Acta med. nagasaki. 5 : 1 – 12 (1960)

Blood Picture of Nagasaki Atomic Bomb Survivors *1

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Received for publication February 8, 1960

The results of hematological studies in Nagasaki on atomic bomb (A-bomb) survivors which were carried out at Second Department of Internal Medicine from 1946 to 1956 have been brought for summary. 1) Anemic and leukopenic tendency revealed in the exposed in 1946 and 1947 has recovered as time went on, no difference being noticed in 1948 in cases of leukopenia and in 1956 in cases of anemia comparing with the control. 2) The incidence of eosinophilia in the exposed showed a characteristic variation from 1947 to 1953, which may be related to the A-bomb radiation. However, in 1956, no difference was noticed between the exposed and control. 3) In general, the tendency of restoring to normal values was extremely strong in the exposed in each item of investigation. Accordingly, so far as concerned with peripheral blood, no significant difference was observed between the exposed and control in 1956. 4) However, the clinical investigation of bone marrow in the exposed performed in 1956, still suggested a possibility of maturation arrest of granulocytic and megakaryocytic series in the short distance exposed. 5) Three cases of chronic myelocytic leukemia were found in these mass survey, two of them being in an early stage of the disease.

The immediate and acute effects of A-bomb radiation on human beings, especially the injuries to hematopoietic organs, were clarified to a large extent by many studies. So it has become very important to determine whether such injuries have recovered or continued, that is, if there could be any delayed, longterm, or chronic effects many years after A-bomb explosion.

Several blood surveys of the Nagasaki A-bomb survivors exposed within 2000m from the hypocenter have been carried out by various staff members of Second Department of Internal Medicine for over ten years. Findings from these investigations have been brought up-to-date for summary.

MATERIALS AND METHODS

Hematological examination (hemoglobin, WBC count and differential) of the survivors exposed within 2000m from the hypocenter of the atomic bombing in Nagasaki were performed, in 1946, 1947, 1948, 1953 and 1956. The number of the survivors examined were 94, 61, 77, 2927 and 3234 respectively and that of the controls who were simultaneously examined were 69, 33, 110, 361 and 1607. They were classified as illustrated in Table 1 into A, B and C, according to presence or abscence of acute radiation symptoms (epilation, hemorrhagic tendency, stomatitis) and were further divided in 18 smaller groups by sex and age. Although

*1 Presented at the 19th General Meeting of the Japan Hematological Society. Tokyo, Japan. April 3, 1957.

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TABLE 1.
The Number of Survivors Examined

1946

Sex	F			T
Group \ Age	Y_1	Y_2	Y_3	
A	89	5	0	94
C	60	9	0	69
T	149	14	0	163
Total	163			

1947

Sex	F			T
Group \ Age	Y_1	Y_2	Y_3	
A	55	6	0	61
C	28	5	0	33
T	83	11	0	94
Total	94			

1948

Sex	F			T
Group \ Age	Y_1	Y_2	Y_3	
A	13	15	2	30
B	18	22	7	47
C	88	22	0	110
T	119	59	9	187
Total	187			

Remarks :

A : Exposed under 2000m with major radiation symtoms.
B : Exposed under 2000m without major radiation symptoms.
C : Control.
T : Total.

Y_1 : 8–23 years.
Y_2 : 24–58 years.
Y_3 : 58 years and over.

1953

Sex	M			F			T
Group \ Age	Y_1	Y_2	Y_3	Y_1	Y_2	Y_3	
A	125	248	44	132	484	54	1,087
B	221	307	111	346	767	127	1,885
C	78	91	22	80	83	7	361
T	430	646	177	558	1,334	188	
Total	1,263			2,080			3,333

1956

Sex	M			F			T
Group \ Age	Y_1	Y_2	Y_3	Y_1	Y_2	Y_3	
A	102	505	86	132	576	76	1,477
B	307	472	97	310	485	86	1,757
C	185	416	146	205	522	133	1,607
T	594	1,393	329	647	1,583	295	
Total	2,316			2,525			4,841

three early surveys were concerned with a small number of female alone, the last two included both male and female of a large number that reached one third of the survivors residing in Nagasaki City as shown in Table 2.

