DISTRIBUTION OF ONSET OF LEUKEMIA AMONG ATOMIC BOMB SURVIVORS IN THE LEUKEMIA REGISTRY BY DOSE, HIROSHIMA AND NAGASAKI, 1946-75

広島・長崎の白血病登録に基づく 線量別にみた被爆者白血病の発病時期の分布, 1946 - 75年

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RADIATION EFFECTS RESEARCH FOUNDATION 財団法人 放射線影響研究所

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In the continued interest of accurately defining the late effects of the atomic bombs, the qualitative and quantitative characteristics of the A-bomb radiation exposure doses are periodically refined. If warranted by future dose assessments, the data reported here will be reanalyzed and subsequently reported.

原爆の後影響を引き続いて正確に究明する目的をもって、原爆放射線被曝線量の質的・量的特質について定期的に 改良を加えている。今後線量評価によって、その必要性が起これば、本報の資料を再解析の上、改めて報告する。

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広島・長崎の白血病登録に基づく 線量別にみた被爆者白血病の発病時期の分布, 1946 ― 75年

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SUMMARY

RERF

The data from the RERF Leukemia Registry for the years 1946-75 were used to determine the distribution of onset of acute leukemia and chronic granulocytic leukemia among atomic bomb survivors in relation to city, dose, and age at the time of the bomb (ATB). A total of 509 confirmed leukemia cases (297 in Hiroshima and 212 in Nagasaki) have occurred among A-bomb survivors in the open populations of these cities in these years.

Analysis revealed that the onset of both acute leukemia and chronic granulocytic leukemia tends to shift to earlier years with increasing dose in Hiroshima, but in Nagasaki, although the onset of both types of leukemia was earlier in the high dose group than in the low dose or control groups, the latter two groups did not differ.

The distribution of onset of acute leukemia in the three dose groups also depended upon age ATB. While the distribution of onset of acute leukemia among those survivors whose age ATB was less than 30 differed significantly in the three dose classes, this tendency was not observed among those individuals whose age ATB was 30 years or more. For chronic granulocytic leukemia, the onset was shifted to earlier years in

1946-75年の放影研白血病登録の資料を用い、都市 別、線量別、原爆時年齢別にみた被爆者の急性白血病 と慢性骨髄性白血病の発病時期の分布について検討 した.調査期間中に両市の全人口における被爆者 から,合計509人(広島297,長崎212)の白血病を tore, the present malyala is restricted to no

広島では急性白血病と慢性骨髄性白血病ともにその 発病時期は線量の増加に伴い早くなる傾向が認めら れた.一方,長崎では二つの病型の白血病とも発病 時期は,高線量群が低線量群と対照群に比較し早 かったが, 低線量群と対照群の間には差異が認めら れないことが観察された.

三つの線量群別にみた急性白血病の発病時期の分布 は、原爆時年齢にも依存していた。30歳未満で被爆 した者の急性白血病の発病時期の分布は, 三つの 線量群間で有意な差が認められたが、30歳以上の 被爆者ではこのような傾向は認められなかった. 慢性 骨髄性白血病についてみると, 広島では原爆時年齢 と関係なく発病時期の分布は高線量群が対照群よりも

the high dose group than in the control group regardless of age ATB in Hiroshima.

These findings support the pattern of leukemogenesis observed in A-bomb survivors in the Life Span Study sample, a fixed cohort, in relation to city, dose, age ATB, and years after exposure.

INTRODUCTION

The leukemia incidence rate among A-bomb survivors in the Life Span Study (LSS) sample, a fixed cohort, has been reported in relation to dose, age ATB, type of leukemia, and years after exposure.1 The ascertainment of leukemia cases among A-bomb survivors through the RERF Leukemia Registry, however, extends beyond this cohort and includes the open populations of Hiroshima and Nagasaki. The Leukemia Registry had identified 1,838 definite and probable leukemia cases in Hiroshima and Nagasaki by the end of 1975; of these 509 had developed in A-bomb survivors during 1946-75 with 297 cases in Hiroshima and 212 cases in Nagasaki.2 It seemed desirable that an analysis be made of the cases of leukemia developing over the years in the open populations to contrast with the findings on the smaller number of cases occurring in the fixed cohort since October 1950. However, an analysis of leukemia cases in the open populations has certain epidemiological limitations (e.g., it is not possible to examine the risk of leukemia by dose and city on an annual basis, because the population at risk is not known reliably). Therefore, the present analysis is restricted to an examination of the distribution of year of onset of acute leukemia and chronic granulocytic leukemia among A-bomb survivors in relation to dose, city, and age ATB during 1946-75. It uses the entire RERF Leukemia Registry to determine whether the analysis of the distribution of onset of leukemia among the survivors in the open populations supports the findings from the cohort in so far as the risk of radiation-induced leukemia by dose, city, age ATB, and years after exposure is concerned.

MATERIALS AND METHODS

The RERF Leukemia Registry is jointly administered by the Department of Hematology, Research Institute for Nuclear Medicine and Biology, Hiroshima University, the Department of Hematology, Atomic Disease Institute, Nagasaki University School of Medicine and

早期に移動していることが認められた。

これらの知見は,固定集団の寿命調査対象の被爆者 について観察された都市別,線量別,原爆時年齢別, 被爆後の経年別にみた白血病の発現様式を裏付け ている.

緒言

固定集団の寿命調査対象者中の被爆者から発生した 白血病発生率と,線量,原爆時年齢,白血病の病型, 被爆後の経過年数との関係については既に報告され ている.1 しかし、放影研白血病登録では、この固定 集団の範囲を越えて,広島・長崎両市の全人口を含 め被爆者からの白血病症例を確認している. 白血病 登録には1975年末までに広島、 長崎で1,838人の 診断確実又はほぼ確実の白血病症例を確認し登録 している。1946-75年の間に被爆者から発生した症例 は合計509例であり、297例が広島、212例が長崎の 症例であった。2 両市の全人口から調査期間中に発生 した白血病症例について、1950年10月以降に固定集団 から発生したより少ない症例についての知見と比較 対照して解析することが望ましいと考えられた. し かし,全人口の白血病症例を用いた解析では,ある 種の疫学的手法に限界がある(例えば線量別、都市 別,経年別にみた白血病の危険率を計算することが 不可能である. なぜならば正確な観察人口が不明で ある). したがって, 今回の解析では, 1946-75年 の間に被爆者から発生した急性白血病と慢性骨髄性 白血病の発病時期の分布を,線量,都市,被爆時 年齢との関係について検討することに限定した。 放 影研の全白血病登録を用い,全人口の被爆者から 発生した白血病の発病時期の分布に関する解析の 結果が、線量別、都市別、被爆時年齢別、被爆後の 経年別にみた放射線誘発白血病の危険率に関する 固定集団について得られた所見を裏付けるかどうか について検討することにした.

