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EFFECTS OF PERIODIC DOSES OF SLOW NEUTRONS ON MICE

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Abstract

Periodic doses of a radiation designated as "slow neutron" were given to two groups of 100 CF-1 female mice. Each arbitrary unit of dose, expressed in a, was composed of slow neutrons considerably contaminated with fast neutrons. The mice were exposed in a manner similar to that used for fast neutron exposures, but in the cart designed specifically for "slow neutron" irradiation.

The results are very similar to those observed as a consequence of periodic fast neutron treatments. A comparison of the shortening of life induced by each radiation indicates that 1 n is as effective as 7.5 a, a ratio roughly equivalent to that observed after single doses. A dose of 10 a per day depressed the leukocyte level to a range between 2000 and 3000 cells/mm.^{3}; more pronounced blood changes probably would have been noted had other strains been used. The terminal pathological condition of the experimental mice was essentially like that observed after periodic fast neutron or gamma ray irradiation.

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EFFECTS OF PERIODIC DOSES OF SLOW NEUTRONS ON MICE

1. Introduction

Two groups of mice, 100 mice per group, were given small, periodic doses of slow neutrons to observe the effects of such treatment. This investigation was the last phase of the extensive study of total body irradiation carried out at Clinton Laboratories. The same effects have been observed in each part of the study to make direct comparisons possible. The effects produced by periodic doses of fast neutrons or gamma rays have been reported in MonH-115, the effects of the same radiations after a single dose in MonH-116, and single slow neutron doses in MonH-117. The primary purpose of the entire study was to provide more adequate experimental data with which to set tolerance levels for radiation workers. In addition, it was hoped to gain some knowledge of the mechanism of radiation effects which would be of significance in protection and therapeutic developments.

2. Exposure Techniques

2.1 Radiation Used:

The radiation utilized for this study, although called "slow neutron", was badly contaminated with fast neutrons. An analysis of the components has indicated that half of the biological effect is contributed by each class of neutron[1]. The radiation was monitored by boron encased chambers of the Victoreen r-meter; doses of this radiation

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1. Zirkle, R. E. - Monthly Report - CH-2808

were expressed in terms of a[2].

2.2 Irradiation Procedure:

The exposure cart described in MonH-117 was also used for these experiments. Each day, before any exposures were made, the rate at which a dose could be given was determined as described in the reference just cited. The duration of any exposure was based upon the daily dose rate and was measured by both a proportional counter and an electric clock to ensure accurate results.

Female mice of the standard CF-1 strain were used exclusively for this study. The method used to put these mice into the experimental cart with a minimum exposure of personnel to radiation from the cart has been described[2]. As pointed out in the description of single slow neutron dose effects, the loading procedure was apt to injure the mice; the periodic exposures greatly increased the probability of injuring any particular mouse. Anticipating that frequent mechanical injury would act to shorten life, specific controls were also put into the cart each day but, of course, given no irradiation. The difference in control and experimental mortality rate indicates, then, the radiation effect.

2.3 Accuracy of Dosage:

The largest source of error in single doses was due to the fact that the radiation intensity varied from front to back of the cart at the exposing position. The dose rate, determined by the preliminary monitor run, was the average rate

2. Henshaw, P. S., R. S. Snider, E. F. Riley, and G. E. Stapleton - Delayed Effects of Single Doses of Slow Neutrons on Mice - MonH-117.

at the center of the cart. Then, since mice were placed at random in the cart, the average dose received by these mice during the course of many treatments was that indicated by the meter. Thus this source of error became unimportant for this study.

Other sources of error during this investigation were (1) error in reading the meter (2) lack of reproducibility of the counter and (3) errors in administering the exact dose prescribed. Since the significance of each source of error is the same as applied for periodic fast neutron exposures[3], it will be sufficient to say that the error was probably not more than 10 percent and tended to make the actual dose greater than the stated dose.