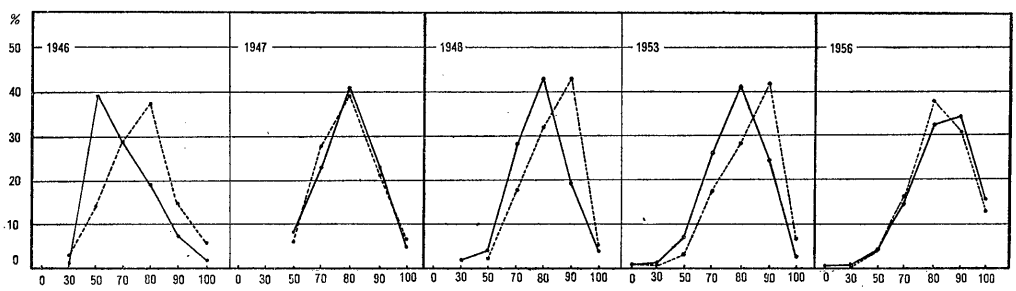
As for the method of analysis, incidence of deviation from the usually normal value which was shown in each item of analysis was compared by the chi square test. As the detailed results of each survey was already reported respectively[1)2)9)10)11)], a particular emphasis has been given to the comparison of changes by year. Chi square analysis were done on two cases between the exposed (refered to as E hereinafter) and the non-exposed (refered to as C hereinafter) of female and between A, B and C group of all examined.

TABLE 2.
The Number of the Exposed Residing in Nagasaki City (Feb. 1956. Nagasaki City Office)

Exposed	Male	Female	Total
Under 2000m	5.123	5.942	11.065
Over 2000m	19.481	25.920	45.401
Total	24.604	31.862	56.466

RESULTS

1) *Anemia.* Hemoglobin level below 80% was considered abnormal (anemic). The distribution of Hb. level is shown in Fig. 1 and 2.



Percentage of under 80%

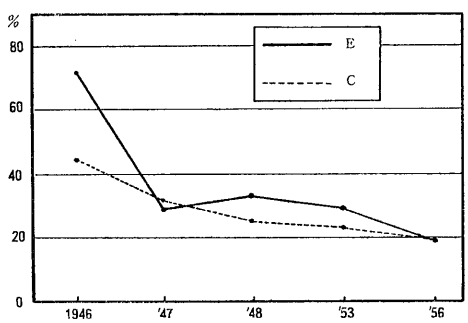
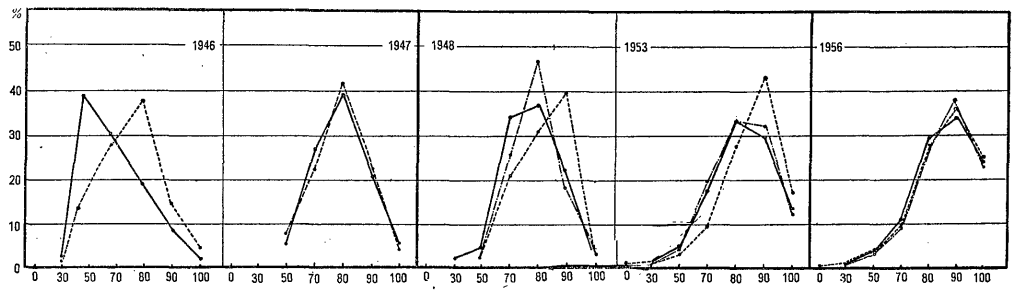


FIG. 1. Hemoglobin (Female).



Percentage of under 80%

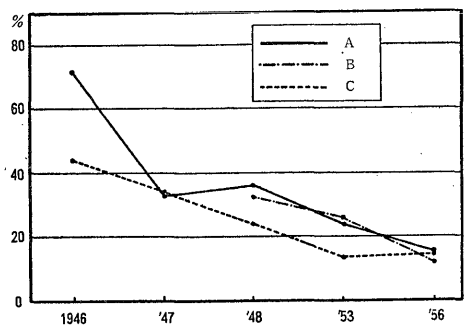


FIG. 2. Hemoglobin (Radiation Symptom).