材料及び方法

放影研白血病登録は,広島大学原爆放射能医学研究所 血液学研究部門,長崎大学医学部原爆後障害医療 研究施設後障害治療部門及び放影研が共同で運営 RERF. The procedures followed by the Leukemia Registry have been described elsewhere. Hematologists confirm the diagnosis of leukemia after reviewing the medical records. The confirmation of all leukemia diagnoses was abandoned in Hiroshima in 1971, however, due to a shortage of hematologists; only cases occurring in the RERF fixed cohort are presently being confirmed.

The T65 dosimetry system⁵ provides estimates of gamma and neutron exposure in rad based on field investigations of the location and shielding configuration ATB of the survivors. The simple sum of these exposures constitutes the T65 total dose. Dose has not yet been calculated for cases in certain complex shielding situations; their exposures are designated as "unknown", as are the exposures of some survivors on whom shielding information is incomplete.

The present analysis is concerned with a comparison of the distribution of time of onset of acute leukemia and chronic granulocytic leukemia among A-bomb survivors in the open populations of Hiroshima and Nagasaki in three dose groups (less than 1 rad, 1-99 rad, and 100 rad or more) by 5-year intervals during 1946-75. The results are given in the form of curves of the cumulative proportions of the two types of leukemia developing in each group in relation to elapsed years after exposure by city and calendar intervals. Each curve begins at zero in 1945 and reaches 100% in 1975. Cumulative proportion curves over the years are compared by city, dose group, and age ATB category. The graphical comparisons are supplemented with nonparametric rank tests6 for difference of the median years between exposure and onset by dose and type of leukemia.

RESULTS

Distribution of Leukemia among A-bomb Survivors, by City, Dose and Major Type of Leukemia, 1946-75

Table 1 shows the distribution of the registered leukemia cases among A-bomb survivors with onset between 1946-75 by city, dose, and three major types of leukemia. In Hiroshima, there were 198 cases of acute leukemia and 99 cases of chronic granulocytic leukemia. The proportions of chronic granulocytic leukemia were 21.8% among survivors exposed to less than 1 rad, 43.2% among those exposed to 1-99 rad, and

している。白血病登録に関する登録要領は別に記述されている。3.4 血液学者は医学記録を検討した後に白血病の診断を確認している。血液学者の不足のため、広島では1971年以降すべての白血病症例の診断の確認を放棄した。しかし、現在では放影研の固定集団から発生した症例についてのみ診断の確認が行われている。

T65線量測定法⁵では、野外調査に基づいて被爆の 位置と遮蔽状態に関する情報を入手し、ガンマ線と 中性子線の被曝線量をrad で計算している。これら 被曝線量の単純和がT65総線量である。ある種の 複雑な遮蔽状態の者は線量が計算されておらず、 遮蔽の情報が不完全な者も同様に線量は"不明"と している。

今回の解析では1946-75年の間に広島・長崎の全人口中の被爆者から発生した急性白血病と慢性骨髄性白血病の発病時期の分布を5年間隔別に三つの線量群(1rad未満、1-99rad、100rad以上)について比較検討した。各群から発生した二つの病型の白血病の発生の累積比率を、都市別、暦年区間別に被爆後の年数の経過とともに曲線の型で表した。各曲線は1945年を0とし、1975年に100%に達する。都市別、線量別、被爆時年齢別にみた全期間にわたる累積比率曲線を比較した。グラフを用いた比較は、線量別、病型別にみた被爆から発病までの年数の中央値の差異をノンパラメトリック順位検定を行って補足した。

維 里

都市別、線量別、白血病の主要病型別にみた被爆者 白血病の分布、1946-75年

都市別,線量別,三つの主要病型別にみた1946-75年の間に発生した被爆者白血病の登録症例の分布を表1に示した。広島では,急性白血病198例,慢性骨髄性白血病99例であった。慢性骨髄性白血病の比率は1rad未満を受けた被爆者で21.8%,1-99rad受けた者で43.2%,100rad以上受けた者では

TABLE 1 DISTRIBUTION OF LEUKEMIA AMONG A-BOMB SURVIVORS
IN THE LEUKEMIA REGISTRIES, BY CITY, DOSE, & TYPE OF LEUKEMIA, 1946-75
表 1 白血病登録に基づく被爆者白血病の分布:
都市別,線量別,白血病病型別.1946-75年

Tuna of Laukamia	T65 Dose in Rad						
Type of Leukemia	<1	1-99	100+	Unknown	Total		
material contraction of the second		Hiroshima	120203-10	AAT TENANT			
Acute	79	50	59	10	198		
	(78.2)	(56.8)	(66.3)	(52.6)	(66.7)		
Chronic granulocytic	22	38	30	9	99		
	(21.8)	(43.2)	(33.7)	(47.4)	(33.3)		
[otal	101	88	89	19	297		
	(100.0)	(100.0)	(100.0)	(100.0)	(100.0)		
		Nagasaki					
Acute	97	25	39	9	170		
	(80.2)	(78.1)	(83.0)	(75.0)	(80.2)		
Chronic granulocytic	14	7	7	3	31		
	(11.6)	(21.9)	(14.9)	(25.0)	(14.6)		
Chronic lymphocytic	10	0	1	0	11		
3 전 2012 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	(8.3)	(0.0)	(2.1)	(0.0)	(5.2)		
Total	121	32	47	12	212		
	(100.0)	(100.0)	(100.0)	(100.0)	(100.0)		

% in parentheses ()内は%.

33.7% among those exposed to 100 rad or more. It appears that the proportion of chronic granulocytic leukemia was greater among individuals who received 1 rad or more. In Nagasaki, there were 170 cases of acute leukemia, 31 of chronic granulocytic leukemia, and 11 of chronic lymphocytic leukemia. It seems that only acute leukemia and chronic granulocytic leukemia were induced by exposure to ionizing radiation from the bombs. The proportion of chronic leukemia was not statistically significantly different, however, among Nagasaki survivors in the three dose groups. There was only one chronic lymphocytic leukemia case among individuals who received 1 rad or more in Nagasaki.

Distribution of Acute Leukemia and Chronic Granulocytic Leukemia among A-bomb Survivors, by City, Dose, and Onset, 1946-75

The distribution of acute leukemia and chronic granulocytic leukemia among A-bomb survivors in the Registry for the period 1946-75 by city, dose, and onset (in 5-year intervals) is shown in Table 2 and Figures 1 and 2. The incidence of acute leukemia among survivors who received 100 rad or more reached its peak during 1951-55 in Hiroshima and Nagasaki, and has gradually

33.7%であった. 慢性骨髄性白血病の比率が1 rad 以上を受けた者では大きいことは明らかである. 長崎では, 急性白血病170例, 慢性骨髄性白血病31例, 慢性リンパ性白血病11例であった. 急性白血病と慢性骨髄性白血病のみが, 原爆による電離放射線の被曝によって誘発されたと思われる. しかしながら, 長崎の被爆者では三つの線量群別で慢性白血病の比率には統計的な有意差が認められなかった. 長崎で1 rad 以上を受けた者からの慢性リンパ性白血病はわずか1例であった.

