THE EFFECT OF CYSTEINE ON THE PERIPHERAL BLOOD OF THE IRRADIATED RAT

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Earlier studies have revealed that cysteine is highly effective in protecting rats against lethal X-irradiation. There is reason to believe that the amino acid, perhaps by preventing oxidations by free radicals, neutralizes a portion of the radiation and thereby decreases its biologic effectiveness. Since the formed elements of peripheral blood are very sensitive indicators of radiation damage, these were selected to evaluate further the influence of cysteine on the irradiated animal.

METHODS

The methods were the same as those reported earlier. Control and experimental rats (male, Sprague-Dawley, 150-250 Gm.) were irradiated simultaneously, caged together, and otherwise similarly handled. Cysteine (950 mg. per Kg., pH 7-8) was injected into a tail vein 5 minutes before irradiation. Irradiated controls received an intravenous injection of 0.5 per cent sodium chloride. The radiation factors were 150 kv, 15 ma, 0.5 mm.-Cu and 3.0-mm. Bakelite filters, 16.5 cm. target distance, 1.5 mm. Cu half value layer, 110 r per minute dose rate. The rats received 800 r total-body x-radiation in a single exposure.

Blood sampling was accomplished by making a deep cut in the tail with a sharp razor blade and using a free flow of blood. Studies of the peripheral blood included total leukocyte, erythrocyte, and reticulocyte counts, hemoglobin, hematocrit and the leukocyte differential using Wright's stain. Control determinations were made before the animals were irradiated and at intervals following treatment. Nonirradiated cysteine and control rats and irradiated cysteine and control rats were sampled at comparable times. Each group consisted of 12 rats with exception of the irradiated cysteine group which contained 9.

RESULTS

The white blood elements of the irradiated controls showed a maximal depression four days after the exposure. Significant recovery ($p < 0.05$) was evident three weeks after irradiation and was essentially complete within 40 days. Change in the leukocyte count of the irradiated rats pretreated with cysteine was less severe. Maximal depression in the latter group also appeared 4 days after the exposure but definite recovery was manifest considerably earlier (9 days post x-ray). The leukocyte count of the nonirradiated controls was increased for several days after the single injection of either cysteine or sodium chloride. The results are presented in figure 1.

Radiation-induced changes in the heterophils and lymphocytes were diminished in rats pretreated with cysteine, and recovery occurred significantly sooner (figs. 2 and 3). An increase of borderline significance was observed in the heterophil count of the irradiated controls one day after exposure. Marked depression of heterophils was noted at 4, 7, 10, and 14 days and significant recovery toward the normal at 21 days. In the irradiated rats receiving cysteine as well as in the cysteine controls, a significant rise in the heterophils ($p < 0.05$) was evident one day after

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the injection. The heterophils of cysteine-irradiated rats were depressed significantly below the normal 4 days after exposure, and appreciable recovery was evident at 7 days.

Maximal depression of lymphocytes in the irradiated controls appeared 4 days after the exposure. The lymphocytic elements remained depressed until the twenty-first day when definite recovery was noted. In the cysteine irradiated group, maximal depression occurred on the first day and significant recovery was apparent by the tenth day after the irradiation. An increased lymphocyte count was seen in both of the nonirradiated control groups (cysteine and sodium chloride) on the first and fourth days after the injection.

The number of circulating erythrocytes in the irradiated controls fell sharply 10 days after the exposure and the maximal anemia occurred at 21 days. The erythrocyte count returned toward normal at 28 days and recovery was essentially complete by 40 days. A comparatively small decrease in erythrocyte count was seen 10 days after exposure in irradiated rats pretreated with cysteine. The erythrocyte level was rapidly restored in these animals; recovery began at 14 days and was
completed by 28 days (fig. 4). There were no significant changes in the erythrocyte counts of the nonirradiated controls. The hematocrit and hemoglobin in the irradiated and nonirradiated groups in general followed closely the change in circulating erythrocytes. Severe depression of the reticulocytes was observed in all of the irradiated animals 4 days after the exposure, but recovery occurred significantly earlier in the animals receiving cysteine (fig. 5). A marked reticulocytosis was noted in the latter on the twenty-first day and in the irradiated controls on the twenty-eighth day.

Four of the 12 irradiated controls were alive 70 days after the exposure. Control fatalities were distributed as follows: one on the seventh day, three on the tenth day, one on the fourteenth day, one on the twenty-first day, one on the twenty-second day, and one on the fifty-sixth day. Only 2 of the 9 cysteine-irradiated rats
FIG. 3.—Influence of cysteine on the lymphocyte count after total-body x-irradiation.

FIG. 4.—Influence of cysteine on the erythrocyte count after total-body x-irradiation.
died during the 70-day postirradiation period; the 2 fatalities occurred on the twenty-first and fifty-third days. None of the nonirradiated controls succumbed.

**Fig. 5.—Influence of cysteine on the reticulocyte count after total-body x-irradiation.**

**DISCUSSION**

Our results reveal that cysteine significantly modified the radiation-induced hematologic changes. Depression of the heterophils, lymphocytes, and erythrocytes was less severe and recovery was more rapid. The protection afforded the heterophils by cysteine appears to be somewhat greater than that observed for the lymphocytes. This is not unreasonable in view of the greater radiosensitivity of the latter. The data derived from the cysteine group receiving 800 r are comparable to those observed by Stearer et al. in rats of the same strain after a sublethal exposure of 300 r. This comparison provides a rough approximation of the protection afforded the blood-forming tissues by cysteine. However, differences in the dose rate employed (15 r per minute by Steamer and 2.15 r per minute in the present work) and in the prevailing LD₅₀ (625 r during the earlier work by Steamer and 750 r at present) should be considered in evaluating this interesting comparison.

There is evidence that depression of the heterophils rather than of the lymphocytes correlates with the lethal radiation dose among the various species of animals. This relationship between the heterophil response and the lethal effect receives further support in other studies where estrogens were employed to alter radiosensitivity. In this connection, it is of interest that there appears to be greater
protection of the heterophils than of the lymphocytes in animals whose resistance to lethal x-irradiation is enhanced by cysteine.

SUMMARY

A single injection of cysteine (950 mg. per Kg., I.V.) 5 minutes before total-body exposure of rats to x-rays (800 r) significantly modified the radiation-induced hematologic changes. Depression of the heterophils, lymphocytes, and erythrocytes was less severe and recovery more rapid. The hematologic observations are consistent with the thesis that cysteine reduces the biological effectiveness of the radiation.

REFERENCES


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