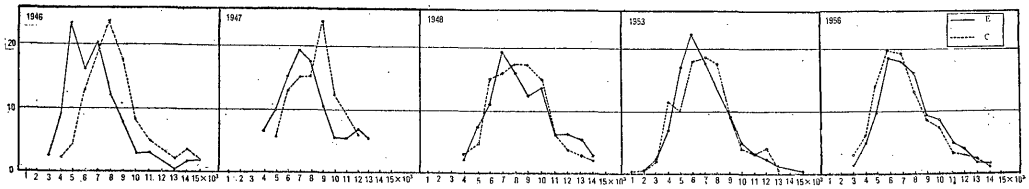
i) Female. In 1946 both E and C showed a tendency to anemia, which significantly marked in E (E=71.4%,** C=43.5%, $p<0.001$). In 1947 C showed no more changes than in 1946, but the recovery from anemia in E was remarkable, so that the difference between the two groups was not significant (E=33.3%, C=31.1%, $0.8<p<0.9$). In 1948 the recovery from anemia was remarkable in C, but E showed no changes since 1947, so that the anemic tendency in E was significantly high (E=33.9%, C=23.8%, $p<0.05$). In 1953 E showed still definite tendency to anemia (E=32.4%, C=22.4%, $p<0.001$), but in 1956 no significant difference was noticed between both groups, because the recovery from anemia was very remarkable in E (E=19.3%, C=19.2%, $p>0.9$).

ii) Comparison between A, B and C. In 1948 both groups A and B showed significant tendency to anemia comparing with C (A=36.6%, B=31.9%, C=23.8%, $p<0.001$, $p<0.001$). No difference was noticed between A and B ($p>0.5$). In 1953 the anemic tendency of these three groups decreased, however significant differences were still noticed between A and C, B and C (A=24.1%, B=24.3%, C=13.3%). In 1956 the recovery from anemia was remarkable in A and B, showing the almost same distribution of Hb. level as in C.

2) *WBC count.* The distribution of WBC count is shown in Fig. 3. WBC count above 10.000 and below 5.000 were considered abnormal (leukocytotic or leukopenic).

i) Female. In 1946 E showed a significant increase of leukopenia than C (E=11.7%, C=1.4%, $p<0.05$). This leukopenic tendency in E was still present in 1947, however, no differences were noticed between E and C since 1948.

** Percentage of the subjects showing an abnormal value.



Percentage of Leukopenia and Leukocytosis

(Female) (Radiation Symptoms)

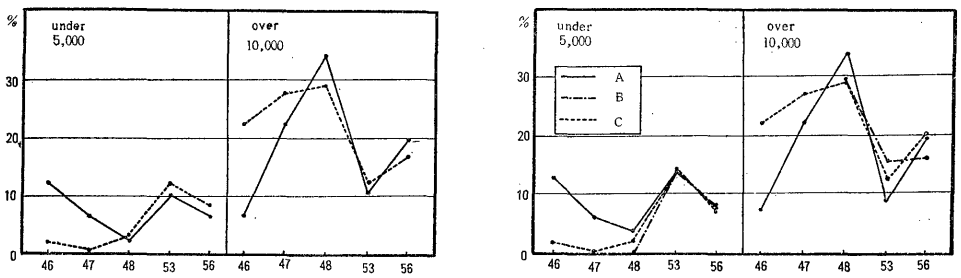
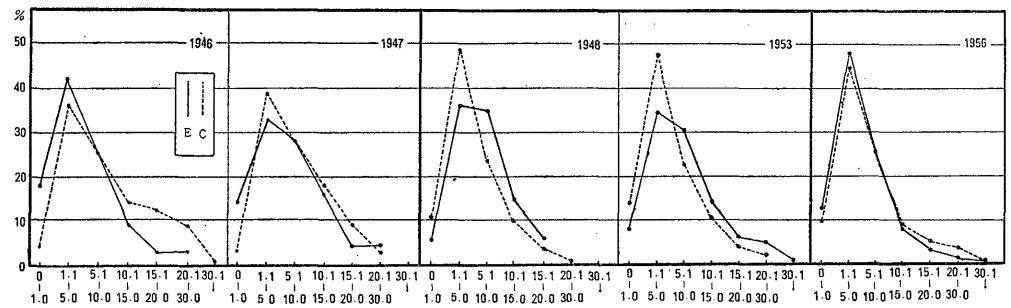


FIG. 3. Leukocyte (Female).

ii) Comparison between A, B and C. No difference was noticed in 1948, 1953 and 1956 respectively.

3) *Eosinophilia.* The percentage of eosinophils in WBC differential is distributed as shown in Fig. 4. An analysis was performed on two cases of the abnormal increase; one was applied to those above 10% and the other to those above 5%.



