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CYTOGENETIC STUDY OF THE OFFSPRING OF ATOMIC BOMB SURVIVORS, HIROSHIMA AND NAGASAKI

原爆被爆者の子供の細胞遺伝学的調査，広島・長崎

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RADIATION EFFECTS RESEARCH FOUNDATION
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SUMMARY

This paper describes the results of a cytogenetic study on 8,322 children born to atomic bomb survivors (4,716 in Hiroshima and 3,606 in Nagasaki) and 7,976 controls (5,112 in Hiroshima and 2,864 in Nagasaki). Because no child was examined before age 12, the data may not be considered valid for the occurrence of chromosomal abnormalities that impose a high risk of early death. Thus, we will restrict our comparison to the sex-chromosome aneuploids and autosomal structural rearrangements of the balanced type, although other abnormalities encountered in this survey will be enumerated.

Among the children born to exposed parents, 19 individuals (0.23%) exhibited sex chromosome abnormalities and 23 (0.28%) exhibited autosomal structural rearrangements, whereas among children born to unexposed parents, 24 (0.30%) and 27 (0.34%), respectively, were observed to exhibit these abnormalities. Only one child with a karyotype of 47,XY,+21 was found in the Hiroshima exposed group. Thus, there was no statistically significant difference in the overall frequencies of

要　約

原爆被爆者の子供8,322名（広島4,716名，長崎3,606名），及び比較対照群7,976名（広島5,112名，長崎2,864名）に対して行った細胞遺伝学的調査結果について報告する．調査対象者の検査時年齢を12歳以上としたことから，本調査結果には，早期死亡の危険度の高い染色体異常例に関する資料の正確さに問題があると考えられる．したがって，本調査では性染色体異数体と均衡型の常染色体構造再配列を中心に比較検討を行うこととしたが，その他の観察し得る異常もすべてこの資料に含まれている．

被爆者の子供には19例（0.23%）の性染色体異常と23例（0.28%）の常染色体構造再配列が観察された．一方，非被爆者の子供では性染色体異常24例（0.30%）と構造再配列27例（0.34%）が認められた．広島被曝群に1例の47，XY，+21のトリソミー個体を確認した．したがって，染色体異常保有個体頻度については，

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cytogenetically abnormal cases between the exposed (0.52%) and control (0.64%) populations. In Hiroshima, frequencies of chromosome abnormalities were similar between exposed and control groups (0.64% vs 0.65%). However, the value observed in the exposed group in Nagasaki was slightly lower (0.36%)—though not statistically significant—than the value observed in the control group (0.63%). This value of the Nagasaki control group was similar to that in Hiroshima.

Family studies on probands with chromosome abnormalities revealed that the majority of cases (about 90%) with autosomal structural rearrangements of the balanced type were inherited from one or the other parent. The mutation rates for these rearrangements were similar between the exposed and control groups, being 0.98 $\times 10^{-4}$ per gamete per generation.

INTRODUCTION

A cytogenetic study of the children born to A-bomb survivors in Hiroshima and Nagasaki and children born to nonexposed parents was initiated in 1967.[1,2] The study was expanded in 1976, as a part of the Genetic Platform Research Program at RERF, and was continued until 1985 in conjunction with an ongoing mortality study and a biochemical genetics survey on the F_1 progeny.[3] The main objective of our study was to evaluate the radiation sensitivity of human germ cell chromosomes by measuring the frequency of certain chromosomal changes in structure or number induced by radiation in the germ cells of exposed parents and transmitted to their progeny.

For practical reasons it is RERF policy not to attempt to obtain blood samples from children below the age of 12. In consequence, the data collected should not be valid for chromosome abnormalities such as autosomal aneuploids or unbalanced chromosomal rearrangements. It is known that most, but not all, situations where autosomal trisomics as well as unbalanced autosomal rearrangements are associated with physical malformations, are incompatible with life. Since the mean age of our study subjects was 24 years at examination, it is unlikely that most liveborn infants with these abnormalities do not survive for two or three decades, or by the time of the examination, even if they survived to term. On the other hand, there should be relatively little selection prior to age 12

被曝群（0.52%）と対照群（0.64%）との間には統計的有意差はなかった．広島では異常個体頻度に関しては両群の間に差は認められなかった（被曝群0.64%，対照群0.65%）．長崎では，統計的に有意ではないが，被曝群（0.36%）の方が対照群（0.63%）よりもやや低い傾向にあった．長崎対照群における異常頻度は広島とほぼ同値である．

染色体異常保有例に対する家族調査の結果から，均衡型の常染色体構造再配列例の多く（約90%）はいずれか一方の親を保有者として遺伝していることが判明した．均衡型構造再配列に対する突然変異率は被曝群，対照群ともに同じ値の 0.98×10^{-4}（1配偶子当たり/1世代当たり）を得た．

緒　言

広島・長崎の原爆被爆者の子供及び非被曝者の子供に対する細胞遺伝学的調査が1967年に開始された．[1,2] この調査は，放影研における遺伝学基盤研究プログラムの一環として1976年に拡充され，現在進行中の F_1 世代の死亡率調査，並びに遺伝生化学的調査[3]と共に1985年まで続けられた．本調査の主たる目的は，被曝した親の生殖細胞中に放射線によって誘発され，かつその子供に伝えられたある種の染色体の構造又は数的変化の頻度を測定することにより，ヒト生殖細胞染色体の放射線感受性を評価することにあった．

実際的な理由により，放影研の方針として12歳未満の子供に対する採血を行わないことを原則とした．その結果，常染色体異数体や不均衡型染色体再配列などの染色体異常に関する限り，本調査資料は妥当性を欠く．すべてではないが，常染色体トリソミーや不均衡型染色体再配列個体では身体的奇形を伴うことが多く，生存不適合である．本研究の対象者の平均年齢は24歳であることから，これらの異常を保有する個体がたとえ生まれることができても，出生後20～30年，もしくは本検査時まで生存するとは考えられない．他方，性染色体異数体や均衡型再配列をもつ個体では，12歳未満に生じ得る淘汰の影響は

against children with sex-chromosome aneuploids or balanced rearrangements, both of which are lesions known to be produced by ionizing radiation in experimental animals.

This paper describes the results of chromosome analysis of peripheral blood leukocytes from 8,322 children born to A-bomb survivors in Hiroshima and Nagasaki and 7,976 children born to parents who had been exposed to less than 1 rad (distally exposed) or were not in the cities (NIC) at the time of the bomb (ATB), based on the old A-bomb radiation dosimetry system, called T65D.[4]

A new system of A-bomb radiation dose estimates, designated DS86,[5] is now available for the majority of survivors in the RERF study cohort. However, calculations of the individual gonadal doses are not fully available at this time for the exposed parents in the F_1 study population. For this reason, no attempt has been made to analyze the present data in terms of parental radiation doses. Further dose-related data analysis is now in progress and will be published in the future.

