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Citation	日本医学放射線学会雑誌. 1973, 33(4), p. 344-350
Version Type	VoR
URL	<a href="https://hdl.handle.net/11094/15241">https://hdl.handle.net/11094/15241</a>
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## Hematological Changes after Partial Body or Whole Body Irradiation in Mice

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Research Code No.: 400

Key Words: Partial body irradiation, Hematological changes, Mice, Blood

### マウスにおける部分照射および全身照射後の血液像の変化

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(昭和47年11月4日受付)

ddN 系雌ハツカネズミ (10~11週令) に 500 R X線全身または部分照射を行ない、末梢血中の白血球数、栓球数、赤血球数およびヘマトクリット値の変化を、経日的に、22日後まで追跡した。部分照射群は、(1) 頭部・上肢群、(2) 胸腹部群、および(3) 骨盤・下肢・尾部群の3群とした。

白血球数は、全身照射群では、4日目頃極小値に達し、10日以後徐々に回復した。部分照射群の中で、減少の程度と回復遅延が最も著しかったのは胸腹部群であった。頭部・上肢群と骨盤・下肢・尾部群とでは、同じ様な変化のパターンがみられた。すなわち、2日目頃の極小値の後、回復し始め旧に復した。

栓球数は、全身照射群では、3日目頃から減少

し始め、10日目頃極小値をとり、その後回復した。部分照射群での変化は、全身照射群でのそれと同じ傾向を示したが、減少の程度はかなり軽かった。

赤血球数およびヘマトクリット値に関しては、全身照射群では10日目頃に極小値がみられたが、部分照射群では有意の変化はみられなかった。

各部分照射群で観察された白血球数、栓球数の減少の程度と、それらの群の照射部位に分布する活性骨髄細胞推定数との間には平行関係がみられた。極小値は、いずれの部位の照射後も赤血球系、栓球系、白血球系の順に小となり、影響が特定の血球系に偏るような照射部位の存在を示唆するような成績は得られなかった。

### Introduction

Many reports are available which concern with hematological changes after a single whole body irradiation. Whereas, only a little attention has been given to the hematological changes which are induced by partial body exposure of animal<sup>8)10)11)</sup>. Present paper deals with changes in number of three cell lines, thrombocyte, erythrocyte and leukocyte, in peripheral blood investigated in parallel after a systematic partial body irradiation of mice. Attention was paid to see if an irradiation of some special

part of the body was in connection with an accentuated change in some special cell lines.

### Materials and Methods

Female mice (ddN) of 10 to 11 weeks old were used throughout the experiment. The radiation was delivered by a 200 kVp x-ray unit having a dose rate of 38.2 R/min. The radiation was filtered through 0.5 mm Cu and 0.5 mm Al. A group of 8 mice, each in a separate compartment of a lucite cage, was irradiated at one time. Prior to and after irradiation, the mice were housed in a quarter air-conditioned at  $24 \pm 1^\circ\text{C}$ .

For partial body irradiation, following three groups were assigned.

1. Head exposure (head and upper limbs)
2. Trunk exposure (chest and abdomen)
3. Lower body exposure (pelvis, lower limbs, and tail)

The relative weights of each exposure region against whole body were as follows. Head:  $24.2 \pm 0.7\%$  (mean  $\pm$  SE), Trunk:  $51.3 \pm 0.9\%$ , Lower body:  $24.5 \pm 0.4\%$ . The above exposure pattern is different from that of previous work<sup>9)</sup> in the head exposure, upper limbs being contained in the present experiment. The shield was accomplished with lead 5 mm thick. The absorbed dose in the shielded area was a few percent of that in the irradiated area. All the mice were anesthetized by intraperitoneal injection of Nembutal (0.1 mg/g body weight) during the irradiation. Since  $LD_{50}$  (30) of whole body exposure under the anesthetic condition was 815 R<sup>9)</sup>, each mice was given 500 R as a sublethal dose.