Percentage of Eosinophilia

(Female) (Radiation Symptoms)

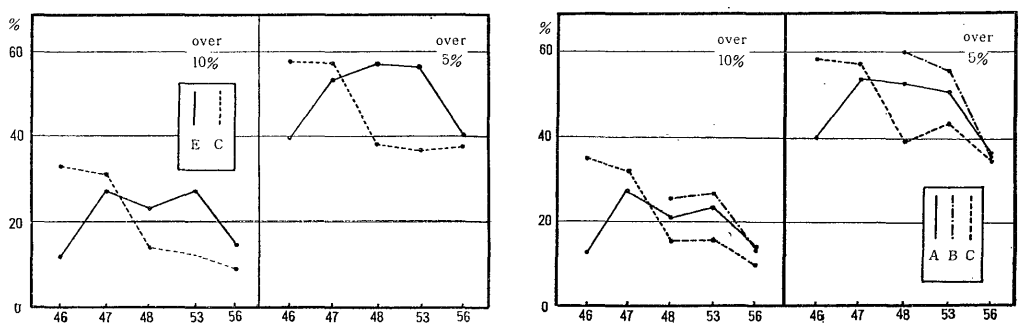


FIG. 4. Eosinophils (Female).

i) In cases when above 5% was considered abnormal.

a) Female. Cases of eosinophilia were extremely high in C in 1946 (E=39.4 %, C=58.0%, $p<0.05$), however, in 1947 no difference were noticed between E and C (E=54.1%, C=57.5%). In 1948 E showed a more significant increase of eosinophilia than C (E=57.1%, C=39.1%, $p<0.05$) and the same relation was still noticed in 1953 (E=56.3%, C=36.5%, $p<0.01$). In 1956 no difference was noticed between both groups (E=40.8%, C=37.1%, $p>0.05$).

b) Comparison between A, B and C. In 1948 no significant difference was noticed between A and B, A and C (A=53.3%, B=59.5%, C=39.0%, $p>0.05$, $p>0.1$), but the difference between B and C was significant ($p<0.05$). In 1953 A and B showed significant increases of eosinophilia than C (A=50.4%, B=56.2%, C=43.4%, $p<0.05$, $p<0.001$), furthermore B showed a significant increase than A ($p<0.01$). In 1956 no significant difference was noticed between each group.

ii) In cases when above 10% was considered abnormal.

a) Female. The almost same courses were observed as in cases of above 5%. In 1946 C showed a significant increase than E (E=12.7%, C=34.8%, $p<0.001$). No difference was noticed in 1947. In 1948 and 1953 E showed a significant increase than C respectively (in 1948 E=22.1%, C=15.4%, $p<0.001$ and in 1953 E=26.2%, C=14.1%, $p<0.001$). Furthermore in 1956 when there was no difference in cases of above 5%, E showed a significant increase than C (E=15.5%, C=11.0%, $p<0.001$).

b) Comparison between A, B and C. In 1948 no significant differences were noticed between each group. In 1953 A and B showed a significant increase than C (A=21.2%, B=25.6%, C=16.0%, $p<0.05$, $p<0.001$) and in 1956 A showed still a significant increase than C (A=12.5%, C=9.2%, $p<0.01$). No differences were noticed between B and C, A and B.

4) *Monocytes*. The percentage of monocytes above 7% in WBC differential was considered abnormal. The percentage of monocytosis in each year is shown in Fig. 5.

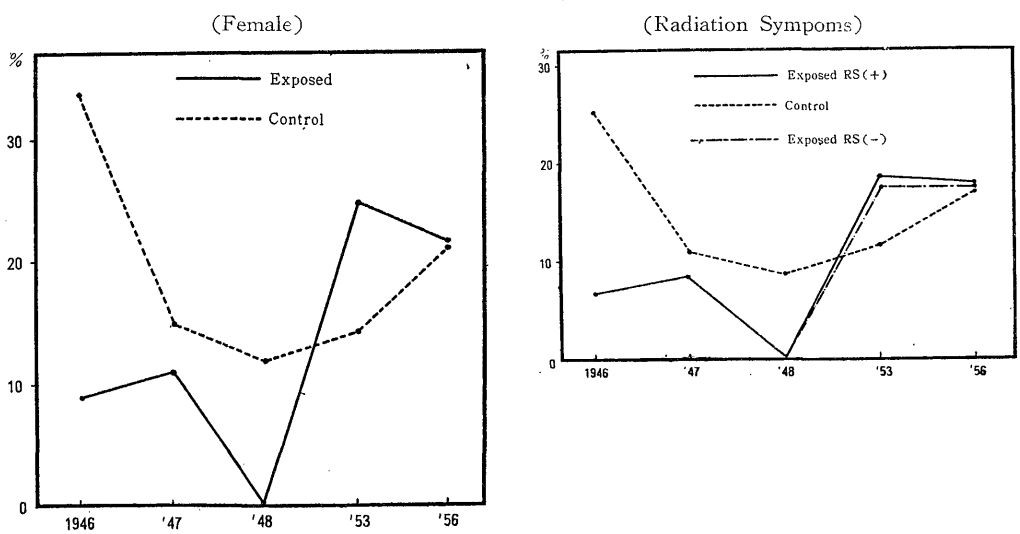


FIG. 5. Monocytosis (over 7%).

