RATS

J. B. Webster

ARMS FORCES RADIOBIOLOGY RESEARCH INSTITUTE
Defense Atomic Support Agency
Bethesda, Maryland

Distribution of this document is unlimited.
All aspects of investigational programs involving the use of laboratory animals sponsored by DOD components are conducted according to the principles associated in the "Guide for Laboratory Animal Facilities and Care," prepared by the National Academy of Sciences - National Research Council.
THE EFFECT OF ORAL NEOMYCIN THERAPY FOLLOWING
WHOLE-BODY X-IRRADIATION OF RATS

J. B. WEBSTER

ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE
Defense Atomic Support Agency
Bethesda, Maryland

Distribution of this document is unlimited.
ACKNOWLEDGMENT

I wish to express my sincere appreciation to Dr. Evelyn Kivy-Rosenberg for her patient and critical assistance in the preparation of this manuscript. The skillful technical assistance of R. L. Gagnon, HMC, USN, is gratefully acknowledged.
ABSTRACT

This study was designed to examine the beneficial effects of oral antibiotic treatment with neomycin following total-body X-irradiation of Sprague-Dawley rats. Survival times of irradiated, neomycin treated male rats were compared with those of irradiated, untreated controls. Eleven selected radiation exposures, beginning at 700 R and extending in increments to 2500 R, were used. Thirty-day lethality was also evaluated at and below exposures of 1100 R.

Neomycin treatment resulted in a significant prolongation of the mean survival times of irradiated animals at exposures between 800 R and 1500 R. At exposures between 1500 R and 2500 R, a small but consistent prolongation of mean survival time resulted. For exposures between 700 R and 1100 R, the 30-day lethality was consistently lower for the neomycin treated rats.

It is suggested that postradiation treatment with oral neomycin, administered every 12 hours, can effect an increase in the mean survival time of whole-body X-irradiated rats.
TABLE OF CONTENTS

Abstract .............................................. i

I. Introduction ........................................ 1

II. Materials and Methods ............................ 2

III. Results ........................................... 5

IV. Discussion ......................................... 7

References ............................................. 11

LIST OF FIGURES

Figure 1. Maxitron exposure array .................. 4

Figure 2. Comparison between mean survival time of whole-body irradiated, untreated rats and whole-body irradiated, neomycin treated rats ........... 6

LIST OF TABLES

Table I. Survival Time Following Whole-Body X-irradiation of Neomycin Treated and Untreated Rats ........ 3

Table II. Lethality Following Whole-Body X-irradiation of Neomycin Treated and Untreated Rats .......... 7
I. INTRODUCTION

Much effort has been directed toward understanding the relationship between infection and radiation injury. Apparently it is important to learn the effect that normally commensal, endogenous bacteria, harbored principally in the gastrointestinal system, have on the physiologically altered, irradiated animal. Work has been done on mice to evaluate the role of bacteria in radiation sickness. This includes studies utilizing antibiotics or germfree animals. The effect of antibiotics on radiation sickness in rats has also been studied.

Although the response of germfree mice to radiation injury has been studied over large dose ranges, the effect of antibiotic therapy on response to radiation injury of conventional rodents has been generally observed over rather short dose ranges. The present study was designed to evaluate the effect of oral neomycin administered to groups of rats after exposure to lethal (LD 50/30 - LD 100/30) or supralethal (LD 100/6) doses of X-radiation. The particular antibiotic used in this study, neomycin, was chosen because of its ability to sterilize the enteric canal after sufficient oral administration, thus placing the test rat's bacteriologic status somewhere between germfree and conventional. It was felt that a comparison of survival times of neomycin treated irradiated rats with similarly irradiated nontreated controls, over a large exposure range (starting with 700 R and extending in increments to 2500 R) would provide some additional information on the role of gastrointestinal bacteria in the postirradiation course of rats.
II. MATERIALS AND METHODS

Male Sprague-Dawley rats from the Charles River Breeding Laboratory, Inc., weighing 180-220 grams, were housed singly in wire mesh bottom cages. They were allowed food (D.N.G. Rat Food, Frederick, Maryland) and water ad libitum and were kept under these conditions for 1 or 2 weeks prior to experimental use. Five dozen unirradiated rats were used to evaluate antibiotic toxicity, and a total of 65 dozen rats were exposed to 11 selected doses of whole-body X-irradiation between 700 R and 2500 R (Table I, columns 1-3). On the day of exposure each of 20 rats was placed in a ventilated plastic box (2-3/4 x 2-3/4 x 6-1/2 inches), and transported to the radiation facility. Twenty animals were exposed simultaneously. Ten were then set aside for observation, and 10 were started on the antibiotic regimen of neomycin (described below) within 30 minutes after exposure. The latter group was considered the "treated" irradiated group as compared with the "untreated" irradiated control group.