Thrombocytes, erythrocytes and leukocytes in the circulating blood were counted by a hemocytometer with blood taken from a tail vein by a method previously described<sup>7)</sup>. Hematocrit values were determined by centrifuging blood taken from the outer iliac artery and vein in a capillary tube. In order to exclude a possible effect of the preceding treatment, the blood sampling was restricted to once a mouse. Each group was consisted of 8 mice and 365 mice were used in this experiment.

### Results

#### 1. Changes in anesthetized controls

The blood cell count and hematocrit value in the anesthetized controls were measured on 0.1.3.6.10. and 21 days after the anesthesia. Over this period there was no statistically significant differences in

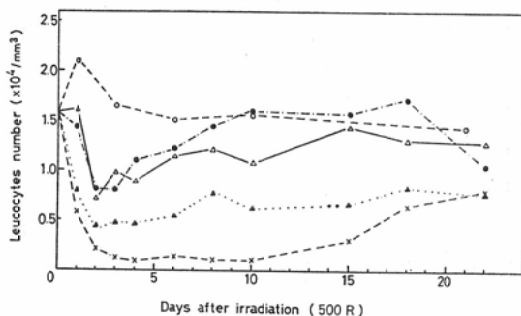


Fig. 1. Changes in leucocyte count in the circulating blood of mice exposed to 500 R. Whole body irradiation (x---x), head irradiation (Δ---Δ), trunk irradiation (▲.....▲), lower body irradiation (●---●), non-irradiated control (○---○). Each point represents the mean of 8 mice.

Table 1. Leucocyte count in the circulating blood of mice after 500 R of whole or partial body irradiation

Days after Irradiation	Non-Irradiated Control ( $\times 10^4/\text{mm}^3$ )	Whole Body Irradiation ( $\times 10^4/\text{mm}^3$ )	Partial Body Irradiation		
			Head ( $\times 10^4/\text{mm}^3$ )	Trunk ( $\times 10^4/\text{mm}^3$ )	Lower Body ( $\times 10^4/\text{mm}^3$ )
0	1.60 $\pm$ 0.11 <sup>a</sup>				
1	2.14 $\pm$ 0.30	0.57 $\pm$ 0.07** <sup>b</sup>	1.63 $\pm$ 0.23	0.77 $\pm$ 0.10**	1.44 $\pm$ 0.12
2		0.21 $\pm$ 0.03**	0.71 $\pm$ 0.09**	0.40 $\pm$ 0.03**	0.81 $\pm$ 0.01**
3	1.66 $\pm$ 0.09	0.12 $\pm$ 0.01**	1.00 $\pm$ 0.10**	0.48 $\pm$ 0.06**	0.81 $\pm$ 0.06**
4		0.09 $\pm$ 0.01**	0.89 $\pm$ 0.10**	0.47 $\pm$ 0.03**	1.10 $\pm$ 0.15**
6	1.51 $\pm$ 0.07	0.14 $\pm$ 0.01**	1.15 $\pm$ 0.12**	0.54 $\pm$ 0.07**	1.23 $\pm$ 0.10**
8		0.11 $\pm$ 0.02**	1.23 $\pm$ 0.20	0.79 $\pm$ 0.05**	1.46 $\pm$ 0.21
10	1.57 $\pm$ 0.12	0.10 $\pm$ 0.02**	1.08 $\pm$ 0.12**	0.62 $\pm$ 0.06**	1.61 $\pm$ 0.19
15		0.30 $\pm$ 0.04**	1.46 $\pm$ 0.17	0.67 $\pm$ 0.08**	1.58 $\pm$ 0.18
18		0.65 $\pm$ 0.12**	1.32 $\pm$ 0.14	0.84 $\pm$ 0.10**	1.73 $\pm$ 0.26
21	1.43 $\pm$ 0.26				
22		0.80 $\pm$ 0.07**	1.28 $\pm$ 0.13	0.77 $\pm$ 0.07**	1.06 $\pm$ 0.16**
Mean of Control Pooled	1.65 $\pm$ 0.08				

a Values are mean  $\pm$  SE. Mice used are 8 for all groups.

b \*\*P<0.01 compared with pooled control value.

the blood cell counts or hematocrit value. Accordingly these values were pooled as a control value which served as a reference for the experimental groups.