i) Female. In 1946 C showed a significant increase than E (E=9.6%, C=34.8%, $p<0.001$). In 1947 and 1948 there were no differences. In 1953 E showed a significant increase than C (E=25.3%, C=14.7%, $p<0.001$). No difference in 1956.

ii) Comparison between A, B and C. In 1953 A and B showed a significant increase than C (A=25.7%, B=24.5%, C=15.9%, $p<0.001$, $p<0.001$). In 1956 there was no significant difference at all between A, B and C (A=24.7%, B=24.1%, C=23,9%).

5) *Lymphocytes.* The percentage of lymphocytes in WBC differential is distributed as shown in Fig. 6. No significant differences were found between E and C in female, and A, B and C each year.

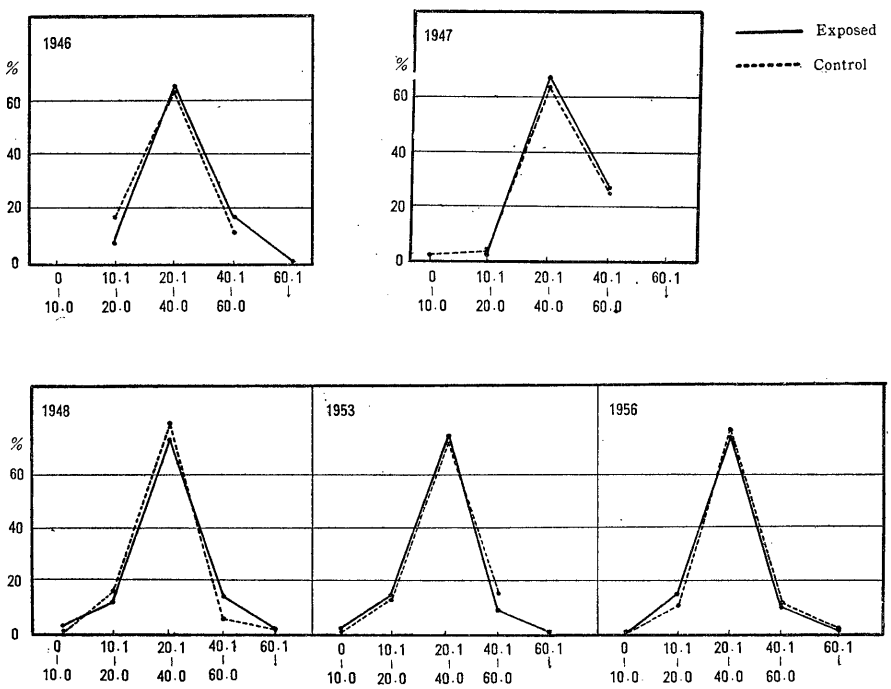


FIG. 6. Lymphocytes (Female).

TABLE 3.
Basophils

1953		T.	0.5−1.0	1.5−2.0	2.5−3.0
Exposed	R.S.(+)	1087	382 (35.14)	79 (7.26)	16 (1.47)
	R.S.(−)	1885	754 (40.00)	150 (7.95)	32 (1.69)
Control		361	60 (16.62)	15 (4.98)	7 (1.93)

1956		T.	0.5−1.0	1.5−2.0	2.5−3.0
Exposed	R.S.(+)	1477	371 (25.12)	20 (1.35)	3 (0.20)
	R.S.(−)	1757	353 (20.09)	24 (1.36)	3 (0.70)
Control		1607	352 (21.91)	22 (1.37)	1 (0.06)

( ) = %

6) *Basophils.* Recently the occurrence of basophilia in the early stage of leukemia have been drawing attention[5] and such two cases were experienced, who were found in the early stage at the mass surveys of survivors. The basophils count of those who showed basophilia above 2.0% on blood smear, were reexamined by a direct method using a Toluidin blue solution. The results are shown in Table 3. There was no case showed the value above 3.0%, and no differences were noticed between E and C both in 1953 and 1956.