Radiation was delivered by a 250 KVP X-ray generator (Maxitron). The physical factors of the X-ray unit during exposure were as follows: 250 KVP, 30 ma, with inherent filtration of 0.95 mm copper and 1.2 mm beryllium, HVL 1.9 mm copper, equivalent to 106 KVE. The dose rate as measured by a Victoreen dosimeter was 70.8 R/min ± 3 percent in air. The exposure geometry was a circular slant array, 60 cm from the tube, with a field width of 12 cm and limited to ± 4 percent variation throughout the 360° arc (Figure 1).

A neomycin solution was administered into the buccal pouch of test rats by way of a 15-gauge cannula with a blunt end. A 0.5 cc disposable syringe was used to
Table I. Survival Time Following Whole-Body X-irradiation of Neomycin Treated and Untreated Rats

<table>
<thead>
<tr>
<th>Dose (Rl)</th>
<th>Group</th>
<th>Number of animals*</th>
<th>Mean survival time (hrs)</th>
<th>Standard error of mean (hrs)</th>
<th>Actual difference of means $\bar{X}_E - \bar{X}_C$</th>
<th>Percent change of control mean</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2500</td>
<td>Treated</td>
<td>30</td>
<td>93.39 : 12.60</td>
<td></td>
<td>2.30</td>
<td>+ 3.58</td>
<td>3.90 N.S.</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>91.11 : 7.42</td>
<td></td>
<td>1.33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2300</td>
<td>Treated</td>
<td>30</td>
<td>98.32 : 11.10</td>
<td></td>
<td>2.15</td>
<td>+ 4.72</td>
<td>5.04 &lt;.05</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>93.60 : 7.73</td>
<td></td>
<td>1.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2100</td>
<td>Treated</td>
<td>30</td>
<td>92.52 : 10.20</td>
<td></td>
<td>1.86</td>
<td>+ 7.71</td>
<td>8.49 &lt;.05</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>90.81 : 7.77</td>
<td></td>
<td>1.24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1900</td>
<td>Treated</td>
<td>30</td>
<td>103.00 : 13.94</td>
<td></td>
<td>2.54</td>
<td>+ 7.80</td>
<td>8.19 &lt;.05</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>95.20 : 8.42</td>
<td></td>
<td>1.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1700</td>
<td>Treated</td>
<td>30</td>
<td>100.40 : 20.94</td>
<td></td>
<td>3.82</td>
<td>+ 4.97</td>
<td>5.21 N.S.</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>95.43 : 8.92</td>
<td></td>
<td>1.63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1500</td>
<td>Treated</td>
<td>30</td>
<td>104.05 : 24.57</td>
<td></td>
<td>4.46</td>
<td>+ 9.33</td>
<td>8.70 &lt;.05</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>95.72 : 11.02</td>
<td></td>
<td>2.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1300</td>
<td>Treated</td>
<td>30</td>
<td>139.91 : 55.52</td>
<td></td>
<td>10.13</td>
<td>+ 58.02</td>
<td>37.31 &lt;.001</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>101.89 : 12.13</td>
<td></td>
<td>2.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1100</td>
<td>Treated</td>
<td>29</td>
<td>203.9 : 74.8</td>
<td></td>
<td>13.9</td>
<td>+ 89.5</td>
<td>76.26 &lt;.001</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>27</td>
<td>114.4 : 29.1</td>
<td></td>
<td>5.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>900</td>
<td>Treated</td>
<td>58</td>
<td>274.0 : 96.9</td>
<td></td>
<td>12.7</td>
<td>+ 98.3</td>
<td>55.95 &lt;.001</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>64</td>
<td>175.7 : 73.3</td>
<td></td>
<td>9.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>800</td>
<td>Treated</td>
<td>24</td>
<td>302 : 124</td>
<td></td>
<td>22</td>
<td>+ 106</td>
<td>54.08 &lt;.001</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>27</td>
<td>196 : 46</td>
<td></td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>700</td>
<td>Treated</td>
<td>13</td>
<td>330 : 116</td>
<td></td>
<td>32</td>
<td>+ 55</td>
<td>18.33 N.S.</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>18</td>
<td>300 : 144</td>
<td></td>
<td>34</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Only animals surviving <30 days are included.