MATERIALS AND METHODS

Study samples

The sample subjects of the present survey were selected primarily from the RERF F_1 mortality study cohort.[6] This cohort included children born between 1 May 1946 and 31 December 1958 to parents, one or both of whom were residents of Hiroshima and Nagasaki ATB. The sample was later expanded to include children who were born after 1959 through the end of 1972. The extended samples were about 10% of the total.

In this analysis, the exposed group consisted of children born to parents, one or both of whom had been located within 2,000 m of the hypocenter and who have been assigned T65DR dose estimates of more than 1 rad. The control group consisted of children born to parents i) one or both of whom were exposed distally (2,500 m or more from the hypocenter), having estimated doses of less than 1 rad, or ii) were NIC ATB.

About 40% of the total individuals in the original sample were not included in this study, because they had died (5%) or migrated outside the contact areas of both cities (35%). Of the remaining individuals, approximately 75% agreed to participate in this

ほとんどないと思われるし，これらの異常が放射線照射によって誘発されることが実験動物系において知られている．

本報は，旧原爆放射線線量推定方式（T65D）[4]に従って抽出した広島・長崎の原爆被爆者の子供8,322名，及び1 rad未満の被爆者（遠距離被爆者）又は原爆時市内にいなかった者（市内不在者）の子供7,976名に対する末梢血白血球の染色体分析結果について記述する．

DS86[5]と呼ばれる原爆放射線新線量推定方式による推定線量が，放影研の研究コホートに属する大部分の被爆者に対して現在用いることができる．しかし，F_1調査集団に属する対象者の被爆した親について，今のところ個別の生殖腺線量計算値が全員について入手できるわけではない．このため，今回のデータに対して親の被曝線量に基づく解析の試みは行わなかった．線量に関するデータの解析は現在進行中であり，将来その結果を発表する．

資料及び方法

調査対象者

本調査の対象者は，主に放影研のF_1死亡率調査のコホート[6]から選んだ．このコホートは，一方又は両方の親が，原爆時に広島又は長崎の居住者であり，かつ1946年5月1日から1958年12月31日までに生まれた子供である．その後，1959年以降1972年末までに生まれた子供を対象者とすることにより対象集団が拡大された．拡大による対象者の増加は全体の約10%であった．

本解析において被曝群を構成している子供は，その親の一方又は両方が爆心地から2,000 m以内で被爆し，かつその T65DR 線量推定値が1 rad以上に該当する者である．対照群となる子供は，その親が，i）一方又は両方とも遠距離で被爆し（爆心地から2,500 m以上），かつ推定線量1 rad未満か，あるいは ii）原爆時市内にいなかった者である．

原集団のうち約40%の者が，死亡（5%）又は両市の対象地域外への転出（35%）などにより，本研究には含まれなかった．残りのうち，約75%の者が本研究への参加を承諾した．結局，本調査への参加率は

study. Thus, the participation rate for this survey was 45% of the total original sample.

After obtaining consent from the F_1 participants and, if necessary, their parents, they were invited to visit the RERF clinic. At that time, a clinic nurse administered a brief medical questionnaire, and a blood sample was drawn. If requested, a physical examination was performed.

As shown in Table 1, the total number of children examined was 16,298 in the two cities; 9,828 in Hiroshima (4,716 exposed and 5,112 controls), and 6,470 in Nagasaki (3,606 exposed and 2,864 controls). The number of females predominated over males in both cities as well as in both the exposed and control groups. The exposed group was further divided into three categories by parental exposure status, i.e., children born to parents in which only the father was exposed, only the mother was exposed, or both parents were exposed. The number of children per parental couple was 1.4 children per couple (or 8,322 in 5,823) in the exposed, and 1.2 per couple (or 7,976 in 6,473) in the controls, when the two cities were combined.

The mean age of the participants at examination was 24 in Hiroshima, and 23 in Nagasaki with a range between 12 and 38.

Cytogenetic methods

Heparinized blood specimens, 1 to 2 ml per person, collected from each participant, were cultured for two days, and then harvested for chromosome preparations using the conventional Giemsa staining methods, the details of which have been described elsewhere.[7]

In each case, 10 well-spread metaphases were examined directly under the microscope, and 3 of them were photographed for detailed karyotype analysis. Cases with less than 10 scorable metaphases were regarded as culture failure. The rate of failure was about 0.1% of the total blood sample in the two cities. When an abnormality was suspected, 100 or more cells were examined.

In addition to the conventional stain, analyses on G-, Q-, and C- banded preparations[8-10] were supplementarily made to cases suspected of having abnormality. When family studies were performed on probands with structural rearrangements, high

原集団の45%であった.

必要に応じては，その親の同意を得たのち，F_1 調査対象者に放影研に来所するよう依頼した．来所時に看護婦が簡単な医学質問票による調査と採血を行った．希望者には診察も行った．

表1に示すように，広島9,828名（被曝群4,716名，対照群5,112名），長崎6,470名（被曝群3,606名，対照群2,864名），計16,298名に対し調査を行った．女性の数が両市において被曝群，対照群ともに男性の数を上回った．被曝群は更に親の被曝状況により，父親のみが被曝者，母親のみが被曝者，両親が被曝者の3群に分類された．夫婦1組当たりの子供の数は両市を合わせて，被曝群では1.4名（5,823組，8,322名），対照群では1.2名（6,473組，7,976名）であった．

被検時の対象者の平均年齢は広島で24歳，長崎で23歳で，12～38歳の範囲内であった．

細胞遺伝学的検査の方法

各対象者から1～2 ml ずつ採血し，ヘパリン処理した末梢血を2日間培養した後に細胞を集め，通常のギムザ染色法による染色体標本を作成した．詳細は既に報告されている論文[7]に記載されている．

観察例1例ごとに，良質の中期分裂像10個を直接顕微鏡下で観察し，そのうちの3個を写真撮影し，詳細にわたる核型分析に供した．観察可能な中期分裂像が10個未満の観察例は，培養失敗例とみなした．失敗率は両市で全試料の約0.1%であった．異常を有する疑いがある場合は，100個以上の細胞を調べた．

異常の疑いのある観察例については，通常の染色に加えてG，Q，Cバンド分染法による解析[8-10]を補足的に行った．構造再配列の発端者についての

TABLE 1 NUMBER AND FREQUENCY (PER 1,000) OF CHILDREN WITH CHROMOSOME ABNORMALITIES BORN TO A-BOMB SURVIVORS AND THEIR CONTROLS, HIROSHIMA AND NAGASAKI