## 2. Changes in leukocyte count

Changes in leukocyte count after exposure to 500 R are shown in Fig. 1. Their standard errors and statistical significances are tabulated in Table 1. Pairs of asterisks indicate significant deviations from the control value with  $p=0.01$ . After the whole body exposure leukocyte count reached its minimum value around the 4th day and began to recover on the 10th day. Whereas, by the partial body exposure

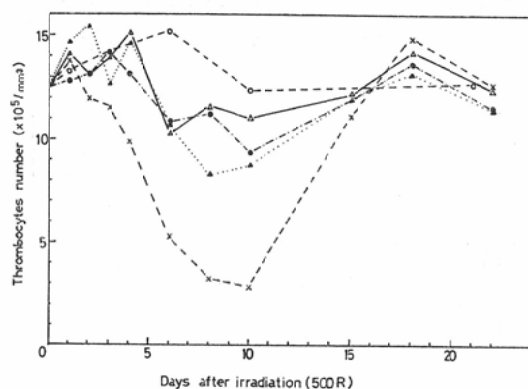


Fig. 2. Changes in thrombocyte count in the circulating blood of mice exposed to 500 R. Whole body irradiation (x---x), head irradiation ( $\Delta$ — $\Delta$ ), trunk irradiation ( $\blacktriangle$ ···· $\blacktriangle$ ), lower body irradiation ( $\bullet$ --- $\bullet$ ), non-irradiated control ( $\circ$ — $\circ$ ). Each point represents the mean of 8 mice.

Table 2. Thrombocyte count in the circulating blood of mice after 500 R of whole or partial body irradiation

Days after Irradiation	Non-Irradiated Control ( $\times 10^5/\text{mm}^3$ )	Whole Body Irradiation ( $\times 10^5/\text{mm}^3$ )	Partial Body Irradiation		
			Head ( $\times 10^5/\text{mm}^3$ )	Trunk ( $\times 10^5/\text{mm}^3$ )	Lower Body ( $\times 10^5/\text{mm}^3$ )
0	12.5 $\pm$ 0.8 <sup>a</sup>				
1	13.3 $\pm$ 0.9	13.8 $\pm$ 0.9	14.1 $\pm$ 0.8	14.7 $\pm$ 0.8	12.8 $\pm$ 0.6
2		11.9 $\pm$ 1.4	13.1 $\pm$ 0.8	15.6 $\pm$ 0.8	13.1 $\pm$ 0.9
3	14.2 $\pm$ 0.7	11.6 $\pm$ 0.6	14.0 $\pm$ 0.5	12.6 $\pm$ 1.0	14.2 $\pm$ 1.1
4		9.9 $\pm$ 0.7**b	15.2 $\pm$ 1.0	14.8 $\pm$ 0.7	13.2 $\pm$ 1.0
6	15.2 $\pm$ 0.7	5.3 $\pm$ 0.4**	10.3 $\pm$ 0.8**	10.7 $\pm$ 0.7**	10.9 $\pm$ 0.7**
8		3.2 $\pm$ 0.3**	11.7 $\pm$ 0.9	8.3 $\pm$ 0.6**	11.2 $\pm$ 0.9
10	12.3 $\pm$ 0.8	2.8 $\pm$ 0.2**	11.1 $\pm$ 0.9	8.8 $\pm$ 0.7**	9.4 $\pm$ 0.5**
15		11.0 $\pm$ 0.9	12.2 $\pm$ 0.8	12.0 $\pm$ 0.4	12.0 $\pm$ 1.0
18		14.9 $\pm$ 0.8	14.3 $\pm$ 0.9	13.2 $\pm$ 0.8	13.7 $\pm$ 1.2
21	12.7 $\pm$ 0.7				
22		12.6 $\pm$ 1.0	12.5 $\pm$ 0.8	11.4 $\pm$ 0.6	11.6 $\pm$ 0.9
Mean of Control Pooled	13.4 $\pm$ 0.3				

a Values are mean  $\pm$  SE. Mice used are 8 for all groups.

b \*\*P&lt;0.01 compared with pooled control value.