* Probability by use of Student's "t" test, treated and untreated compared at each dose indicated.

$p = .25 - .20$

$p = .10 - .05$

measure the dose. Between 0.10 and 0.15 cc of neomycin solution, containing 87 to 130 mg of neomycin sulfate, constituted a single dose. The animals readily accepted the material, which was prepared by dissolving 100 gm of micronized, unsterile, neomycin sulfate, U.S.P. (assayed 648 mg of neomycin base per gm of neomycin sulfate) in 100 cc of distilled water. Treated rats, fed the neomycin solution within 30 minutes after exposure, received a second dose in 10 ± 1 hours, and twice daily, about every 12 hours, thereafter. This regimen was continued until the demise of the animals or for a maximum of 14 days. The 60 unirradiated rats were randomly separated into two groups of 30 each, one group of which was fed the neomycin solution (described above) twice daily for 10 days. Both groups were allowed food.
and water ad libitum. These 60 rats were weighed daily and observed for the appearance of diarrhea, and any other adverse response to the antibiotic.

In order to establish accurate postirradiation survival, all rats which received between 1100 R and 2500 R were observed at hourly intervals beginning on the 4th day after exposure. Rats exposed to lower doses were observed every 6 hours for 14 days, and thereafter every 12 hours through 30 days postirradiation.

Figure 1. Maxitron exposure array
III. RESULTS

The 30 unirradiated, neomycin treated rats developed no diarrhea and the mean daily weight gain for the 10 days of treatment paralleled that of the untreated rats. Treated rats had a mean daily weight gain of 4.31 gm/rat, compared to 4.16 gm/rat for untreated rats.

Survival times of all X-irradiated, untreated rats surviving less than 30 days after exposure were tabulated and the usual acute death mean survival time versus exposure dose curve was obtained. Similar data were then tabulated for the neomycin treated rats (Table I). At exposures of 1500 R and greater, there was always an increase in the mean survival time of the treated rats when compared to the untreated rats. However, in only two of the six selected exposures in this dose range, specifically 1900 R and 2100 R, was the difference between the means of the two groups statistically significant when evaluated by Student's "t" test. Probabilities from the statistical tests are listed in Table I, column 8. Between 1300 R and 800 R the difference in mean survival times of the two groups at each exposure was much greater than at the higher doses, and at these lower doses, the differences between the means are highly significant. The difference in the mean survival times of the two groups decreased abruptly at 700 R, where this difference was again not statistically significant. In all cases, however, the mean survival time of the neomycin treated rats was longer than the mean survival time of the untreated rats (Table I, column 6). The largest increase of rat mean survival time (Table I, column 7) occurred with neomycin treatment after whole-body X-irradiation of 1100 R.

Figure 2 demonstrates graphically the comparison of mean survival times of the
treated and untreated rats as a function of exposure dose of whole-body irradiation. The ranges plotted vertically are plus and minus one standard error of the mean (Table I, column 5).

Below 1100 R, acute death mean survival time was only one parameter of injury which changed. Another change occurred in the 30-day lethality (Table II) and consistently less mortality was noted among the neomycin treated rats when compared to equivalently irradiated untreated rats.