7) *Leukocytes enzymes.*

i) Peroxydase. Peroxydase index which was calculated on cytochemically stained smear using the same method as the mean lobulation of nucleus by Sugiyama, showed no difference between E and C as shown in Table 4.

ii) Catalase and alkaline phosphatase: The activities of catalase and alkaline phosphatase of leukocytes which were separated by using the high molecular Dextran solution, were biochemically determined by a permanganate method and Fiske-Subbrow's method respectively. No differences were noticed between E and C as shown in Fig. 7.

TABLE 4.
Peroxydase Index of Neutrophils

		No.	Mean	Max.	Min.
Exposed	R.S.(+)	47	2.931±0.027	3.35	2.42
	R.S.(−)	173	2.923±0.017	3.75	2.04
Control		193	20884±0.016	3.68	2.03

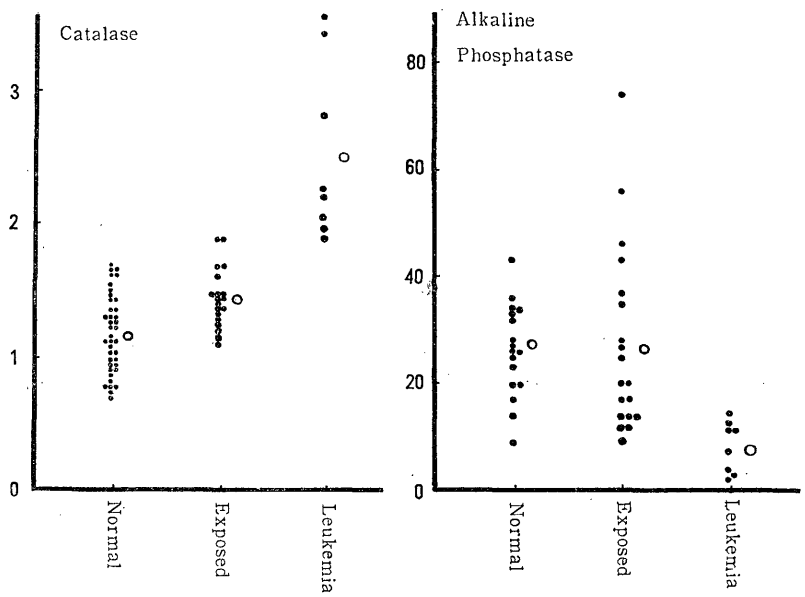


FIG. 7. Enzyme activities of leukocytes.

8) *Finding of leukemia patients.* At these mass surveys of A-bomb survivors, one case of chronic myelocytic leukemia in 1953 and two cases of the same type in 1956 were detected. In the both cases the leukemic process was in the early stage and the characteristics of blood pictures were basophilia, remarkable decrease of leuko-

cytic alkaline phosphatase and abnormal increase of leukocytic catalase. The other patient showed a typical picture of splenomegaly and remarkable increase of WBC count and juvenile granulocytes in spite of no subjective complaints when detected.

9) *Classification of anemia in the exposed.* The detailed reexamination was performed in 335 males and 529 females revealed the presence of anemia at the survey in 1953. The majority of anemia was macrocytic or normocytic, no difference in the rate of macro, normo, microcytic anemia being noticed between E and C. as shown in Table 5.

TABLE 5.

Classification of Anemia

Male

Age	R.S.	MCV≧94.1 MCHC≧30.0	MCV 80.0–94.0 MCHC≧30.0	MCV≦79.9 MCHC≧30.0	MCV≦79.9 MCHC≦29.9	T.
5	A	6(21.57)	13(78.43)			19
↓	B	18(26.47)	45(66.17)	1(1.47)	4(5.82)	98
19	C	1(12.5)	6(75.0)		1(12.5)	8
20	A	27(44.26)	31(50.81)	1(1.63)	2(3.27)	61
↓	B	77(47.11)	68(42.23)	3(1.86)	13(8.07)	161
	C	12(66.66)	6(33.33)			18