表1　広島・長崎の原爆被爆者及び対照者の子供における染色体異常を有する者の数及び頻度（1,000名当たり）

		Hiroshima				
		Exposed				Control
		Father	Mother	Both	Total	
No. of cases:	Males	638	1,348	274	2,260	2,477
	Females	636	1,490	330	2,456	2,635
	Total	1,274	2,838	604	4,716	5,112
No. of parental couples		968	2,018	467	3,453	4,242
Mean dose (rad, T65D)	Father	115.8	0	88.1	42.6	0
	Mother	0	91.3	61.3	62.8	0
Abnormalities:						
A. Sex chromosomes						
Males**	1. XYY	–	–	–	–	5 (2.02)
	2. XXY	1 (1.57)	4 (2.97)	1 (3.65)	6 (2.65)	4 (1.61)
	3. Mosaic	1 (1.57)	–	–	1 (0.44)	–
	4. Other	–	–	–	–	2 (0.81)
	T	2 (3.13)	4 (2.97)	1 (3.65)	7 (3.10)	11 (4.44)
Females**	5. X	–	–	–	–	–
	6. XXX	2 (3.14)	1 (0.67)	1 (3.03)	4 (1.63)	3 (1.14)
	7. Mosaic	–	–	1 (3.03)	1 (0.41)	3 (1.14)
	8. Other	–	–	–	–	–
	T	2 (3.14)	1 (0.67)	2 (6.06)	5 (2.04)	6 (2.28)
Subtotal		4 (3.14)	5 (1.76)	3 (4.97)	12 (2.54)	17 (3.33)
B. Rearrangements						
Balanced:	1. rob(D/D)	2 (1.57)	3 (1.06)	–	5 (1.06)	4 (0.78)
	2. rob(D/G)	–	1 (0.35)	–	1 (0.21)	–
	3. rcp	3 (2.35)	2 (0.70)	2 (3.31)	7 (1.48)	6 (1.17)
	4. inv	–	1 (0.35)	–	1 (0.21)	6 (1.17)
Subtotal		5 (3.92)	7 (2.47)	2 (3.31)	14 (2.97)	16 (3.13)
Unbalanced:						
	5. rob	–	–	–	–	–
	6. rcp	–	–	–	–	–
	7. del	–	–	–	–	–
	8. Supern.	1 (0.78)	–	–	1 (0.21)	–
	9. Other	1 (0.78)	1 (0.35)	–	2 (0.42)	–
Subtotal		2 (1.57)	1 (0.35)	0	3 (0.64)	0
C. Trisomics						
	1. +21	1 (0.78)	–	–	1 (0.21)	–
	2. Other	–	–	–	–	–
Subtotal		1 (0.78)	0	0	1 (0.21)	0
Grand total		12 (9.42)	13 (4.58)	5 (8.28)	30 (6.36)	33 (6.46)

*Cited from Hook and Hamerton.[22]　Hook and Hamerton[22] より引用.　(Continued 続く)

**The rates for the sex chromosome abnormalities apply only to the affected sex, not the total studied.
性染色体の異常率は対象者総数に対するものではなく，その異常が認められた性別における割合である.

rob: Robertsonian translocation ロバートソン型転座　rcp: Reciprocal translocation 相互転座　inv: Inversion 逆位
del: Deletion 欠失
Supern: Supernumerary with minute marker (Details of individual abnormalities are given in Appendix Table 1.)
微小マーカーによる過剰染色体（個々の異常については付表1で詳述.）

TABLE 1 Continued 表 1 続き

		Nagasaki				
		Exposed				Control
		Father	Mother	Both	Total	
No. of cases:	Males	543	912	199	1,654	1,205
	Females	623	1,123	206	1,952	1,659
	Total	1,166	2,035	405	3,606	2,864
No. of parental couples		802	1,305	263	2,370	2,231
Mean dose (rad, T65D)	Father	131.3	0	124.6	56.4	0
	Mother	0	117.7	83.7	75.8	0
Abnormalities:						
A. Sex chromosomes						
Males**	1. XYY	2 (3.68)	1 (1.10)	–	3 (1.81)	–
	2. XXY	–	1 (1.10)	–	1 (0.60)	5 (4.15)
	3. Mosaic	–	–	–	–	–
	4. Other	–	1 (1.10)	–	1 (0.60)	–
	T	2 (3.68)	3 (3.29)	0	5 (3.02)	5 (4.15)
Females**	5. X	–	–	–	–	–
	6. XXX	1 (1.61)	–	–	1 (0.51)	1 (0.60)
	7. Mosaic	–	1 (0.89)	–	1 (0.51)	–
	8. Other	–	–	–	–	1 (0.60)
	T	1 (1.61)	1 (0.89)	0	2 (1.02)	2 (1.21)
Subtotal		3 (2.57)	4 (1.97)	0	7 (1.94)	7 (2.44)
B. Rearrangements						
Balanced:	1. rob(D/D)	2 (1.72)	–	–	2 (0.55)	2 (0.70)
	2. rob(D/G)	1 (0.86)	–	1 (2.47)	2 (0.55)	–
	3. rcp	–	–	–	–	7 (2.44)
	4. inv	–	–	–	–	–
Subtotal		3 (2.57)	0	1 (2.47)	4 (1.11)	9 (3.14)
Unbalanced:						
	5. rob	–	–	–	–	–
	6. rcp	–	–	–	–	–
	7. del	–	–	–	–	–
	8. Supern.	1 (0.86)	–	–	1 (0.28)	–
	9. Other	–	1 (0.49)	–	1 (0.28)	2 (0.70)
Subtotal		1 (0.86)	1 (0.49)	0	2 (0.55)	2 (0.70)
C. Trisomics						
	1. +21	–	–	–	–	–
	2. Other	–	–	–	–	–
Subtotal		0	0	0	0	0
Grand total		7 (6.00)	5 (2.46)	1 (2.47)	13 (3.61)	18 (6.28)

(Continued 続く)