都市別、線量別、発病時期別にみた被爆者からの 急性白血病と慢性骨髄性白血病の分布、1946-75年 表2、図1及び2には、都市別、線量別、発病時期 別(5年間隔)にみた1946-75年の間に発生した急性 白血病と慢性骨髄性白血病の分布を示した。100rad 以上の線量に被曝した者における急性白血病の発生 は広島・長崎ともに1951-55年の間にピークに達し、

TABLE 2 DISTRIBUTION OF ONSET OF ACUTE LEUKEMIA & CHRONIC GRANULOCYTIC LEUKEMIA AMONG A-BOMB SURVIVORS IN THE LEUKEMIA REGISTRIES BY CITY, DOSE, & YEAR OF ONSET (5-YEAR INTERVALS), 1946-75

表 2 白血病登録に基づく被爆者の急性白血病と慢性骨髄性白血病の発病時期の分布: 都市別,線量別,発病年度別(5年間隔).1946-75年

TCS Danie Bod		Year of Onset						
T65 Dose in Rad	1946-50	1951-55	1956-60	1961-65	1966-70	1971-75	Total	
			Hiroshima					
Acute Leukemia								
Unknown	2	1	2	2	1	2	10	
100+	11	17	14	6	8	3	59	
1-99	6	9	12	8	4	11	50	
<1	4	11	21	19	13	11	79	
Total	23	38	49	35	26	27	198	
Test of significance*	x² [10]	= 20.96		.01 < P	< .05			
Chronic Granulocytic Leu	ıkemia							
Unknown	2	2	3	2	0	0	9	
100+	9	14	2	1	1	3	30	
1-99	5	14	7	9	3	0	38	
<1	2	1	6	3	6	4	22	
Total	18	31	18	15	10	7	99	
Test of significance*	x2 [10	= 32.88		P	< .001			
	. Rensale		Nagasaki					
Acute Leukemia								
Unknown	2	1	1	2	2	W 1 - 1	9	
100+	7	11	7	9	2	3 0		
1-99	3	3	3	6	5	5	25	
<1	2	20	19	18	13	25	97	
Total .	14	35	30	35	22	34	170	
Test of significance*	x^{2} [10] = 20.59		.01 < 1	P < .05			
Chronic Granulocytic Le	1 10000000							
Unknown	1	1	0	1	0	0	3	
100+	1	5	0	0	0	1	7	
1-99	2	0	2	1	0	2	7	
<1	2	1	3	2	4	2 5	14	
Total	6	7	5	4	4	5	31	
Test of significance*	x ² [10	l = 19.00		.01 < 1	P < .05			

Three dose groups (<1, 1-99 and 100+rad) and six onset periods 三つの線量群(1 rad 未満, 1 - 99 rad, 100 rad 以上), 6 発病年度別.

declined with time in both cities. In the low dose region (1-99 rad), the cases were quite uniformly distributed over time in Hiroshima and Nagasaki. In the control group (less than 1 rad), the number of cases was small in the period 1946-50, large in both cities during 1950-65, and decreased after 1965, especially in Hiroshima. This may reflect the efficiency of case detection or a change of population in the area covered by the case detection program over the years.

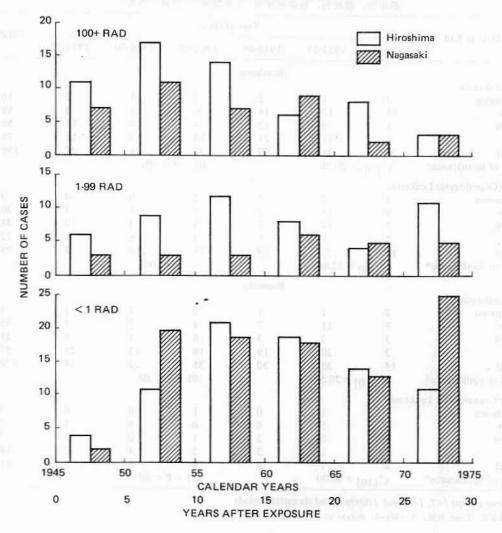
For chronic granulocytic leukemia, the peak incidence was observed during 1951-55 in the high dose group (100 rad or more) as well as in

その後は両市とも徐々に経時的に減少した。低線量群(1-99rad)では、両市とも全期間にわたりほぼ均一に分布していた。対照群(1rad未満)についてみると発生数は1946-50年は少なく、両市とも1950-65年が多く、1965年以後減少し、特に広島でその傾向が著しい。これらは症例探知の効率か、症例探知プログラムの対象となった地域の人口の期間中の変動を反映しているのであろう。

慢性骨髄性白血病についてみると,広島では,高線 量群(100rad 以上)も低線量群(1-99rad)も共に

FIGURE 1 DISTRIBUTION OF ONSET OF ACUTE LEUKEMIA AMONG A-BOMB SURVIVORS IN LEUKEMIA REGISTRIES BY CITY, DOSE, & YEAR OF ONSET (5-YEAR INTERVALS), 1946-75 図 1 白血病登録に基づく被爆者の急性白血病の発病時期の分布:

都市別,線量別,発病年度別(5年間隔). 1946-75年

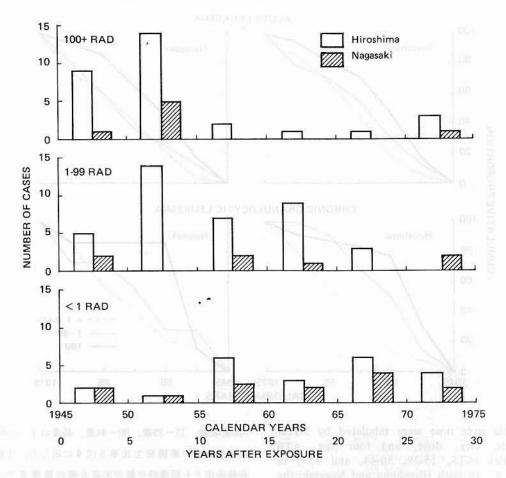


the low dose group (1-99 rad) in Hiroshima. After 1955, the number of cases declined gradually with time among survivors in Hiroshima who received less than 100 rad, and more rapidly among those who received 100 rad or more. In Nagasaki, the peak incidence was observed in only the high dose region during 1951-55. There have been few cases in the control group in the two cities by 5-year intervals.