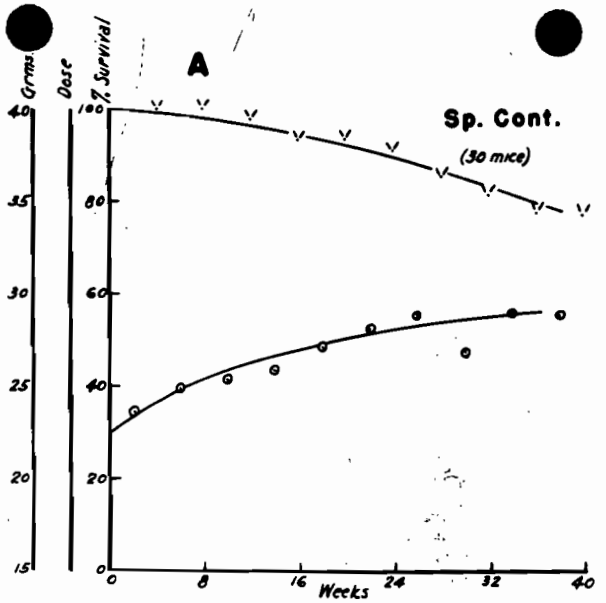
3. Experimental Results

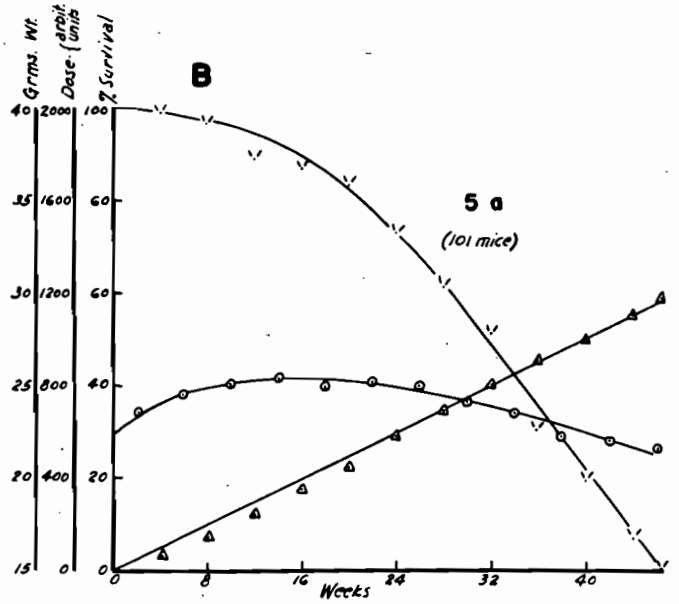
3.1 Shortening of Life:

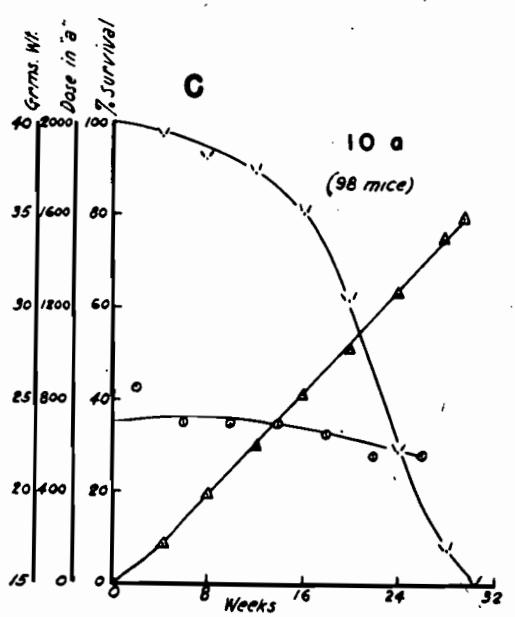
The ability of mice to survive repeated treatments of slow neutrons is presented in the graphs of Figure 1. The

Figure 1. Dose-weight-survival relationships observed in groups of CF-1 female mice: A the specific controls, B the 5a per day, and C the 10a per day group.

3. Henshaw, P. S., R. S. Snider, E. F. Riley, G. E. Stapleton, and R. E. Zirkle - Comparative Late Effects of Periodic Doses of Fission Neutrons and of Gamma Rays - MonH-115.


A
Sp. Cont.
(30 mice)
Grms.
Dose
% Survival
Weeks


B
5 a
(101 mice)
Grms. Wt.
Dose (droit. units)
% Survival
Weeks


C
10 a
(98 mice)
Grms. Wt.
Dose in "a"
% Survival
Weeks

curves drawn through the V symbols show percent survival; the accumulated dose is indicated by triangular symbols and the average group weight by circular symbols. The treatment given to each group and the numbers upon which the curves were based are noted by the respective curves. The scales used were the same for all three sets of curves.