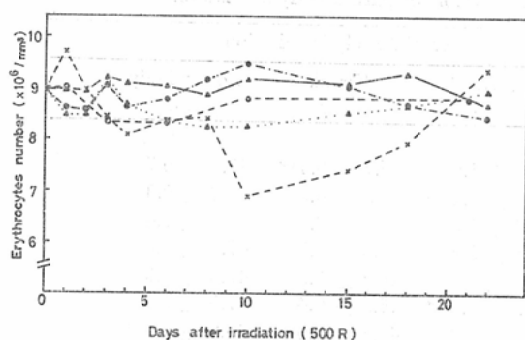


Fig. 3. Changes in erythrocyte count in the circulating blood of mice exposed to 500 R. Whole body irradiation (x---x), head irradiation (Δ---Δ), trunk irradiation (▲.....▲), lower body irradiation (●---●), non-irradiated control (○---○). Each point represents the mean of 8 mice.

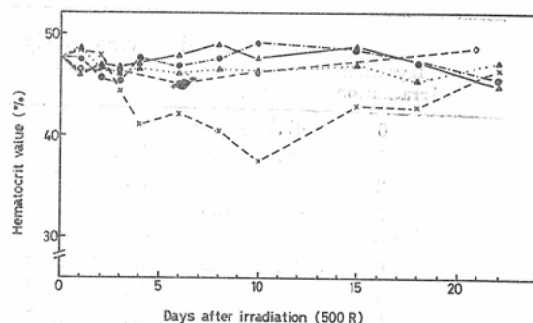


Fig. 4. Changes in hematocrit value of mice exposed to 500 R. Whole body irradiation (x---x), head irradiation (Δ---Δ), trunk irradiation (▲.....▲), lower body irradiation (●---●), non-irradiated control (○---○). Each point represents the mean of 8 mice.

of head or lower body, the decrease in count was slighter and the start of recovery was earlier than in whole body group. The degree of these changes was intermediate in the trunk group.

### 3. Changes in thrombocyte count

Changes in thrombocyte count after 500 R exposure are shown in Fig. 2 and Table 2. After the whole body exposure thrombocyte count decreased to a minimum value on the 10th day and recovered to normal level by the 18th day. The other three groups of partial body exposure showed changes of

Table 3. Erythrocyte count in the circulating blood of mice after 500 R of whole or partial body irradiation

Days after Irradiation	Non-Irradiated Control ( $\times 10^6/\text{mm}^3$ )	Whole Body Irradiation ( $\times 10^6/\text{mm}^3$ )	Partial Body Irradiation		
			Head ( $\times 10^6/\text{mm}^3$ )	Trunk ( $\times 10^6/\text{mm}^3$ )	Lower Body ( $\times 10^6/\text{mm}^3$ )
0	8.96 $\pm$ 0.22 <sup>a</sup>				
1	9.03 $\pm$ 0.25	9.73 $\pm$ 0.44	8.98 $\pm$ 0.32	8.47 $\pm$ 0.22	8.61 $\pm$ 0.33
2		8.99 $\pm$ 0.32	8.93 $\pm$ 0.31	8.46 $\pm$ 0.14	8.57 $\pm$ 0.31
3	8.34 $\pm$ 0.34	8.43 $\pm$ 0.48	9.02 $\pm$ 0.30	9.22 $\pm$ 0.32	9.05 $\pm$ 0.36
4		8.08 $\pm$ 0.35	9.09 $\pm$ 0.44	8.64 $\pm$ 0.29	8.61 $\pm$ 0.48
6	8.30 $\pm$ 0.19	8.37 $\pm$ 0.32	9.03 $\pm$ 0.39	8.36 $\pm$ 0.32	8.78 $\pm$ 0.23
8		8.44 $\pm$ 0.58	8.87 $\pm$ 0.43	8.24 $\pm$ 0.16	9.17 $\pm$ 0.35
10	8.82 $\pm$ 0.28	6.89 $\pm$ 0.35 <sup>**b</sup>	9.18 $\pm$ 0.39	8.25 $\pm$ 0.33	9.47 $\pm$ 0.23
15		7.41 $\pm$ 0.26 <sup>**</sup>	9.09 $\pm$ 0.38	8.51 $\pm$ 0.32	9.04 $\pm$ 0.43
18		7.94 $\pm$ 0.24	9.31 $\pm$ 0.17	8.66 $\pm$ 0.26	8.68 $\pm$ 0.31
21	8.82 $\pm$ 0.45				
22		9.40 $\pm$ 0.47	8.69 $\pm$ 0.45	8.96 $\pm$ 0.43	8.44 $\pm$ 0.36
Mean of Control Pooled	8.71 $\pm$ 0.12				