TABLE 1 Continued 表 1 続き

		Two cities combined					Newborn infants*
		Exposed				Control	
		Father	Mother	Both	Total		
No. of cases:	Males	1,181	2,260	473	3,914	3,682	37,779
	Females	1,259	2,613	536	4,408	4,294	19,173
	Total	2,440	4,873	1,009	8,322	7,976	56,952
No. of parental couples		1,770	3,323	730	5,823	6,473	–
Mean dose (rad, T65D)	Father	123.0	0	102.7	48.6	0	–
	Mother	0	102.3	70.3	68.4	0	–
Abnormalities:							
A. Sex chromosomes							
Males**	1. XYY	2 (1.69)	1 (0.44)	–	3 (0.77)	5 (1.36)	35 (0.93)
	2. XXY	1 (0.85)	5 (2.21)	1 (2.11)	7 (1.79)	9 (2.44)	35 (0.93)
	3. Mosaic	1 (0.85)	–	–	1 (0.26)	–	14 (0.37)
	4. Other	–	1 (0.44)	–	1 (0.26)	2 (0.54)	14 (0.37)
	T	4 (3.39)	7 (3.10)	1 (2.11)	12 (3.07)	16 (4.35)	98 (2.59)
Females**	5. X	–	–	–	–	–	2 (0.10)
	6. XXX	3 (2.38)	1 (0.38)	1 (1.87)	5 (1.13)	4 (0.93)	20 (1.04)
	7. Mosaic	–	1 (0.38)	1 (1.87)	2 (0.45)	3 (0.70)	7 (0.37)
	8. Other	–	–	–	–	1 (0.23)	–
	T	3 (2.38)	2 (0.77)	2 (3.73)	7 (1.59)	8 (1.86)	29 (1.51)
Subtotal		7 (2.87)	9 (1.85)	3 (2.97)	19 (2.28)	24 (3.01)	127 (2.23)
B. Rearrangements							
Balanced:	1. rob(D/D)	4 (1.64)	3 (0.62)	–	7 (0.84)	6 (0.75)	40 (0.70)
	2. rob(D/G)	1 (0.41)	1 (0.21)	1 (0.99)	3 (0.36)	–	11 (0.19)
	3. rcp	3 (1.23)	2 (0.41)	2 (1.98)	7 (0.84)	13 (1.63)	51 (0.90)
	4. inv	–	1 (0.21)	–	1 (0.12)	6 (0.75)	8 (0.14)
Subtotal		8 (3.28)	7 (1.44)	3 (2.97)	18 (2.16)	25 (3.13)	110 (1.93)
Unbalanced:							
	5. rob	–	–	–	–	–	4 (0.07)
	6. rcp	–	–	–	–	–	7 (0.12)
	7. del	–	–	–	–	–	5 (0.09)
	8. Supern.	2 (0.82)	–	–	2 (0.24)	–	10 (0.18)
	9. Other	1 (0.41)	2 (0.41)	–	3 (0.36)	2 (0.25)	8 (0.14)
Subtotal		3 (1.23)	2 (0.41)	0	5 (0.60)	2 (0.25)	34 (0.60)
C. Trisomics							
	1. +21	1 (0.41)	–	–	1 (0.12)	–	71 (1.25)
	2. Other	–	–	–	–	–	11 (0.19)
Subtotal		1 (0.41)	0	0	1 (0.12)	0	82 (1.44)
Grand total		19 (7.79)	18 (3.69)	6 (5.95)	43 (5.17)	51 (6.39)	353 (6.20)

resolution banding techniques[11,12] were also employed for the precise identification of break points of the chromosomes involved in the aberrations. Description of the type of chromosome abnormalities followed the standardized International System for Human Cytogenetic Nomenclature (ISCN).[13]

In the present study, a number of heteromorphic variants have been detected with the conventional staining method, and most of these cases were reanalyzed by the application of C-, Q- and other banding techniques. Since cytogenetic characteristics of heteromorphic variants have been reported elsewhere,[14–16] these variants will not be described in this report.

RESULTS

The results of the cytogenetic observations are shown in Table 1, and every abnormal case is fully described in Appendix Table 1.

Chromosome abnormalities were classified into the following four groups: i) sex chromosome abnormalities, ii) balanced autosomal structural rearrangements, iii) unbalanced autosomal structural rearrangements, and iv) autosomal trisomics. As noted above, the latter two classes were thought to be of little research importance under the circumstances of this study.

Sex chromosome abnormalities

As shown in Table 1, items A1–8, 43 cases exhibited sex chromosome anomalies—19 out of 8,322 in the exposed group (2.28 per 1,000) and 24 out of 7,976 in the controls (3.01 per 1,000). No increased frequency of sex chromosome abnormalities, ascribable to parental radiation exposure, was observed.

The majority of the abnormalities were due to sex-chromosome aneuploidy, mostly XYY and XXY in males and XXX in females, which constituted 75% of the total sex anomaly cases. Except for mosaic situations, no female with 45,X was detected in any of the groups studied.

When the data from the two cities were combined, no significant differences were noted between the frequencies of sex chromosome abnormalities in the exposed group when compared to the controls.

Furthermore, no statistically significant difference was noted in the mean maternal age at birth of

家族調査を実施した際には，異常を有する染色体の切断箇所を正確に同定するため高精度分染技法[11,12]も用いた．染色体異常の種類の表記は，International System for Human Cytogenetic Nomenclature (ISCN)[13]に従った．

本調査では，多くの異形染色体変異体が通常染色法により検出された．それらのうち大部分をC，Q，又はその他の分染法を用いて再分析した．異形変異体の細胞遺伝学的特性については既に報告しているので，[14–16]本報では省略した．

結　果

細胞遺伝学的観察の結果は表1に示し，異常例についてはすべて付表1に詳述した．

染色体異常を以下の4群，すなわち，i）性染色体異常，ii）均衡型常染色体構造再配列，iii）不均衡型常染色体構造再配列，iv）常染色体トリソミーに分類した．前述のように，後者の2群は本調査ではあまり研究上の重要性がないと考えた．

性染色体異常

表1のA1～8項に示すように43例の性染色体異常が認められ，被曝群では8,322名中19例（1,000例当たり2.28例），対照群では7,976名中24例（1000例当たり3.01例）であった．親の放射線被曝に起因すると考えられる性染色体異常の増加は認められなかった．

異常の大多数は性染色体異数体によるものであり，男性ではそのほとんどがXYYかXXY，女性ではXXXで，全性染色体異常のうち異数体に起因するものは75%を占めた．モザイク型を除けば，女性ではどの観察群においても45,Xは検出されなかった．

両市のデータを合計した場合，被曝群と対照群との間に性染色体異常の頻度に関して有意な差は認められなかった．

更に，XXY又はXXXの子供出生時における母親の

XXY and XXX children between the exposed and control groups: for XXY, 28.3±4.1 years old in the exposed and 28.9±5.8 years old in the control, and for XXX, 27.5±6.2 years old in the exposed and 27.2±4.2 years old in the control.

The frequency of mosaic cases was higher in females (two in 4,408 exposed and three in 4,294 controls) than in males (one in 3,914 exposed and none in 3,682 controls). Among the mosaics, a woman in the Hiroshima control showed a mosaic of 45,X/46,X,r(X). A family study revealed that the abnormality was the result of a de novo mutant, since both parents showed the normal karyotype.

Three cases were noted with structural rearrangements involving sex chromosomes, all of which belonged to the control group: two unrelated males—each with a pericentric inversion of the Y chromosome in Hiroshima—and a female with a distally deleted long arm of one of the X chromosomes in Nagasaki.