The cumulative proportions of acute leukemia and chronic granulocytic leukemia over time were tabulated by 5-year intervals, city, three 発生のピークは1951-55年に観察された、1955年 以後、広島の被爆者では、100rad 未満を受けた者 の症例数は経時的に除々に減少したが、100rad 以上 を受けた者では急速に減少した。長崎では、発生の ピークは1951-55年の間に高線量群のみに認められ た、対照群においては両市とも5年間隔別にみれば、 その症例数はごく少数にすぎなかった。

5年間隔別,都市別,三つの線量群別,二つの白血病 病型別に,急性白血病と慢性骨髄性白血病の累積 FIGURE 2 DISTRIBUTION OF ONSET OF CHRONIC GRANULOCYTIC LEUKEMIA AMONG A-BOMB SURVIVORS IN LEUKEMIA REGISTRIES BY CITY, DOSE, & YEAR OF ONSET (5-YEAR INTERVALS), 1946-75

2 白血病登録に基づく被爆者の慢性骨髄性白血病の発病時期の分布: 都市別,線量別,発病年度別(5年間隔).1946-75年



dose groups, and two types of leukemia (Figure 3). For acute leukemia, in Hiroshima the high dose (100 rad or more) curve was to the left of the low dose (1-99 rad) and the latter curve was to the left of the control group (less than 1 rad) curve. In Nagasaki, the high dose curve was to the left of both the low dose and control group curves which differed little. For chronic granulocytic leukemia, the shape of the curves of cumulative proportions over time by city and three dose groups was identical with those observed for acute leukemia.

Cumulative Proportions of Incidence over Time of Acute Leukemia and Chronic Granulocytic Leukemia by City, Dose, and Age ATB

The cumulative proportions of incidence of acute

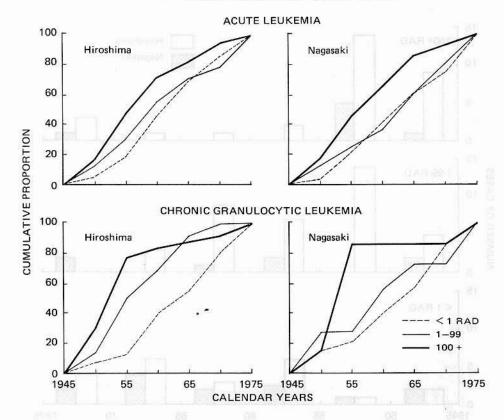
比率を計算し図3に示した. 急性白血病についてみると, 広島では高線量群(100rad 以上)の曲線は, 低線量群(1-99rad)の曲線の左側に位置し, 低線量群の曲線は対照群(1rad未満)の曲線の左側にそれぞれ位置した. 長崎では, 高線量群の曲線は, ほとんど差異のない低線量群と対照群の両曲線の左側に位置した. 慢性骨髄性白血病では, 都市別, 三つの線量群別にみた累積比率曲線の形状とほぼ同一であった.

都市別、線量別、原爆時年齢別にみた急性白血病と 慢性骨髄性白血病の累積発生比率

5年間隔別,都市別,線量別,四つの原爆時年齢別

FIGURE 3 CUMULATIVE PROPORTIONS OVER TIME OF ACUTE LEUKEMIA & CHRONIC GRANULOCYTIC LEUKEMIA INCIDENCE AMONG A-BOMB SURVIVORS IN LEUKEMIA REGISTRIES BY CITY, & DOSE, 1946-75

図3 白血病登録に基づく被爆者の急性白血病と慢性骨髄性白血病の期間中の累積発生比率: 都市別,線量別,1946-75年



leukemia over time were tabulated by 5-year intervals, city, dose, and four age ATB categories (<15, 15-29, 30-44, and 45+) in Figure 4. In both Hiroshima and Nagasaki the high dose curve was to the left of the low dose or control curves for those survivors whose age ATB was less than 30. However, the curves of the three dose groups where the age ATB was 30-44 and 45 or more were very similar.

Figure 5 shows the cumulative proportions of incidence over time for chronic granulocytic leukemia tabulated by 5-year intervals, city, dose, and three age ATB groups (<15, 15-29, and 30+). In Hiroshima, the curves were more to the left the higher the dose at all ages ATB. In Nagasaki, the curve of the high dose group was to the left of those for the low dose or control groups which behaved inconsistently.

Table 3 and 4 indicate the median for year and month of onset of acute leukemia and chronic

(15歳未満,15-29歳,30-44歳,45歳以上)にみた 急性白血病の累積発生比率を図4に示した。広島・ 長崎両市とも原爆時年齢が30歳未満の被爆者では, 高線量群の曲線は低線量群又は対照群の曲線の左側 に位置した。しかし、原爆時年齢が30-44歳と45歳 以上の者についてみると,三つの線量群の曲線は極 めて類似していた。

5年間隔別,都市別,線量別,三つの原爆時年齢別(15歳未満,15-29歳,30歳以上)にみた慢性骨髄性白血病の累積発生比率を図5に示した.広島では,すべての原爆時年齢で曲線は線量が高いほど左側に位置した.長崎では,高線量群の曲線は不整形な形状の低線量群と対照群の曲線の左側に位置した.

表3と4は、都市別、原爆時年齢別、三つの線量群

FIGURE 4 CUMULATIVE PROPORTIONS OVER TIME OF ACUTE LEUKEMIA INCIDENCE AMONG A-BOMB SURVIVORS IN LEUKEMIA REGISTRIES BY CITY, DOSE, & AGE ATB, 1946-75