A comparison of these controls with the corresponding fast neutron controls shows that the ability to survive is much the same in both cases. Accordingly, we may conclude that the mechanical injury suffered during the loading procedure did not contribute as much as was expected to a shortening of life. The slow neutron control group appears to be dying at a slightly higher rate so the average life span will probably not be as long as that of the fast neutron control group. Since 80 percent of the mice were still living when the survival curve of Figure 1A was drawn, the average life expectancy was estimated by extrapolation based upon experience with other control groups, the value so derived being between 56 and 60 weeks.

Analysis of the curves obtained with the two experimental groups shows that repeated doses cause both a loss in weight and premature death. The average life span of the 10a group was found to be 22 weeks, that of the 5a group 32 weeks. Then, if 58 weeks is assumed to be a fair estimate of the length of life of the average control mouse, it follows that the 10a group lived 38 percent as long and the 5a group 55 percent as long as the controls. Thus 10a per day shortens a mouse's life 62 percent. When this value is plotted on a curve of percent shortening of life by periodic fast neutron doses, 10a appears to have shortened life as much as 1.3 n per day would have. On the basis of

this comparison 1 n would seem to be about 7.5 times as effective as 1 a. This value is probably a better comparative value than any quoted in MonH-117 since the periodic doses were more accurate than single doses and not subject to as many correction factors.

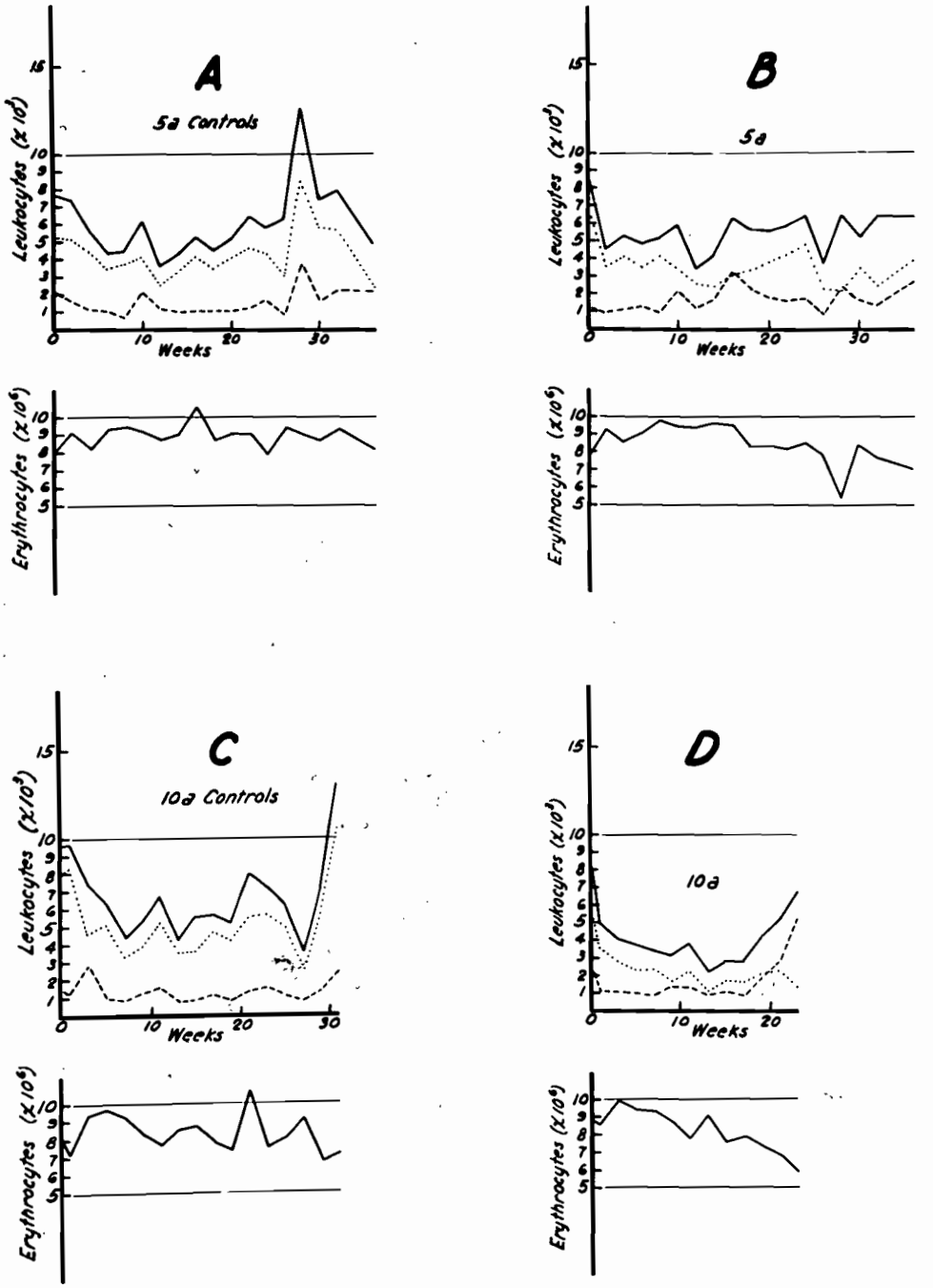
3.2 Hematology and Pathology:

Figure 2 shows the hematological findings associated with

Figure 2. Peripheral blood changes associated with daily exposure to slow neutrons. A and C specific controls; B and D: 5 and 10 a daily treatments, respectively.

5 and 10 a daily exposures of slow neutrons. Because of the specific control picture, it is doubtful whether the continuous low leukocyte level obtained with 5 a animals is due to irradiation. The results obtained with 10 a animals, however, are definitely on the positive side. Total leukocyte levels dropping to the range of 2000 and 3000 rarely happens in normal animals. But as pointed out on other occasions, CF-1 animals proved to be rather unsatisfactory for hematologic studies because of the downward drift in controls. It seems likely that rather dramatic blood changes might be obtained with 5 and 10 a daily doses in other strains of animals.

The terminal pathology in periodic slow neutron treated animals revealed the same conditions as obtained with fast neutrons and gamma rays - a gradual emaciation and decline and occasional mediastinal lymphomatoses. It should be noted that about one fourth of the animals in this series


A
5a Controls
Leukocytes (x10³)
Weeks
Erythrocytes (x10⁶)
B
5a
Leukocytes (x10³)
Weeks
Erythrocytes (x10⁶)
C
10a Controls
Leukocytes (x10³)
Weeks
Erythrocytes (x10⁶)
D
10a
Leukocytes (x10³)
Weeks
Erythrocytes (x10⁶)

died with a lung infection of unknown type. Great numbers of small pustules formed throughout the lungs and on the walls of the pleural cavity. Since at first these were seen only in treated groups there was a tendency to attribute the reaction to some specific action of the radiation being used. Later a few cases were seen in other groups including controls and there were groups in this series that showed no such infections. Hence, this was regarded merely as an accidental infection. Because of the infection, however, the incidence figures for tumors have little value.

4. General Summary

Slow neutrons administered in small periodic treatments have been found to shorten life, cause loss of weight, and change bodily organs. Repeated doses of 10 a shorten life to 38 percent of the normal expectancy; 5 a per day reduces the life span to 55 percent of normal. The kinds of effects observed in this experiment are very similar to those observed after daily fast neutron exposures. Since the same observation was made in connection with the single dose investigation, it may be stated that slow neutron radiation does not have a unique biologic action, rather it is much like fast neutron or gamma radiation.

On the basis of the dose-effect relationships noted here and in the corresponding fast neutron investigation, 1 n appears to be as effective as 7.5 a as defined. This is not greatly different from the ratio obtained with single doses where 92 n and 525 a constitued an LD-50. When comparing single and periodic gamma and fast neutron effects it was found that the biological effectiveness ratio changed from 1 n/9r for single doses to 1 n / 15 - 30 r for periodic doses. The stability of the fast and slow neutron ratio in contrast to the different gamma to n ratios suggests that slow neutrons act biologically more like fast neutrons than like gamma rays. However, the radiation used for slow neutron exposures was by no means pure. Therefore, before making any conclusions based upon quantitative results as observed, the components of the various radiations should be more carefully analyzed and the methods of dose measuring carefully evaluated. In fact, the difficulty encountered in evaluating quantitative effects emphasizes the need for a satisfactory biological unit of dose which can be applied to and measured for each of the various radiations.

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