Figure 2. Comparison between mean survival time of whole-body irradiated, untreated rats and whole-body irradiated, neomycin treated rats.
Table II. Lethality Following Whole-Body X-irradiation of Neomycin Treated and Untreated Rats

<table>
<thead>
<tr>
<th>Dose (R)</th>
<th>Group</th>
<th>Number of animals</th>
<th>Number of 30-day survivors</th>
<th>Lethality</th>
</tr>
</thead>
<tbody>
<tr>
<td>2500</td>
<td>Treated</td>
<td>30</td>
<td>0</td>
<td>LD 100/5</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>0</td>
<td>LD 100/5</td>
</tr>
<tr>
<td>2300</td>
<td>Treated</td>
<td>30</td>
<td>0</td>
<td>LD 100/6</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>0</td>
<td>LD 100/5</td>
</tr>
<tr>
<td>2100</td>
<td>Treated</td>
<td>30</td>
<td>0</td>
<td>LD 100/5</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>0</td>
<td>LD 100/5</td>
</tr>
<tr>
<td>1900</td>
<td>Treated</td>
<td>30</td>
<td>0</td>
<td>LD 100/6</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>0</td>
<td>LD 100/5</td>
</tr>
<tr>
<td>1700</td>
<td>Treated</td>
<td>30</td>
<td>0</td>
<td>LD 100/8</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>0</td>
<td>LD 100/5</td>
</tr>
<tr>
<td>1500</td>
<td>Treated</td>
<td>30</td>
<td>0</td>
<td>LD 100/9</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>0</td>
<td>LD 100/5</td>
</tr>
<tr>
<td>1300</td>
<td>Treated</td>
<td>30</td>
<td>0</td>
<td>LD 100/12</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>30</td>
<td>0</td>
<td>LD 100/6</td>
</tr>
<tr>
<td>1100</td>
<td>Treated</td>
<td>30</td>
<td>1</td>
<td>LD 97/30</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>27*</td>
<td>0</td>
<td>LD 100/30</td>
</tr>
<tr>
<td>900</td>
<td>Treated</td>
<td>70</td>
<td>11</td>
<td>LD 84/30</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>70</td>
<td>5</td>
<td>LD 93/30</td>
</tr>
<tr>
<td>800</td>
<td>Treated</td>
<td>40</td>
<td>16</td>
<td>LD 60/30</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>40</td>
<td>13</td>
<td>LD 68/30</td>
</tr>
<tr>
<td>700</td>
<td>Treated</td>
<td>40</td>
<td>27</td>
<td>LD 33/30</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
<td>40</td>
<td>22</td>
<td>LD 45/30</td>
</tr>
</tbody>
</table>

* Records for hours of deaths were misplaced for 3 animals.

IV. DISCUSSION

The present study, planned to evaluate the effect of neomycin treatment on survival time, over a wide range of whole-body exposures, indicated prolongation of survival over this whole range. As seen in Table I, however, at the larger doses (1500 R through 2500 R) the prolongation of survival times of treated rats compared to untreated rats was quite small. Although this prolongation of survival time was not statistically significant, its constancy over a wide dose range indicates an apparent beneficial effect. Strikingly significant prolongation of mean survival times occurred for treated rats exposed in the dose range from 1100 R to 1500 R, at which doses there is known to be severe hematopoietic and significant gastrointestinal
damage. This beneficial effect of neomycin treatment, as measured by mean survival time, becomes much less significant as the exposure dose is further lowered from 1100 R to 700 R (Figure 2), but the effectiveness is reflected in the 30-day mortality. Between 1100 R and 700 R, consistently more treated rats survived 30 days than did untreated ones (Table II).

Although these findings are not in complete agreement with those of Quastler, they do support work reported by Taketa. Early work by Quastler described the "intestinal radiation death" and laid emphasis on the role of the intestinal mucosa in this form of radiation death by accentuating the role of water and electrolyte loss, suggesting the possible role of proteolytic enzymes and other toxins, but minimizing the role of the intestinal bacteria. However, a subsequent study by Taketa indicated that microorganisms play a prominent role in the genesis of acute intestinal death in the rat.