One unusual observation was made in the Nagasaki series. A male child, born to an exposed mother, was found to have 46 chromosomes with two X chromosomes. Molecular basis for the etiology of the XX males has recently been investigated extensively, and it is interpreted that XX males carry certain Y-specific DNA sequences, or the testis-determining factor, produced most likely by an interchange of a portion of the Y chromosome with a portion of the paternal X chromosome.[17,18] It is yet known whether the altered function of an X chromosome in this particular child was related to maternal exposure to A-bomb radiation, although it may be unlikely as suggested above.

Balanced autosomal structural rearrangements

The majority of structural rearrangements involving autosomes were translocations of the Robertsonian or reciprocal types and pericentric inversions. They would, therefore, result in no loss or gain of chromosome material, and they would be genetically balanced without any phenotypic effect. The present study sample consisted of seven families (three exposed and one control from Hiroshima, and one exposed and two controls from Nagasaki) in which two or more siblings in a family showed identical karyotypic abnormalities.

Among these cases 10 children (7 D/D and 3 D/G) from eight exposed families exhibited Robertsonian

平均年齢に関して，被曝群と対照群との間に統計的に有意な差は認められなかった．XXYの場合，被曝群は28.3±4.1歳，対照群は28.9±5.8歳であり，XXXの場合，被曝群が27.5±6.2歳，対照群は27.2±4.2歳であった．

モザイク例の観察頻度は女性の方が（被曝群4,408名中2例，対照群4,294名中3例）男性（被曝群3,914名中1例，対照群3,682名中0例）より高かった．モザイクのうち，広島対照群の女性1例が，45,X/46,X,r(X)のモザイク型を呈した．家族調査によると両親ともに正常な核型であるので，この異常は新たに発生した突然変異の結果によるものと判明した．

性染色体の構造再配列が3例に認められ，すべて対照群であった．2例は広島の互いに血縁関係のない男性で，共にY染色体の挟動原体逆位を示した．残りの1例は長崎の女性で，1個のX染色体長腕に端部欠失が認められた．

長崎で特異な例が観察された．被曝母親から生まれた男性1例は染色体数46で2個のX染色体構成を示した．XX型男性の成因を探るための分子レベルの研究が，近年入念に行われており，その解釈としてXX型男性は，ある種のY特異性DNA配列，あるいは睾丸決定因子をもつことを示しており，Y染色体の一部が父親由来のX染色体の一部に相互交換に基づく転移によって形成されたと思われる．[17,18] この男性のX染色体の機能変化が，母親の原爆放射線被曝に関係があるのか否かは分からないが，上述の理由から考えてその可能性は低い．

均衡型常染色体構造再配列

常染色体の構造再配列の大部分は，ロバートソン型若しくは相互型の転座，及び挟動原体逆位であった．したがって，これらの異常により染色体の欠失や増加を生じることはなく，表現型にも影響がなく遺伝的に均衡していると考えられる．本調査対象者には，同一家族内に同じ核型異常を示す同胞が2名以上存在する家族が7例認められた（広島では被曝群3家族と対照群1家族，長崎では被曝群1家族と対照群2家族）．

これらのうち，被曝群の8家族中10名の子供がロバートソン型転座（7名がD/D，3名がD/G）を呈

translocations, and six children (all D/D) from three control families showed similar rearrangements. In addition, seven children from five exposed families and 13 children from 12 control families exhibited reciprocal translocations. Only one child among the exposed families, and six children from five control families had inversions.

Table 1, items B1-4, shows that a high incidence of pericentric inversion was observed among the Hiroshima controls (Table 1, item B4), and in Nagasaki a high rate of reciprocal translocations was observed in the controls, while no such cases were found in the exposed group (Table 1, item B3).

As shown in Appendix Table 1, chromosomes No. 5 and No. 8 were found to be involved more frequently than the others in the formation of reciprocal translocations. Furthermore, chromosome No. 2 was frequently involved in pericentric inversions in the Hiroshima sample.

Pooled data on the frequencies of balanced structural rearrangements indicated that, although there is no significant difference in the frequencies of children with stable autosomal rearrangements, a relatively low frequency of rearrangements was observed in the exposed group in Nagasaki (see subtotal in Table 1, item B). The data were further compared with the frequencies of the same types of abnormality derived from cytogenetic surveys on 59,542 consecutive newborn infants.[19] The results obtained in this study of both exposed and control groups were approximately 50% higher than those reported for neonatal surveys.

Family studies of abnormal cases were undertaken to determine whether the observed structural rearrangements arose de novo or were inherited from one or the other parent. Family studies in all cases were not possible because of the death of parents or because parents did not wish to cooperate in this study. When two or more siblings from a family were found to carry an identical rearrangement, their abnormalities were judged to be inherited even though a family study may not have been done.

Ample evidence indicates that the majority of cases with rearrangements were preexisting. Only two de novo mutants were identified; both mutants (one in the exposed and one in the control group) were

し，対照群の３家族の６名の子供も同様の再配列（すべて D/D）を示した．被曝群５家族中７名の子供，及び対照群12家族中13名の子供に相互転座が観察された．被曝群１家族中１名と対照群５家族中６名の子供に逆位があった．

表１の項目 B1～4 は，広島対照群における挟動原体逆位発生率が高いことを示しており（表１，項目 B4），長崎対照群では相互転座が高率である反面，被曝群にはそのような例は認められない（表1，項目 B3）．

付表１に示すように，５番及び８番染色体が，他の染色体よりも相互転座形成に関与する頻度が高いことが分かった．更に，広島の対象者では，２番染色体が頻繁に挟動原体逆位に関与していた．

均衡型構造再配列の頻度についてデータをプールした場合，安定型常染色体再配列を有する子供の頻度には有意な差はないが，長崎被曝群における再配列頻度が相対的に低いことが認められた（表１の項目Ｂの小計参照）．このデータを更に，連続出生の新生児59,542名に対して行われた細胞遺伝学的調査に基づく同型の異常頻度データ[19]と比較した．本調査で得られた結果は，被曝群，対照群ともに，新生児調査で報告された結果より約50％高い値であった．

観察された構造再配列が新たに起こったものか，それともどちらか一方の親から遺伝したものなのかを明らかにするために，異常例に対する家族調査を行った．親が死亡していたり，また本調査への協力を希望しない場合もあるために，全観察例について家族調査を行うことはできなかった．１家族内に同一再配列を有する同胞が２名以上いることが認められた場合は，家族調査が行われていない場合であっても，その異常は遺伝によるものと判定した．

これまで報告されている多くの知見によれば，再配列例の大部分が遺伝によるものであることを示している．新たな突然変異は２例のみに確認され，両方ともに広島の対象者（被曝群，対照群それぞれ１例ず

from the Hiroshima group. Thus far, none have been detected in the Nagasaki sample.