図 4 白血病登録に基づく被爆者の急性白血病の期間中累積発生比率: 都市別,線量別,原爆時年齢別. 1946-75年

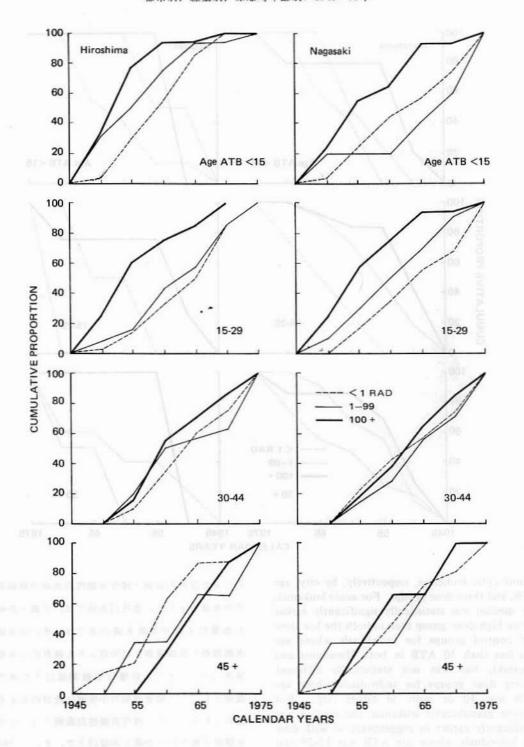
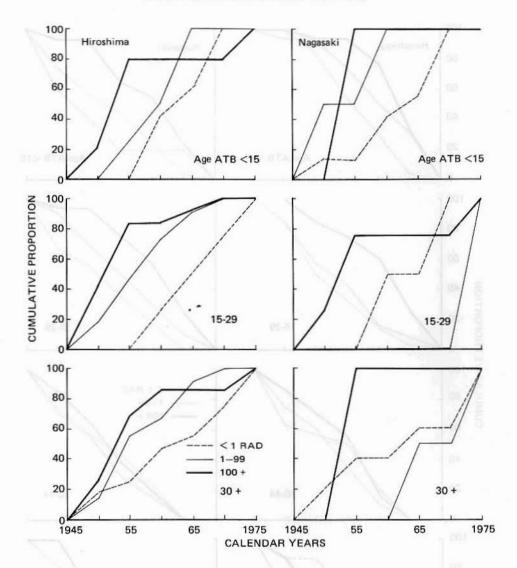


FIGURE 5 CUMULATIVE PROPORTIONS OVER TIME OF CHRONIC GRANULOCYTIC LEUKEMIA INCIDENCE AMONG A-BOMB SURVIVORS IN LEUKEMIA REGISTRIES BY CITY, DOSE, & AGE ATB, 1946-75

図 5 白血病登録に基づく被爆者の慢性骨髄性白血病の期間中累積発生比率: 都市別,線量別,原爆時年齢別,1946-75年



granulocytic leukemia, respectively, by city, age ATB, and three dose groups. For acute leukemia, the median was statistically significantly earlier in the high dose group than in both the low dose and control groups for individuals whose age was less than 30 ATB in both Hiroshima and Nagasaki, but was not statistically different among dose groups for individuals whose age ATB was 30 or more in either city. For chronic granulocytic leukemia, the median was significantly earlier or suggestively so with dose for individuals whose age ATB was 15-29 and

別にみた急性白血病と慢性骨髄性白血病の発病年月の中央値を示した。急性白血病では、広島・長崎とも原爆時年齢が30歳未満の者では、その中央値は高線量群が低線量群と対照群よりも統計的に有意に早かった。しかし、原爆時年齢30歳以上の者では両市とも三つの線量群間の中央値は統計的有意差が認められなかった。慢性骨髄性白血病では、広島で原爆時年齢が15-29歳と30歳以上で、また、長崎で

TABLE 3 MEDIAN ONSET OF ACUTE LEUKEMIA AMONG A-BOMB SURVIVORS BY CITY, AGE ATB, & DOSE, 1946-75

表3 被爆者の急性白血病の発病年月の中央値: 都市別、原爆時年齢別、線量別、1946-75年

A ATD	T65 Dose in Rad	Hiro	shima	Nagasaki		
Age ATB	165 Dose in Rad	No.	Median	No.	Median	
<15	100 +	18	March 1952	14	January 1956	
	1-99	16	January 1957	5	December 1970	
	< 1	20	March 1959	27	May 1963	
	Total	54	July 1955	46	July 1961	
		(H=8.76)	.01 < P < .05)	(H=6.38)	.01 < P < .05	
15-29	100+	20	July 1953	16	March 1954	
	1-99	12	May 1962	10	July 1959	
	< 1	18	January 1966	22	July 1964	
	Total	50	December 1960	48	September 1959	
		(H=8.56)	.01 < P < .05)	(H=8.98)	.01 < P < .05)	
30-44	100+	14	March 1961	6	March 1964	
	1.00	16	May 1962	7	August 1965	
	41 × 1	25	June 1963	27	November 1961	
	Total	55	April 1962	40	November 1963	
		(H=1.84	P > .10)	(H=.25)	P > .10)	
45 +	100 +	7	August 1962	3	April 1958	
	1-99	6	May 1962	3	November 1965	
	< 1	16	April 1959	21	January 1961	
	Total	29	January 1961	27	January 1961	
		(H=1.86	P >.10)	(H=.23)	P > .10)	
Total	100+	59	February 1957	39	November 1957	
	1-99	50	July 1960	25	June 1965	
	<1	79	February 1962	97	November 1961	
	Total	188	August 1959	161	July 1961	
	F ATEL THEFT	(H=13.69	0.001 < P < .01	(H=13.3	3.001 < P < .01)	

Cases with unknown dose are excluded. 線量不明は除いた.
Nonparametric rank test (Kruskal-Wallis test) in parentheses
()内はノンパラメトリック順位検定(Kruskal-Wallis の検定 6).

30 or more in Hiroshima, and whose age ATB was less than 15 in Nagasaki. As a whole, the median was significantly earlier with increasing dose in only Hiroshima survivors.

Table 5 shows the median for year and month of onset of acute granulocytic leukemia, acute lymphocytic leukemia, acute leukemia other type, and chronic granulocytic leukemia among those who received 100 rad or more for three age ATB groups. According to Kruskal-Wallis rank test, 6 there was no statistically significant difference in the distribution of onset for the types of leukemia and three age ATB groups. The appendix contains the distribution of cases by 5-year interval, city, dose, type of leukemia, and age ATB as presented in Figures 4 and 5.

は原爆時年齢15歳未満の者で中央値は有意又は示唆 的に線量とともに早くなることが認められた。全体 としては、広島の被爆者についてのみ中央値は線量 の増加とともに有意に早くなった。

表5には、三つの原爆時年齢群別に100rad以上を受けた者の急性骨髄性白血病、急性リンパ性白血病、その他の病型の急性白血病、慢性骨髄性白血病の発病年月の中央値を示した。Kruskal と Wallis の順位検定⁶によると、白血病病型と三つの原爆時年齢群についてみた発病時期の分布には統計的有意差が認められなかった。付録には、図4と5に示した5年間隔別、都市別、線量別、白血病病型別、原爆時年齢別にみた症例の分布を示した。

TABLE 4 MEDIAN ONSET OF CHRONIC GRANULOCYTIC LEUKEMIA AMONG A-BOMB SURVIVORS BY CITY, AGE ATB, & DOSE, 1946-75 表 4 被爆者の慢性骨髄性白血病の発病年月の中央値:

都市別,原爆時年齡別,線量別. 1946-75年

1 1 TD	TCE Dans in Bod	Hiro	oshima	Nagasaki		
Age ATB	T65 Dose in Rad	No.	Median	No.	Median	
<15	100 +	5	November 1954	2	February 1955	
	1-99	4	May 1960	4	October 1953	
	< 1	5	July 1961	7	August 1964	
	Total	14	February 1959	13	August 1957	
		(H=2.95)	P > .10)	(H=5.23)	.05 < P < .10)	
15-29	100 +	12	August 1951	4	August 1952	
	1-99	11	May 1956	1	July 1971	
	< 1	4 5891	August 1964	2	August 1961	
	Total	27	June 1953	7	November 1957	
		(H=6.44	.01 < P < .05)	(H=1.45)	P > .10)	
30 +	100 +	13	December 1952	1	January 1954	
	1-99	23	May 1955	2	January 1967	
	<1	13	March 1962	5	February 1965	
	Total	49	July 1955	8	April 1963	
		(H=5.48)	.05 < P < .10)	(H=1.20)	P > .10)	
Total	100 +	30	September 1952	7	January 1954	
	1-99	38	November 1955	7	August 1957	
	<1	22	December 1961	14	November 1964	
	Total	• ~90	November 1955	28	November 1957	
		(H=15.19	P < .001	(H=2.32)	P > .10)	

See footnote Table 3 脚注は表3に同じ.