Further evidence for definite influence of gastrointestinal bacteria on the response to radiation injury includes the finding of a significant prolongation of mean survival time for X-irradiated germfree mice when compared to conventional controls, a prolongation of survival time when rats, mice, or dogs are treated with antibiotics, and rather dramatic survival of whole-body irradiated rats and dogs after combined treatment including antibiotics and fluid replacement therapy or blood transfusion. For mice, well documented relationships exist between gastrointestinal epithelial cell villus transit time and the presence or absence of gastrointestinal bacteria, suggesting the possibility that bacteria might have a direct effect on radiation-induced intestinal injury and repair. Bacterial agents that
exist commonly in the enteric canal are frequently isolated from the blood, spleen, or lymph nodes of whole-body irradiated animals in the moribund state, implying a relationship between gastrointestinal bacteria and radiation limited hematopoietic defense mechanisms. Antibiotics which affect the intestinal flora may then exert an eventual beneficial effect on either or both of these radiation-injured systems.

Neomycin will, when administered orally, essentially sterilize the gastrointestinal tract, yet is minimally absorbed from this route making large doses desirable. Orally administered after irradiation it theoretically removes only enteric bacteria and, therefore, appeared to be ideally suited to study the effect that the presence of enteric bacteria has on the irradiated, conventional rat. An encouraging study had been done using neomycin by gavage therapeutically for whole-body X-irradiated Wistar rats over a radiation exposure range from 325 R to 675 R. The study evaluated the effect of administering 10-15 mg of neomycin daily for 10-21 days and indicated that survival could occur after whole-body irradiation at levels lethal for controls, and that if survival occurred, it was related to the absence of coliform organisms in the rats' stools. The present study reinforces the evidence suggesting that microorganisms play a prominent role in the genesis of acute intestinal death in the rat.

As pointed out by Bond et al., the "radiation gastrointestinal syndrome" is the generalized response to whole-body irradiation and includes the result of a combination of injury to both the hematopoietic system and the gastrointestinal system. For animals exhibiting the radiation gastrointestinal syndrome, the postirradiation survival time may well be determined by the result of the combined injury, rather
than by the gastrointestinal injury alone. In the present study, because there are two parameters changing (i.e., the 30-day lethality and the acute death mean survival time), it is difficult to interpret the overall beneficial effect of treatment with oral neomycin after radiation exposures which do not result in 100 percent lethality within 30 days. Although the beneficial effect of oral neomycin is small for exposures at and above 1500 R, postirradiation treatment with this agent at lower exposures appears to cause an increase in survival time of whole-body irradiated rats, perhaps by delaying bacterial overgrowth during a time of severe hematopoietic depression.
REFERENCES


DISTRIBUTION LIST

ARMY
The Surgeon General, U. S. Department of the Army, Washington, D. C. 20315 (1)
USACDC CSSG, Doctrine Division, Fort Lee, Virginia 23801 (1)
CG, USCONARC, ATTN: ATUTR-TNG (NBC), Fort Monroe, Virginia 23651 (1)
Commanding Officer, U. S. Army Medical Research Laboratory, Fort Knox, Kentucky 40121 (1)
Commanding Officer, USA Nuclear Medical Research Detachment, Europe, APO New York, New York 09180 (2)
Army Research Office, ATTN: Chief, Scientific Analysis Branch, Life Sciences Division, 3045 Columbia Pike, Arlington, Virginia 22204 (1)
Division of Nuclear Medicine, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C. 20012 (5)

NAVY
Chief, Bureau of Medicine and Surgery, U. S. Navy Department, Washington, D. C. 20390 (1)
Commanding Officer and Director (222A), U. S. Naval Radiological Defense Laboratory, San Francisco, California 94135 (2)
Head, Division of Biology and Medicine, U. S. Naval Radiological Defense Laboratory, San Francisco, California 94135 (1)
Commanding Officer, Naval Aerospace Medical Institute, Naval Aviation Medical Center, ATTN: Director of Research, Pensacola, Florida 32512 (3)
Commanding Officer, Nuclear Weapons Training Center, Atlantic, Nuclear Warfare Department, Norfolk, Virginia 23511 (1)
Director, Biological Sciences Division, Office of Naval Research, Washington, D. C. 20360 (1)
Commanding Officer, U. S. Naval Hospital, ATTN: Director, REEL, National Naval Medical Center, Bethesda, Maryland 20014 (1)