つ）であった．今までのところ，長崎の対象者からは1例も検出されていない．

The chromosomal mutation rate can be estimated using the following formula:

下記の式を用いて，染色体突然変異率を推定することができる．

$$\text{Mutation rate} = \frac{\text{No. of de novo cases observed} + \frac{\text{No. of de novo cases}}{\text{de novo cases} + \text{inherited cases}} \times \text{No. of rearrangements of unconfirmed origin}}{\text{Total number of individuals examined}}$$

突然変異率 = （新規突然変異例観察数 + 新規例数 / 新規例数 + 遺伝例数 × 起源未確認の再配列例数） / 被検者総数

For the gametic mutation rate, the value derived from the above formula is further divided by 2.[19] As shown in Table 2, the gametic mutation rates for balanced structural rearrangements were estimated as 0.98×10^{-4} in the exposed and 0.98×10^{-4} in the controls, indicating no statistical difference between the two groups. However, these values were much lower than the value of 1.88×10^{-4} per gamete per generation on the liveborn infant survey.[19]

配偶子突然変異率は，上式で得られた値を更に2で割ると得られる．[19] 表2に示すように，均衡型構造再配列の配偶子突然変異率は被曝群では 0.98×10^{-4}，対照群では 0.98×10^{-4} と推定され，両群間に統計的な差がないことが示された．しかし，これらの値は，新生児調査[19]で求められている1世代1配偶子当たりの値 1.88×10^{-4} よりかなり低かった．

TABLE 2 PARENTAL ORIGIN OF BALANCED STRUCTURAL REARRANGEMENTS*
表2 均衡型構造再配列*の親別の由来

	Hiroshima		Nagasaki		Hiroshima + Nagasaki		Neonates**
	Exposed	Control	Exposed	Control	Exposed	Control	
No. of individuals	4,716	5,112	3,606	2,864	8,322	7,976	59,452
de novo	1	1	0	0	1	1	18
Inherited	8	8	2	7	10	15	73
Father	(2)	(4)	(2)	(4)	(4)	(8)	(37)
Mother	(0)	(1)	(0)	(1)	(0)	(2)	(36)
Undetermined	(6)	(3)	(0)	(2)	(6)	(5)	(0)
Subtotal	9	9	2	7	11	16	91
Not studied	5	7	2	2	7	9	22
Grand total	14	16	4	9	18	25	113
Gametric mutation rate ($\times 10^{-4}$)	1.65	1.74	-	-	0.98	0.98	1.88

*Including reciprocal and Robertsonian translocations plus pericentric inversions.
相互転座，ロバートソン型転座，挟動原体逆位を含む．

**Cited from Jacobs.[19]
Jacobs[19]より引用．

Unbalanced autosomal structural rearrangements

Unbalanced autosomal structural rearrangements were noted in seven cases: five among the exposed and two among the controls. All of them were characterized by the presence of an extra small metacentric element (or elements), termed "mar," according to ISCN.[13] The element (or elements) was present either as a "supernumerary" piece of chromosomal material in addition to the normal chromosome complement in all cells,[20] or was in the form of a mosaic (Table 1, items B5-9, also Appendix Table 1). Five of the cases were mosaics (three exposed and two controls).

In one male observed among the Nagasaki controls, three extra minute elements, each of which differed in size and shape, existed as cell lines with different combinations of markers.[21] Family studies revealed that most of these marker cases were found to arise as de novo mutants (Appendix Table 1).

Autosomal trisomics

Only one male Down's syndrome case (47,XY,+21) was born in 1966 to an exposed father in Hiroshima. This child's age at cytogenetic examination was 15. No other trisomic cases, such as D- and E-trisomy, have been observed in the F_1 population.

The overall frequency of cases with abnormalities by parental exposure and by city is shown at the bottom of Table 1. It can be seen that, for sex chromosome abnormalities and structural rearrangements, the frequencies are consistently higher in the controls than in the exposed, and also higher in Hiroshima than in Nagasaki. Yet none of these differences is statistically significant.

The data from the two cities were combined, regardless of parental radiation exposure, and each of the frequencies was compared with that of the corresponding abnormalities in the cytogenetic surveys on 56,952 consecutive liveborn infants.[22] Here again, the frequencies of both sex abnormalities and rearrangements were found to be somewhat higher in the children included in this study as compared to the neonates.

DISCUSSION

As mentioned previously, the main objective of this study was to demonstrate whether any measurable increase in the frequency of children with chro-

不均衡型常染色体構造再配列

不均衡型常染色体構造再配列は，7例に観察され，5例は被曝群，2例は対照群であった．これらはすべて，ISCN[13]による"mar"と命名される極めて小さな中部動原体様構造を示し，1個若しくはそれ以上存在することがその特徴であった．この染色体は，どの細胞においても通常の染色体全量に加えて染色体状構成物質から"過剰"に存在するか，[20]若しくはそのモザイク型として存在した(表1の項目B5～9及び付表1)．5例(被曝群3例，対照群2例)はモザイク型であった．

長崎対照群の男性1例に大きさや形が各々異なる微小な染色体様構造物が3個認められ，これらのマーカーが様々の組み合わせをもつ細胞集団を形成していることが観察された．[21]家族調査により，これらマーカーの大部分が，新規の突然変異として生じたことが明らかとなった(付表1)．

常染色体トリソミー

ダウン症候群の男性(47, XY, ＋21) 1名のみが観察された．1966年に出生，父親が広島で被曝しており，細胞遺伝学的検査の被検時年齢は15歳であった．DあるいはEトリソミーのような他のトリソミーはF_1集団では観察されなかった．

都市別，親の被曝別からみた観察異常例の全頻度を表1の最下欄に示した．この表からも明らかなように，性染色体異常例も構造再配列例も，その頻度は一貫して被曝群より対照群の方が，また長崎より広島の方が高い．しかし，これらの差はいずれも統計的に有意ではなかった．

親の被曝に関係なく両市のデータを合計し，それぞれの異常頻度について，連続出生の生産児56,952名に対する細胞遺伝学的調査結果[22]のそれぞれに対応する異常頻度と比較してみた．ここでも性染色体異常，再配列異常の両頻度ともに，新生児調査に比べて本調査対象者の方が幾分高いことが認められた．

考　察

前述のとおり本調査の主要な目的は，染色体異常を有する子供の頻度の増加があるとすれば，その増加

mosome abnormalities might be associated with A-bomb radiation exposure of parental germ cell chromosomes. Thus, this study was conducted to compare the frequency of births to A-bomb survivors of children exhibiting chromosome abnormalities—especially structural rearrangements—against the frequency of such births to nonexposed parents.