Female

Age	R.S.	MCV≧94.1 MCHC≧30.0	MCV 80.0–94.0 MCHC≧30.0	MCV≦79.9 MCHC≧30.0	MCV≦79.6 MCHC≦29.9	T.
5	A	6(46.15)	7(53.84)			13
↓	B	9(27.27)	21(63.64)		3(9.09)	33
19	C	3(21.44)	11(78.60)			14
20	A	23(25.84)	55(41.79)	5(5.62)	6(6.74)	89
↓	B	47(25.68)	112(61.20)	4(2.19)	20(10.92)	183
40	C	13(36.09)	21(58.30)		2(5.55)	36
41	A	1(14.28)	6(85.71)			7
↓	B	3(21.43)	8(57.14)	1(7.14)	2(14.29)	14
44	C	1(33.33)	1(33.33)	1(33.33)		3
45	A	4(11.11)	29(80.56)	2(5.56)	1(2.78)	36
↓	B	18(20.69)	55(63.21)	4(4.60)	10(11.49)	87
	C	3(21.23)	8(57.14)		3(21.23)	14

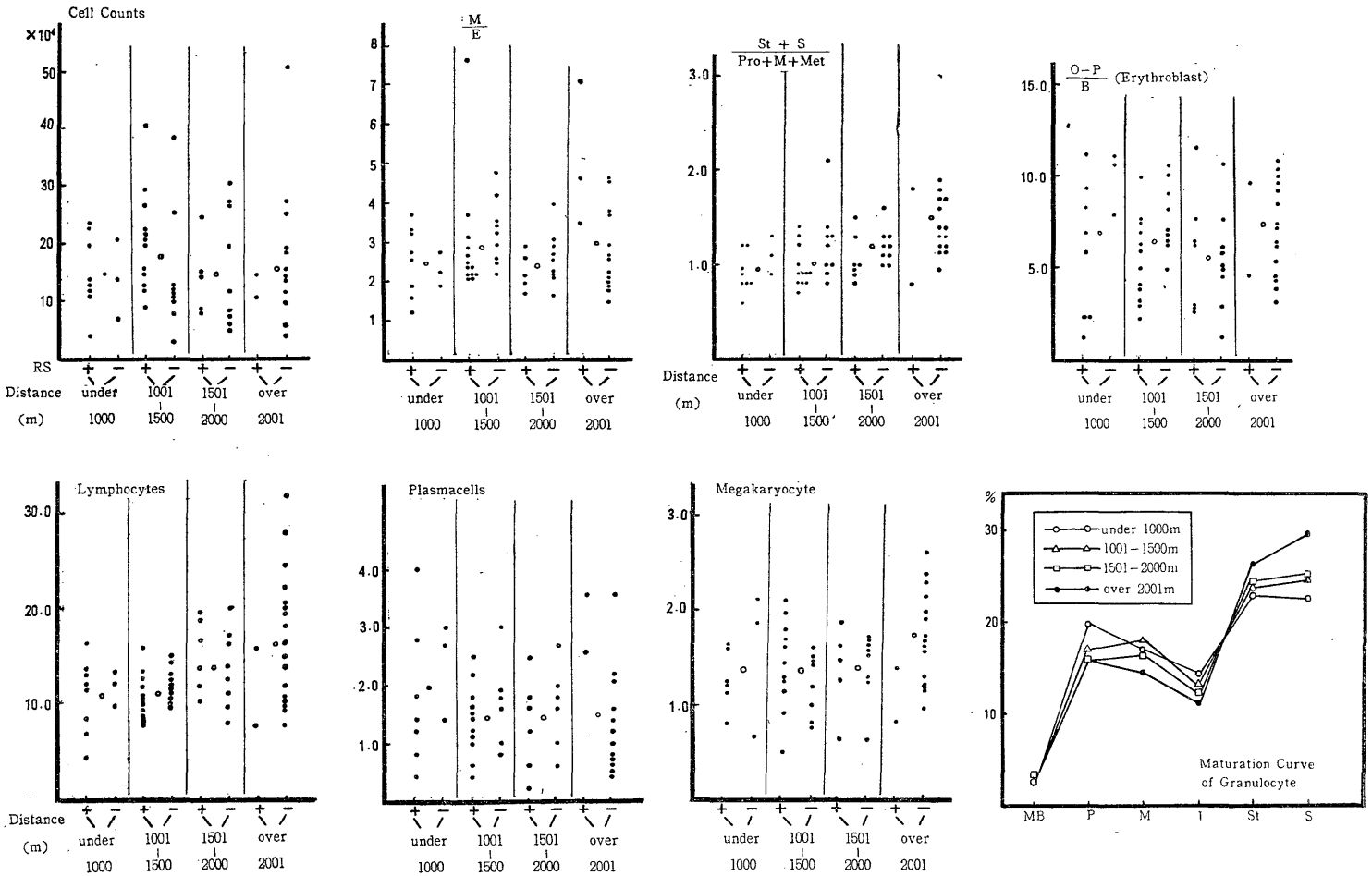


FIG. 8. Myelogram of the exposed.