a Values are mean  $\pm$  SE. Mice used are 8 for all groups.b <sup>\*\*</sup>P<0.01 compared with pooled control value.

Table 4. Hematocrit value of mice after 500 R of whole or partial body irradiation

Days after Irradiation	Non-Irradiated Control (%)	Whole Body Irradiation (%)	Partial Body Irradiation		
			Head (%)	Trunk (%)	Lower Body (%)
0	47.7 $\pm$ 0.5 <sup>a</sup>				
1	46.3 $\pm$ 0.9	48.3 $\pm$ 0.6	45.9 $\pm$ 1.0	48.7 $\pm$ 0.4 <sup>**</sup>	47.7 $\pm$ 0.7
2		48.0 $\pm$ 1.1	47.0 $\pm$ 0.6	46.5 $\pm$ 0.6	45.6 $\pm$ 0.8
3	46.3 $\pm$ 0.5	44.4 $\pm$ 0.7	46.7 $\pm$ 1.0	46.1 $\pm$ 0.6	45.4 $\pm$ 1.4
4		41.0 $\pm$ 0.7 <sup>**b</sup>	47.1 $\pm$ 0.8	46.6 $\pm$ 0.7	47.6 $\pm$ 0.6
6	45.1 $\pm$ 1.9	42.2 $\pm$ 1.3 <sup>**</sup>	47.9 $\pm$ 1.9	46.2 $\pm$ 0.5	46.8 $\pm$ 0.5
8		40.5 $\pm$ 0.9 <sup>**</sup>	49.0 $\pm$ 0.6 <sup>**</sup>	46.5 $\pm$ 0.4	47.5 $\pm$ 0.6
10	46.3 $\pm$ 1.0	37.5 $\pm$ 1.1 <sup>**</sup>	47.6 $\pm$ 0.8	46.4 $\pm$ 0.5	49.2 $\pm$ 0.6 <sup>**</sup>
15		42.9 $\pm$ 1.4	48.8 $\pm$ 0.9	47.0 $\pm$ 0.8	48.6 $\pm$ 1.0
18		42.7 $\pm$ 1.3	47.3 $\pm$ 0.8	45.4 $\pm$ 0.8	47.4 $\pm$ 1.1
21	48.6 $\pm$ 1.0				
22		46.4 $\pm$ 0.5	44.9 $\pm$ 1.8	47.1 $\pm$ 0.5	45.6 $\pm$ 0.9
Mean of Control Pooled	46.7 $\pm$ 0.4				

a Values are mean  $\pm$  SE. Mice used are 8 for all groups.b <sup>\*\*</sup>P<0.01 compared with pooled control value.

similar pattern to that of the whole body exposure group with less decrease.