Our results show no statistically significant increases in the frequency of chromosome abnormalities, especially sex-chromosome aneuploids and structural rearrangements of the balanced type, among children of the exposed. This does not imply that genetic effects ascribable to parental A-bomb exposure have not occurred. It simply indicates that such effects have not been detectable by current cytogenetic methods or that the total number of cases in the present study is too small to be observed. The reason for the absence of cytogenetic effects of A-bomb radiation among the children of survivors remains unresolved. One possible interpretation is that germ cells with chromosome damage could have been eliminated either in the course of gametogenesis or in the very early period of gestation as "unrecognized" spontaneous abortions, or in early postnatal life.

Extensive cytogenetic surveys on consecutive live-born infants, undertaken as international collaborative studies in several European and North American countries, have provided very useful and relevant information on the natural incidence of various types of constitutional chromosome abnormalities in the human population,[23−29] (also refer to Hook and Hamerton[22] for a review).

Cytogenetic data based on the above-mentioned surveys were compared with our findings (Tables 1 and 2). It is apparent that the frequencies of both sex chromosome abnormalities and balanced autosomal structural rearrangements were slightly higher in our study than in the neonatal surveys. The situation was reversed when we compared unbalanced rearrangements and autosomal trisomics. Here again, we must emphasize that the mean age of our study subjects was 24 years at examination, which was markedly different from the neonatal surveys. It is conceivable that the majority of infants with the abnormalities in question did not survive for 20 to 30 years, and thus did not reach the mean age of our study.

が親の生殖細胞染色体に及ぼす原爆放射線の影響と関連があるか否かを明らかにすることであった．したがって，染色体異常，特に構造再配列，を有する個体頻度について，被爆者の子供と非被爆者の子供の比較を目的として本調査を行った．

我々の結果では，被曝群の子供における染色体異常，特に性染色体異数体及び均衡型の構造再配列の頻度に関して，統計的に有意な増加は認められなかった．これは，親の原爆放射線被曝に起因する遺伝的な影響がなかったことを意味するわけではない．原爆放射線の遺伝的影響が現在の細胞遺伝学的方法では検出不可能であるか，又は，影響を証明するためには本調査の観察例数が少なすぎるということを単に示すものである．現状における被爆者の子供に対する原爆放射線の細胞遺伝学的影響が認められない真の理由はまだ分からない．一つの可能な解釈としては，染色体に損傷をもつ生殖細胞が，配偶子形成の過程，妊娠の極めて初期の段階において「無自覚」の自然流産，若しくは出生後ごく初期に淘汰（死亡）されたなどが考えられる．

連続出生児についての広範な細胞遺伝学的調査が，ヨーロッパや北米など数か国で国際的協同調査研究として行われており，ヒト集団における様々な先天性染色体異常の自然発生率に関して極めて有用な情報を提供している[23-29]（総説については Hook and Hamerton[22] を参照のこと）．

上記調査の細胞遺伝学的データと我々の知見とを比較した（表１及び２）．性染色体異常と均衡型常染色体構造再配列の頻度は，新生児調査結果より本調査結果の方がわずかに高かった．不均衡型再配列と常染色体トリソミーを比較した場合，逆の結果を示した．本調査対象者の被検時平均年齢は24歳であり，新生児調査の場合とは大いに異なるという点をここで強調する必要がある．トリソミーなどに関する異常を有する幼児の多くが，20～30年も生き延びる可能性はなく，当然のことながら本調査の平均年齢にまで達しないと思われる．

A question arises as to whether the F_1 cohort in this study truly reflected the entire population of offspring of A-bomb survivors. As mentioned earlier, we were able to obtain a high cooperation rate among the children of survivors, about 75% of them being in the "contact areas" of Hiroshima and Nagasaki. Nevertheless, since the final participation rate in this study was only 45% of the original sample, there was good reason to believe that some of the individuals with chromosome abnormalities could not participate in this survey due either to early death or to being institutionalized. Furthermore, because the cytogenetic survey was not begun until more than two decades after the A-bomb explosion and because of the age limitation for blood drawing (allowed at the age of 12 years or older), the data may not be considered valid for the occurrence of chromosome abnormalities associated with impaired phenotypes, such as autosomal trisomics and unbalanced autosomal structural rearrangements, which impose a high risk of early death. There should, however, be little or no selection against individuals with autosomal structural rearrangements of the balanced type. Thus, the mutation rate estimated for this type of abnormality is relevant for evaluating the genetic effects of A-bomb radiation.

Recently, attempts have been made to reevaluate cytogenetic surveys of neonates using banding techniques to obtain more precise information on the frequency of abnormalities associated with structural chromosomal changes in the general human population.[30–33] The results obtained in such studies are discordant. Some studies indicated an increase in the frequency of reciprocal translocations,[31] and inversions,[31,33] or an increase in the Q-band variants.[32] In contrast, the frequency of all types of chromosome abnormalities detected when G-banding techniques were used has been found to be similar to that observed previously when conventional staining preparations were used.[30] In our experience, there seemed to be no difference in the detectability of structural rearrangements between conventional stain and G- and Q-banding methods, although the latter were found to be more efficient in detecting heteromorphic variants than the conventional method.

Maeda et al[34] have reported the results of a cytogenetic survey on 2,626 consecutive liveborn infants in Japanese. They found 8 cases with sex chromosome abnormalities (0.30%) and 10 autosomal ab-

本調査の F_1 コホートが，原爆被爆者子孫の全集団を真に反映しているのか否かという疑問がある．前述のように，広島・長崎の「連絡可能地域」居住者の約75％が本調査に協力するという高い協力率を得ることができた．それにもかかわらず，本調査における最終的な参加率は原集団の45％にしかならなかったために，染色体異常保有者の中で早期死亡や施設入所などの理由により，本研究に参加できなかった者が存在することなどが十分に考えられる．更に，原爆被爆後20年以上も経ってから細胞遺伝学的調査が行われたこと，更に採血時年齢を12歳以上としたために，常染色体トリソミーや不均衡型構造再配列のような表現型異常を伴う染色体異常の場合には，早期死亡のリスクが高いため，かかる染色体異常発生率に関しては本研究からは有効な資料が求められない．しかし，均衡型常染色体構造再配列保有者に対する淘汰現象は，ほとんど，あるいは全く生じなかったと思われる．したがって，この種の異常について推定される突然変異率は，原爆放射線の遺伝学的影響の評価に用いることができる．

近年，一般的なヒト集団における染色体の構造変化に関連のある異常の頻度について，より正確な情報を得るために，新生児を対象として各種の分染法を用いて細胞遺伝学的調査の再評価が試みられている．[30–33] このような調査から得られた結果については一致がみられない．相互転座[31]や逆位[31,33]の頻度の増加，又はQバンド変異体の増加[32]を示す幾つかの調査結果がある．それとは対照的に，G分染法によって検出された全染色体異常頻度が，通常の染色法による以前の観察結果と同様であるという結果がある．[30] 我々の経験では，構造再配列の検出能に関して，通常の染色法とG若しくはQ分染法との間に差はないように思われた．ただし，後者の方が通常の方法より，異形性変異体の検出に関してはより有効であることが認められた．

前田ら[34]が，日本人の連続出生児2,626名に対する細胞遺伝学的調査結果を報告している．彼らは，8例（0.30％）の性染色体異常と10例の常染色体異常を認めた．10例の常染色体異常の内訳は，均衡型の

normalities, including 5 with Robertsonian translocation of the balanced type (0.19%), 1 with 13-trisomy associated with rob translocation (0.04%), 1 with a supernumerary marker (0.04%), and 3 with 21-trisomy (0.11%). Although the sample size of their survey was rather small, the results agreed to a certain extent with our findings with respect to the frequency of sex chromosome abnormalities and the types and patterns of autosomal abnormalities.