TABLE 5 MEDIAN ONSET OF LEUKEMIA CASES WHO RECEIVED 100 RAD OR MORE AMONG A-BOMB SURVIVORS, HIROSHIMA & NAGASAKI,

BY FOUR MAJOR TYPES OF LEUKEMIA & AGE ATB, 1946-75 表 5 100rad 以上を受けた広島・長崎の被爆者白血病の発病年月の中央値:

Age ATB	No. of Cases	Median	Kruskal-Wallis Test ⁶ df = 2
Acute Granu	locytic Leukemia		
<15	5	December 1963	
15-29	19	September 1953	
30 +	20	January 1962	H = 5.84
Total	44	May 1959	.05 < P < .10
Acute Lymp	hocytic Leukemia		
<15	14	February 1952	
15-29	8	August 1951	H = 4.60
30 +	5	August 1962	P > .10
Total	27	June 1952	
Acute Leuke	emia, Other Type		
<15	13	July 1954	
15-29	9	October 1957	H = 2.92
30 +	5	October 1959	P > .10
Total	27	April 1958	
Chronic Gra	nulocytic Leukemia		
<15	7	November 1954	
15-29	16	September 1951	H = 2.38
30 +	14	December 1952	P > .10
Total	37	January 1953	

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DISCUSSION

It has been reported that examination of the distribution of time of death from leukemia in mice after irradiation revealed an earlier mean time of death with increasing dose.7-9 Among humans, however, the latent period of radiationinduced leukemia has been found to be affected by various factors. According to Court Brown and Doll10 who studied the mortality from leukemia among individuals receiving radiotherapy for ankylosing spondylitis in relation to the period after irradiation, the peak in excess leukemia deaths was observed 3-5 years after exposure, while the peak incidence of leukemia among A-bomb survivors who received 1 rad or more was observed 5 or 6 years after exposure in both Hiroshima and Nagasaki. 11 The difference of the peak between two instances may be due to the difference of average dose.

A rigorous analysis of the leukemia data on the open populations of Hiroshima and Nagasaki, insofar as radiation-induced leukemia is concerned, is compromised by our present inability to determine the population at risk by dose and city over the years. Moreover, the area covered by the ABCC-RERF Leukemia Registry has expanded to surrounding areas with the reconstruction and annexation in each city and improvement of medical care with time. Thus, the entire Leukemia Registry is of limited value in evaluating the pattern of onset of radiation-related leukemia.

Based on the material of Bizzozero et al, ¹² Land and Norman¹³ reported the distribution of onset of acute leukemia and chronic granulocytic leukemia in the entire Leukemia Registry, Hiroshima and Nagasaki, in the years 1946-64 for two exposure distance groups (less than 1,500 m and between 1,500 and 9,999 m). They found the onset of acute leukemia in the proximally exposed to be earlier than in the distally exposed survivors who were less than 20 years age ATB, but the relationship was reversed for survivors who were 50 or older age ATB. The onset of chronic granulocytic leukemia appeared earlier in proximally exposed cases than in distally exposed cases regardless of age ATB.

They aslo compared the age-weighted average of onset times between high dose and low dose cases in the LSS fixed cohort in the years 1950-71. They concluded that radiogenic leukemias occurred earlier than so-called

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放射線照射後のハツカネズミの白血病による死亡時期の分布の調査では、線量の増加に伴い平均死亡時期が早くなることが報告されている.7-9 しかし、人間では放射線による誘発白血病の潜伏期は種々の要因の影響を受けていることが判明している。Court Brown と Doll¹⁰ の強直性脊椎炎で放射線治療を受けた患者からの白血病の死亡と被曝後の期間についての研究によると、白血病の過剰死亡のビークは被曝後3-5年であったが、1 rad 以上を受けた被爆者からの白血病発生のビークは、広島・長崎とも被爆後5-6年に観察された.11二つの事例のピークの差異は平均線量の差異によるかもしれない。

放射線による誘発白血病に関して、広島・長崎の全人口からの白血病資料について厳密な解析ができないのは、全期間にわたって線量別、市別の観察人口が現在確認できないことによるものである。更に、ABCC-放影研の白血病登録の調査地域は、年月の経過とともに各市の復興、行政区域の拡大、医療の向上によって両市の周辺地域に拡大した。したがって、全白血病登録は放射線による誘発白血病の発現様式を評価するには限られた価値しかもっていない。

Bizzozero ら12 の報告した資料に基づいて、Land と Norman 13 は、1,500 m 未満と1,500 ー 9,999 m の二つ の被爆距離群について、1946 ー 64年の間の広島・長崎の全白血病登録における急性白血病と慢性骨髄性白血病の発病時期の分布を報告している。原爆時年齢が20歳未満の被爆者では、近距離被爆者が遠距離被爆者よりも急性白血病の発病時期が早かったが、原爆時年齢50歳以上の被爆者では逆になっていることを彼らは認めた。慢性骨髄性白血病の発病時期は原爆時年齢に関係なく、近距離被爆者が遠距離被爆者よりも早いことを明らかにした。

また、1950-71年の寿命調査固定集団における高線 量と低線量の症例の年齢加重平均発病時期の比較を した。同年齢群ではいわゆる自然発生の白血病より

spontaneous leukemias among members of the same age cohort, but they were uncertain whether dose had a different effect on the latent period among radiogenic leukemias. analysis did not provide for possible city differences and different levels of dose effect with respect to the distribution of onset of leukemia among A-bomb survivors. It is known that the quality of radiation of the A-bombs differs between the two cities and that the total dose is greater in Nagasaki than in Hiroshima at the same distance from the hypocenter.5 There is suggestive evidence that the pattern of disappearance of radiation-induced leukemia among A-bomb survivors in the high dose group differs by city, age ATB, and type of leukemia.14 It was desirable, therefore, to examine the distribution of onset of leukemia among A-bomb survivors in relation to city, dose, age ATB, and type of leukemia. The present analysis assumes that there has been no bias in the in- and outmigration or in ascertainment of case findings among A-bomb survivors by city, dose and age ATB over the years, but this may not be so.