#### 4. Changes in erythrocyte count and hematocrit value

Changes in erythrocyte count and hematocrit value are shown in Figs. 3 and 4 and in Tables 3 and 4. Significant decreases in erythrocyte count were observed 10 and 15 days after whole body exposure. Three types of partial body irradiation produced no effect on erythrocyte count. Decrease in hematocrit

value was statistically significant in whole body exposure group on days 4, 6, 8, and 10 after irradiation.

### Discussion

Changes of the blood cell counts in peripheral blood after an exposure are induced mainly through damages on their precursor cells irradiated<sup>2)6)</sup>. Accordingly the time course of the blood cell counts are determined by amount of damages on the precursor cells, their transit times and the life spans of the matured cells. In a partial body irradiation, it is critical to estimate how many cells of the precursors are irradiated. Distributions of active erythropoietic bone marrow of mice measured by <sup>59</sup>Fe uptake were reported by Chervenick et al.<sup>5)</sup> and Carsten<sup>4)</sup>. According to the reports, the amounts of erythropoietic bone marrow are tentatively estimated for each exposure pattern as shown in Table 5. The

Table 5. Irradiated portions of erythropoietic bone marrow

Irradiated Area	Irradiated Portions of Erythropoietic Bone Marrow (%)	
	Estimation I <sup>a</sup>	Estimation II <sup>b</sup>
Whole Body	100.0	100.0
Head	20.7	24.8
Trunk	48.9	54.2
Lower Body	30.4	21.0

a,b Estimation I and II were calculated with the data of Chervenick et al.<sup>5)</sup> and that of Carsten<sup>4)</sup>, respectively.

depressions of leukocyte counts and of thrombocyte counts roughly reflect the amount of erythropoietic bone marrow irradiated. This may suggest that granulopoietic or thrombopoietic bone marrow may distribute similarly in the body as the erythropoietic one does. In other words there may be no cell line specificity among the three portions of the body.

The changes of thrombocyte counts in Fig. 2 resembles the changes produced by whole body irradiation with graded doses<sup>2)8)</sup>. Namely a partial body irradiation with a given dose is approximately equivalent to a whole body irradiation with a smaller dose as far as thrombocyte counts are concerned. This may also suggest an uniform distribution of thrombopoietic precursor cells in the bone marrow throughout the body.

Erythrocytes number after whole body irradiation reached a minimum value (about 80% of control) at the 10th day. If one assumes a complete stop of supply of erythrocyte from marrow to peripheral blood after the exposure, erythrocyte count gradually decreases due to their own decay with life span of 45 days<sup>1)</sup>. In that case erythrocyte count will decrease to about 80% of normal level at the 10th day which is in agreement with the experiment. However there is no evidence on complete stop of erythrocyte production and moreover, the abrupt fall on the 10th day of irradiation would not be explained by this assumption alone. It might be valuable to consider another possibility, such as a release of erythrocytes out of blood vessels. In effect a coincidence of the times at which the thrombocyte count and the erythrocyte count reach their minimums may suggest an anemia due to thrombocytopenia<sup>12)13)</sup>.

In summary these data given in the text suggest that the precursor cells of three cell lines have similar distribution throughout the body.

### Summary

Mice were given head, trunk or lower body, or whole body exposures to 500 R of x-ray under the anesthetic condition. Comparisons were made of the effects of these 4 groups of exposure on leukocyte, thrombocyte and erythrocyte count in the circulating blood.

The change in leukocyte count followed essentially the same pattern in all types of exposure, although the extent of the radiation induced reduction was more severe and the recovery less rapid in order of whole, trunk, head=lower body group.

The severity of thrombocyte depression occurred on 6 to 10 days after exposures. It was more marked in whole body group than in partial body groups.

No significant reduction was detectable in erythrocyte count and hematocrit value after all types of partial body irradiation.

The results suggest that precursor cells of three cell lines distribute in general uniformly in the bone marrow throughout the body.

### Acknowledgements

We wish to thank Mr. N. Kawashima and Mr. Y. Nishimoto for their valuable technical assistance.

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