AIRC FORCE
Executive Officer, Director of Professional Services, Office of the Surgeon General, Hq. USAF (AFMSPA) T-8, Washington, D. C. 20333 (1)
Headquarters, U. S. Air Force (AFMSPA), Washington, D. C. 20333 (1)
Chief, Radiobiology Branch, USAF School of Aerospace Medicine, Aerospace Medical Division (AFSC), Brooks AFB, Texas 78235 (2)
Air Force Weapons Laboratory, ATTN: WLIL, Kirtland AFB, New Mexico 87117 (1)
Chief, Nuclear Medicine Department, P. O. Box 5088, USAF Hospital Wright-Patterson, Wright-Patterson AFB, Ohio 45433 (1)

D.O.D.
Director, Defense Atomic Support Agency, Washington, D. C. 20301 (1)
Deputy Director Scientific, Defense Atomic Support Agency, Washington, D. C. 20301 (1)
Director, Defense Atomic Support Agency, ATTN: Chief, Medical Division, Washington, D. C. 20301 (1)
Director, Defense Atomic Support Agency, ATTN: Document Library Section, Washington, D. C. 20301 (1)
Commander, Field Command, Defense Atomic Support Agency, ATTN: PC Technical Library, Sandia Base, Albuquerque, New Mexico 87115 (1)
Director, Armed Forces Institute of Pathology, Washington, D. C. 20305 (1)
Administrator, Defense Documentation Center, Cameron Station, Bldg. 5, Alexandria, Virginia 22314 (20)

OTHER GOVERNMENT
U. S. Atomic Energy Commission, Division of Technical Information, P. O. Box 62, Oak Ridge, Tennessee 37831 (10)
U. S. Atomic Energy Commission, Headquarters Library, Reports Section, Mail Station G-17, Washington, D. C. 20545 (1)
U. S. Atomic Energy Commission, Division of Biology and Medicine, Washington, D. C. 20545 (1)
National Bureau of Standards, ATTN: Chief, Radiation Physics Division, Washington, D. C. 20234 (1)
U. S. Public Health Service, Deputy Chief, Division of Radiological Health, Washington, D. C. 20201 (1)
U. S. Public Health Service, Radiological Health Laboratory, ATTN: Library, 1901 Chapman Avenue, Rockville, Maryland 20852 (1)
U. S. Public Health Service, Northeastern Radiological Health Laboratory, 109 Holton Street, Winchester, Massachusetts 01890 (1)
U. S. Public Health Service, Southwestern Radiological Health Laboratory, P. O. Box 684, Las Vegas, Nevada 89101 (1)
1. ORIGINATING ACTIVITY (Corporate author)
   Armed Forces Radiobiology Research Institute
   Defense Atomic Support Agency
   Bethesda, Maryland 20014

2. REPORT TITLE
   THE EFFECT OF ORAL NEOMYCIN THERAPY FOLLOWING WHOLE-BODY X-IRRADIATION OF RATS

4. AUTHOR(S) (Last name, First name, Initial)
   Webster, J. B.

6. REPORT DATE
   October 1966

8. CONTRACT OR GRANT NO
   AFRRI SR66-5

9. PROJECT NO
   DB 03.1463

10. DISTRIBUTION OF THIS DOCUMENT
    Distribution of this document is unlimited.

11. SUPPLEMENTARY NOTES

12. SPONSORING MILITARY ACTIVITY
    Defense Atomic Support Agency
    Washington, D. C. 20301

13. ABSTRACT

   This study was designed to examine the beneficial effects of oral antibiotic treatment with neomycin following total-body X-irradiation of Sprague-Dawley rats. Survival times of irradiated, neomycin treated male rats were compared with those of irradiated, untreated controls. Eleven selected radiation exposures, beginning at 700 R and extending in increments to 2500 R, were used. Thirty-day lethality was evaluated at and below exposures of 1100 R. Neomycin treatment resulted in a significant prolongation of the mean survival times of irradiated animals at exposures between 800 R and 1500 R. At exposures between 1500 R and 2500 R, a small but consistent prolongation of mean survival time resulted. For exposures between 700 R and 1100 R, the 30-day lethality was consistently lower for the neomycin treated rats. It is suggested that postradiation treatment with oral neomycin, administered every 12 hours, can effect an increase in the mean survival time of whole-body X-irradiated rats.
<table>
<thead>
<tr>
<th>KEY WORDS</th>
<th>LINK A</th>
<th>LINK B</th>
<th>LINK C</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray irradiation</td>
<td>ROLE</td>
<td>HT</td>
<td>ROLE</td>
</tr>
<tr>
<td>dosage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>survival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>antibiotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>neomycin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rat</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**INSTRUCTIONS**

1. **ORIGINATING ACTIVITY:** Enter the name and address of the contractor, subcontractor, grantee, Department of Defense activity or other organization (corporate author) issuing the report.