The analysis showed that during 1946-75 the cumulative distributions of onset for both acute leukemia and chronic granulocytic leukemia were shifted to earlier years with increasing dose and the median for year and month of onset was significantly earlier as dose increases in Hiroshima survivors. In Nagasaki, however, the cumulative distributions of onset for both types of leukemia were shifted to the earlier side in the high dose group than in the low dose and less than 1 rad groups, and the latter two groups did not differ. The median for year and month of onset of acute leukemia was significantly earlier in the high dose than in the low dose and less than I rad groups; there were no significant differences in the onset of chronic granulocytic leukemia among the three dose classes. These observations based on the entire Leukemia Registry generally support the findings in the fixed cohort. The excess risk of both types of leukemia in the cohort appeared to increase with dose in Hiroshima survivors, but no excess risk was seen for either type of leukemia in the low dose region in Nagasaki survivors.

Examination of the cumulative distribution and the median onset for acute leukemia by dose and age ATB revealed a tendency for an earlier onset in survivors whose age ATB was less than 30 in the high dose group than in the low dose も放射線による誘発白血病の方が早期に発病すると 結論したが、線量が放射線による誘発白血病の潜伏 期に及ぼす影響については明確には述べることが できなかった,彼らの解析は被爆者白血病の発病 時期の分布に関し、都市別の差と被曝線量の異なる レベルにおける影響について検討していない. 原爆 放射線の線質は両市で差異があり、また、同一の 被爆距離では長崎が広島よりも総線量は大きいこと が知られている.5高線量群の被爆者における放射 線による誘発白血病の消失様式は、都市別、原爆時 年齢別、白血病の病型別で異なることを示唆する 所見が報告されている.14 したがって、被爆者白血病 の発病時期の分布を都市,線量,原爆時年齢,白血病 の病型との関係について検討することが望ましい. 今回の解析では,全期間にわたって都市別,線量別, 原爆時年齢別にみた転入・転出,及び症例の探知 確認状態に偏りがないと仮定したが、そうでないか もしれない.

1946-75年の間に広島の被爆者では、急性白血病と 慢性骨髄性白血病は共に発病時期の累積分布は線量 の増加に伴い早くなり, 発病年月の中央値は線量の 増加とともに有意に早くなることが今回の解析で示 された. しかし, 長崎では二つの病型の白血病の発病 時期の累積分布は、高線量群は低線量群と 1 rad 未満 の群より早期に位置していたが、低線量群と1rad 未満の線量群の間には差異はなかった. 急性白血病 の発病年月の中央値は、高線量群が低線量群と1rad 未満の群に比較して有意に早かったが、慢性骨髄性 白血病では三つの線量群間で発病時期には有意差が 認められなかった、全白血病登録に基づくこれらの 観察結果は, 固定集団における所見を一般に裏付ける ものであった. 広島の被爆者では両病型の白血病の 固定集団における過剰リスクは線量とともに増加する ようであるが、長崎における低線量域の被爆者では どちらの病型の白血病も過剰リスクは認められな かった.

線量別,原爆時年齢別にみた急性白血病発生の累積 分布及び発病年月の中央値は,原爆時年齢30歳未満 の被爆者では,両市とも高線量群が低線量群と対照 and control groups in both cities. No difference among dose groups in the distribution of onset emerged in either city among survivors whose age ATB was 30 or more. However, a significant excess risk of acute leukemia in the high dose group was demonstrated and it still persists in the older age ATB groups in the cohort through 1978. For chronic granulocytic leukemia, the cumulative distribution and median onset revealed the onset to be earlier with dose regardless of age ATB in Hiroshima survivors, but the same tendency was not observed in Nagasaki survivors, perhaps, due to the small number of cases.

As we have stated, the leukemia data based on the open populations of Hiroshima and Nagasaki are of limited value in the assessment of the latent period for radiation-induced leukemia in relation to dose. However, the present analysis showed that the distribution of onset among these cases depends upon city, dose, type of leukemia, and age ATB. A significantly shorter interval between exposure and onset was observed among the high dose group where an excess risk has been indicated in the cohort analysis, except for acute leukemia among those whose age ATB was 30 or more. This exception probably stems from the persistent excess risk of leukemia in these age groups in the present study period. Geographic differences in chronic lymphocytic leukemia between Hiroshima and Nagasaki have previously been reported.15

群よりも発病が早い傾向が認められた。原爆時年齢30歳以上の被爆者では、いずれの都市でも発病時期の分布は線量群で差異が認められなかった。しかしながら、1978年まで固定集団における高年齢被爆者では高線量群における急性白血病の有意な過剰リスクは依然続いている。14慢性骨髄性白血病についてみると、発生の累積分布と発病年月の中央値は広島の被爆者では原爆時年齢に関係なく、線量に伴って発病時期が早くなっているが、長崎では恐らく例数が少なかったために同様な傾向は認められなかった。

前述したように、広島・長崎の全人口に基づく白血病の資料は、放射線による誘発白血病の潜伏期と線量の関係を評価するには、限られた価値しかない。しかし、今回の解析によって、白血病の発病時期の分布が都市、線量、白血病の病型、被爆時年齢に依存することが示された。原爆時年齢が30歳以上の急性白血病を除けば、固定集団で過剰リスクが観察された高線量群においては、被爆から発病までの期間が有意に短くなることが観察された。上記の例外は、本調査期間ではこの年齢群における白血病の過剰リスクが継続していることに多分起因していると考えられる。広島と長崎における慢性リンパ性白血病の地理的差異については既に報告されている。15

[98] AS A [87] 2 [28] 3 [28] 3 [28] 3 [28] 1 [100] 1 [

APPENDIX 1

DISTRIBUTION OF ONSET OF ACUTE LEUKEMIA & CHRONIC GRANULOCYTIC LEUKEMIA AMONG A-BOMB SURVIVORS IN LEUKEMIA REGISTRY BY CITY, DOSE, AGE ATB, & YEAR OF ONSET (5-YEAR INTERVALS), 1946-75 付録