10) *Bone marrow picture of the exposed.* The bone marrow aspiration was performed in 65 cases of the exposed during a period from August to December 1956. They were classified into four groups according to the distance from the hypocenter, namely within 1000m (A), 1000 — 1500m (B), 1500 — 2000m (C) and over 2000m (D), and the results were compared with each other as shown in Fig. 8.

i) Total nucleated cell count and the ratio of granulocyte and erythrocyte (M/E). No differences were noticed among the four groups.

ii) Maturation of granulocyte. The mean values of the maturation ratio ($\frac{St + S}{Pro + M + Met}$) of A, B, C and D were 0.96 ($\mu^2 = 0.048$), 1.07 ($\mu^2 = 0.11$), 1.11 ($\mu^2 = 0.057$) and 1.52 ($\mu^2 = 0.26$) respectively. The three groups A, B and C showed a significant decrease of the ratio compared with D respectively and A and B decreased significantly than C. No difference was noticed between A and B.

iii) Maturation of erythroblast. No differences were noticed between the four groups.

iv) Percentage of lymphocytes. The mean value of lymphocytes percentage of each group was 10.9%, 11.1%, 13.9%, and 16.7% respectively. A and B decreased sgnificantly than D. No differences were noticed between C and D, A and C, B and C, A and B.

v) Plasmacell. No differences were noticed among the four groups.

vi) Megakaryocytes. According to the Morita's classification method[6], the maturation ratio of megakaryocytes were calculated. The mean value of each group was 1.37, 1.36, 1.41 and 1.76 respectively and A, B and C showed a significant decrease than C respectively.

vii) No abnormality of mitosis was found in all cases.

DISCUSSION

The high rate of anemia in the control groups in 1946 is considered to be due to poor post-war conditions and took a smooth recovery course afterwards. On the other hand, the recovery from anemia in the exposed was slow, being about as the controls in 1956. From these results the disturbance of the hematopoietic organs may be assumed to be due to the A-bomb radiation. Especially, the more remarkable recovery of anemia in 1947 than in 1946 may indicate most clearly that the high rate of anemia in 1946 was caused by A-bomb radiation.

The WBC count of the exposed which showed a leukopenic tendency in 1946 and 1947, did not vary from the controls since 1948. This rapid recovery of leukopenia and the slow recovery of anemia above mentioned consist with the general recognition that the reproduction of granulocytic series is faster than the erythrocytic one after the bone marrow injuries.

The change of eosinophilia in the exposed is very characteristic. It has been already reported that eosinophilia appeared in the convalescence of acute A-bomb radiation injuries[3][4][7][8]. As eosinophilia appears easily at allergic disease or parasite infection, it is more difficult and dangerous to connect eosinophilia noticed in the exposed many years after A-bomb explosion with its radiation than anemia or variation of WBC count. However, the incidence of eosionphilia in the controls showed a gradual and remarkable decrease from the very high value in 1946 year by year.

On the contrary, that of the exposed increased from the relatively low value in 1946, maintaining high values till 1953 and then decreased, no difference being noticed comparing with the control in 1956. This specific course of incidence of eosinophilia in the exposed may show the relation with A-bomb radiation.

There is nothing specific to say about lymphocytes and monocytes and basophils.

As mentioned above, it can be said in general that the tendency of recovering to normal in the exposed who had taken an abnormal course in 1946, 1947, 1948 and 1953, was so remarkable that there was no difference from the control group in 1956. However, such conclusion was obtained from the statistical disposition of results of mass surveys as to peripheral blood picture alone. Therefore, the bone marrow examination was performed in 1956 and the maturation arrest of granulocytic and megakaryocytic series was noticed in the short distance exposed. It is no doubt that the reliability of clinical bone marrow picture is relatively low to determine such maturation grade. However, considering the patterns of blastfocus and perivascular blast-focus in the bone marrow which were histologically found in the exposed cases as a specific change 7 — 11 years after the exposure, this maturation arrest may have some meanings. The incidence of leukemia in the exposed still shows a high rate and the significance to pursue the cause of individual case of the exposed who shows a deviation normal values is quite another problem from the results of statistical investigation. Such being the case, the importance of the medical examination of an individual exposed person should not be disregarded in order to clarify the late effects of A-bomb radiation and to discover and treat the disease in the early stage. The detection of leukemia cases in our mass surveys has presented a good example.

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