2a. **R. ORT SECURITY CLASSIFICATION:** Enter the overall security classification of the report. Indicate whether "Restricted Data" is included. Marking is to be in accordance with appropriate security regulations.

2b. **GROUP:** Automatic downgrading is specified in DoD Directive 5200.10 and Armed Forces Industrial Manual. Enter the group number. Also, when applicable, show that optional markings have been used for Group 3 and Group 4 as authorized.

3. **REPORT TITLE:** Enter the complete report title in all capital letters. Titles in all cases should be unclassified. If a meaningful title cannot be selected without classification, show title classification in all capitals immediately following the title.

4. **DESCRIPTIVE NOTES:** If appropriate, enter the type of report, e.g., interim, progress, summary, annual, or final. Give the inclusive dates when a specific reporting period is covered.

5. **AUTHOR(S):** Enter the name(s) of author(s) as shown on or in the report. Enter last name, first name, middle initial. If military, show rank and branch of service. The name of the principal author is an absolute minimum requirement.

6. **REPORT DATE:** Enter the date of the report as day, month, year; or month, year. If more than one date appears on the report, use date of publication.

7a. **TOTAL NUMBER OF PAGES:** The total page count should follow normal pagination procedures, i.e., enter the number of pages containing information.

7b. **NUMBER OF REFERENCES:** Enter the total number of references cited in the report.

8a. **CONTRACT OR GRANT NUMBER:** If appropriate, enter the applicable number of the contract or grant under which the report was written.

8b. & 8d. **PROJECT NUMBER:** Enter the appropriate military department identification, such as project number, subproject number, system numbers, task number, etc.

9a. **ORIGINATOR'S REPORT NUMBER(S):** Enter the official report number by which the document will be identified and controlled by the originating activity. This number must be unique to this report.

9b. **OTHER REPORT NUMBER(S):** If the report has been assigned any other report numbers (either by the originator or by the sponsor), also enter this number(s).

10. **AVAILABILITY/LIMITATION NOTICES:** Enter any limitations on further dissemination of the report, other than those imposed by security classification, using standard statements such as:

   (1) "Qualified requesters may obtain copies of this report from DDC."

   (2) "Foreign announcement and dissemination of this report by DDC is not authorized."

   (3) "U. S. Government agencies may obtain copies of this report directly from DDC. Other qualified DDC users shall request through...

   (4) "U. S. military agencies may obtain copies of this report directly from DDC. Other qualified users shall request through...

   (5) "All distribution of this report is controlled. Qualified DDC users shall request through..."

If the report has been furnished to the Office of Technical Services, Department of Commerce, for sale to the public, indicate this fact and enter the price, if known.

11. **SUPPLEMENTARY NOTES:** Use for additional explanatory notes.

12. **SPONSORING MILITARY ACTIVITY:** Enter the name of the departmental project office or laboratory sponsoring (paying for) the research and development. Include address.

13. **ABSTRACT:** Enter an abstract giving a brief and factual summary of the document indicative of the report, even though it may also appear elsewhere in the body of the technical report. If additional space is required, a continuation sheet shall be attached.

It is highly desirable that the abstract of classified reports be unclassified. Each paragraph of the abstract shall end with an indication of the military security classification of the information in the paragraph, represented as (TS), (S), (C), or (U).

There is no limitation on the length of the abstract. However, the suggested length is from 150 to 225 words.

14. **KEY WORDS:** Key words are technically meaningful terms or short phrases that characterize a report and may be used as index entries for cataloging the report. Key words must be selected so that no security classification is required. Identifiers, such as equipment model designation, trade name, military project code name, geographic location, may be used as key words but will be followed by an indication of technical context. The assignment of links, rules, and weights is optional.