白血病登録に基づく被爆者の急性白血病と慢性骨髄性白血病の発病時期の分布: 都市別,線量別,原爆時年齡別,発病年度別(5年間隔).1946-75年

			Hiroshima	and promote the	gal serventi.	Nagasaki		
Age ATB	Year of Onset	Total Dose in Rad			Total Dose in Rad			
		< 1	1-99	100+	<1	1-99	100 +	
Acute Leuk	cemia				Herbital All	PARTIE CA	WI DO	
< 15	1946-50	1 (5.0)	5 (31.3)	6 (33.3)	1 (3.7)	1 (20.0)	3 (21.4	
	1951-55	5 (30.0)	3 (50.0)	8 (77.8)	6 (25.9)	0 (20.0)	4 (50.0	
	1956-60	5 (55.0)	4 (75.0)	3 (94.4)	5 (44.4)	0 (20.0)	2 (64.3	
	1961-65	6 (85.0)	3 (93.8)	0 (94.4)	4 (59.3)	1 (40.0)	4 (92.9	
	1966-70	3 (100.0)	0 (93.8)	1 (100.0)	4 (74.1)	1 (60.0)	0 (92.9	
	1971-75	0 (100.0)	1 (100.0)	0 (100.0)	7 (100.0)	2 (100.0)	1 (100.0	
	Total	20 (100.0)	16 (100.0)	18 (100.0)	27 (100.0)	5 (100.0)	14 (100.0	
15-29	1946-50	1 (5.6)	1 (8.3)	5 (25.0)	0 (0.0)	1 (10.0)	4 (25.0	
	1951-55	2 (16.7)	1 (16.7)	7 (60.0)	4 (18.2)	2 (30.0)	5 (56.3	
	1956-60	3 (33.3)	3 (41.7)	3 (75.0)	4 (36.4)	2 (50.0)	3 (75.0	
	1961-65	3 (50.0)	2 (58.3)	2 (85.0)	4 (54.5)	2 (70.0)	3 (93.8	
	1966-70	6 (83.3)	3 (83.3)	3 (100.0)	3 (68.2)	2 (90.0)	0 (93.8	
	1971-75	3 (100.0)	2 (100.0)	0 (100.0)	7 (100.0)	1 (100.0)	1 (100.0	
	Total	18 (100.0)	12 (100.0)	20 (100.0)	22 (100.0)	10 (100.0)	16 (100.0	
30-44	1946-50	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0(0.0	
	1951-55	3 (12.0)	3 (18.8)	2 (14.3)	6 (22.2)	1 (14.3)	1 (16.7	
	1956-60	6 (36.0)	5 (50.0)	6 (57.1)	5 (40.7)	1 (28.6)	1 (33.3	
	1961-65	6 (60.0)	1 (56.3)	2 (71.4)	5 (59.3)	2 (57.1)	2 (66.7	
	1966-70	4 (76.0)	1 (62.5)	2 (85.7)	4 (74.1)	1 (71.4)	1 (83.3	
	1971-75	6 (100.0)	6 (100.0)	2 (100.0)	7 (100.0)	2 (100.0)	1 (100.0	
	Total	25 (100.0)	16 (100.0)	14 (100.0)	27 (100.0)	7 (100.0)	6 (100.0	
45 +	1946-50	2 (12.5)	0 (0.0)	0 (0.0)	1 (4.8)	1 (33.3)	0(0.0	
	1951-55	1 (18.8)	2 (33.3)	0 (0.0)	4 (23.8)	0 (33.3)	1 (33.3	
	1956-60	7 (62.5)	0 (33.3)	2 (28.6)	5 (47.6)	0 (33.3)	1 (66.7	
	1961-65	4 (87.5)	2 (66.7)	2 (57.1)	5 (71.4)	1 (66.7)	0 (66.7	
	1966-70	0 (87.5)	0 (66.7)	2 (85.7)	2 (81.0)	1 (100.0)	1 (100.0	
	1971-75	2 (100.0)	2 (100.0)	1 (100.0)	4 (100.0)	0 (100.0)	0 (100.0	
	Total	16 (100.0)	6 (100.0)	7 (100.0)	21 (100.0)	3 (100.0)	3 (100.0	
Chronic Gr	anulocytic Leuke	mia						
< 15	1946-50	0 (0.0)	0 (0.0)	1 (25.0)	1 (14.3)	2 (50.0)	0(0.0	
	1951-55	0(0.0)	1 (25.0)	3 (80.0)	0 (14.3)	0 (50.0)	2 (100.0	
	1956-60	2 (40.0)	1 (50.0)	0 (80.0)	2 (42.9)	2 (100.0)	0 (100.0	
	1961-65	1 (60.0)	2 (100.0)	0 (80.0)	1 (57.1)	0 (100.0)	0 (100.0	
	1966-70	2 (100.0)	0 (100.0)	0 (80.0)	3 (100.0)	0 (100.0)	0 (100.0	
	1971-75	0 (100.0)	0 (100.0)	1 (100.0)	0 (100.0)	0 (100.0)	0 (100.0	
	Total	5 (100.0)	4 (100.0)	5 (100.0)	7 (100.0)	4 (100.0)	2 (100.0	
15-29	1946-50	0 (0.0)	2 (18.2)	5 (41.7)	0 (0.0)	0 (0.0)	1 (20.0	
	1951-55	0(0.0)	3 (45.5)	5 (83.3)	0 (0.0)	0 (0.0)	2 (60.0	
	1956-60	1 (25.0)	3 (72.7)	0 (83.3)	1 (50.0)	0 (0.0)	0 (60.0	
	1961-65	1 (50.0)	2 (90.9)	1 (91.7)	0 (50.0)	0 (0.0)	0 (60.0	
	1966-70	1 (75.0)	1 (100.0)	1 (100.0)	1 (100.0)	0(0.0)	0 (60.0	
	1971-75	1 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	1 (100.0)	2 (100.0	
	Total	4 (100.0)	11 (100.0)	12 (100.0)	2 (100.0)	1 (100.0)	5 (100.0	

Cumulative proportion (%) in parentheses ()内は累積比率(%).

Appendix 1 Continued 付録 1 続き

Age ATB			Hiroshima			Nagasaki		
	Year of Onset	Total Dose in Rad			Total Dose in Rad			
		< 1	1-99	100 +	<1	1-99	100 +	
30 +	1946-50	2 (15.4)	3 (13.0)	3 (23.1)	1 (6.7)	0(0.0)	0 (0.0)	
	1951-55	1 (23.1)	10 (56.5)	6 (69.2)	1 (13.3)	0(0.0)	1 (100.0)	
	1956-60	3 (46.2)	3 (69.6)	2 (84.6)	3 (33.3)	0(0.0)	0 (100.0)	
	1961-65	1 (53.8)	5 (91.3)	0 (84.6)	4 (60.0)	1 (50.0)	0 (100.0)	
	1966-70	3 (76.9)	2 (100.0)	0 (84.6)	4 (86.7)	0 (50.0)	0 (100.0)	
	1971-75	3 (100.0)	0 (100.0)	2 (100.0)	2 (100.0)	1 (100.0)	0 (100.0)	
	Total	13 (100.0)	23 (100.0)	13 (100.0)	15 (100.0)	2 (100.0)	1 (100.0)	

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