Disagreement does exist in regard to the possible association between maternal radiation and 21-trisomy.[35-37] In the A-bomb exposed population, Schull and Neel[35] have reported that the frequency of children with Down's syndrome born to exposed mothers (the fathers were not exposed) was 0.54 per 1,000 (3 in 5,579), and 1.27 per 1,000 (12 in 9,440) in children born to nonexposed mothers. These results suggest that no association exists between Down's syndrome and maternal radiation. Our results did not indicate an increase in children with 21-trisomy or aneuploidy involving any other chromosome.

ロバートソン型転座が5例（0.19%），ロバートソン型転座に伴う13番染色体トリソミーが1例（0.04%），過剰マーカー1例（0.04%），21番染色体トリソミー3例（0.11%）であった．彼らの調査の対象者数はかなり少ないが，性染色体異常の頻度及び常染色体異常の種類やパターンに関する結果は，我々の知見とかなりの程度の一致をみた．

母親被曝と21番染色体トリソミーとの関連性の可能性については，論議が別れている．[35-37] Schull と Neel[35] は，原爆放射線被曝者集団においてダウン症候群の子供が生まれる頻度は，母親が被曝者の場合（父親は非被曝者）1,000名当たり0.54例（5,579名中3例），母親が非被曝者の場合1,000名当たり1.27例（9,440名中，12例）であったと報告している．これらの結果は，ダウン症候群と母親の被曝との間には関連性がないことを示唆するものである．我々の結果では，21番染色体トリソミー，又は他の染色体が関与する異数体の子供の増加は示されなかった．

APPENDIX TABLE 1 LIST OF CHILDREN WITH CHROMOSOME ABNORMALITIES

付表1　染色体異常を有する子供の一覧表

Case No.	Sex	Age ATE	Year of birth	Age at birth Mo	Age at birth Fa	Exposure status	Type of abnormality	Remarks
			Hiroshima					
FH3321	M	28	1948	32	38	C	A1. 47,XYY	
FH4305	M	22	1956	30	38	C	〃 〃	
FH4998	M	29	1949	25	29	C	〃 〃	
FH7308	M	17	1964	28	32	C	〃 〃	
FH9913	M	15	1969	25	27	C	〃 〃	
FH0757	M	17	1953	26	34	Mo	A2. 47,XXY	
FH0801	M	22	1948	23	27	Fa	〃 〃	
FH0815	M	13	1957	31	48	B	〃 〃	
FH4223	M	22	1956	34	31	Mo	〃 〃	
FH4727	M	29	1949	33	38	Mo	〃 〃	
FH5953	M	26	1953	21	24	C	〃 〃	
FH6415	M	30	1950	32	40	C	〃 〃	
FH6662	M	28	1952	27	31	C	〃 〃	
FH8632	M	24	1958	24	28	Mo	〃 〃	
FH8718	M	33	1949	35	41	C	〃 〃	
FH8454	M	17	1965	25	30	Fa	A3. 46,XY/47,XYY	46:48 cells, 47:152 cells
FH6505	M	24	1956	32	38	C	A4. 46,X,inv(Y)(p11.2q11.2)	
FH7417	M	23	1958	33	31	C	〃 46,X,inv(Y)(p11.2q11.23)pat	Paternal origin
FH0492	F	21	1948	25	29	Fa	A6. 47,XXX	
FH1870	F	15	1957	34	33	B	〃 〃	
FH3886	F	30	1947	25	27	C	〃 〃	
FH5852	F	21	1958	30	36	Mo	〃 〃	
FH8291	F	24	1958	23	27	Fa	〃 〃	F_1:one (liveborn)
FH8912	F	16	1967	37	39	C	〃 〃	Sib (dizygotic co-twin)—normal
FH9339	F	15	1967	28	30	C	〃 〃	
FH0092	F	18	1949	33	36	B	A7. 45,X/47,XXX	45:95 cells, 47:4 cells
FH3033	F	22	1954	33	38	C	〃 〃	45:82 cells, 47:15 cells
FH8020	F	24	1957	24	28	C	〃 〃	45:44 cells, 47:49 cells. F2; one (liveborn), also pregnant at examination
FH8590	F	33	1948	25	38	C	〃 45,X/46,X,r(X)§	§*de novo* mutant. 45:141 cells, 46:59 cells

(Continued 続く)

ATE: At the time of examination. 被検時　Age at birth: Parental age. 出生時の親の年齢　Mo: Mother 母親　Fa: Father 父親
Exposure status: 被曝の有無　B=Both parents exposed 両親とも被曝　Fa=Father exposed 父親のみ被曝　Mo=Mother 母親のみ被曝　C=Control 対照群

APPENDIX TABLE 1 Continued 付表 1 続き

Case No.	Sex	Age ATE	Year of birth	Age at birth Mo	Age at birth Fa	Exposure status	Type of abnormality	Remarks
FH0381	M	18	1951	21	30	Fa	B1. 45,XY,t(DqDq)	
FH1988	F	16	1956	27	32	Mo	〃 45,XX,t(DqDq)	Sibs; inherited, origin unknown (ND)
FH2443	F	21	1952	23	28	Mo	〃 45,XX, 〃	
FH4989	M	28	1951	29	39	Mo	〃 45,XY,t(13q14q)	
FH6456	M	30	1949	24	27	C	〃 45,XY,t(13q14q)	
FH6664	F	29	1951	26	29	C	〃 45,XX, 〃	Sibs; inherited, origin unknown (ND)
FH6757	F	26	1954	29	32	C	〃 45,XX, 〃	
FH6538	F	30	1950	20	23	C	〃 45,XX,t(14q15q)	
FH8096	F	16	1966	30	35	Fa	〃 45,XX,t(13q14q)	
FH3496	F	22	1954	26	34	Mo	B2. 45,XX,t(14q21q)	
FH0405	F	18	1951	29	43	Fa	B3. 46,XX,t(5;11)(q13;p15)	
FH8076	M	33	1949	27	41	Fa	〃 46,XY, 〃	Sibs; inherited, origin unknown (ND)
FH2209	F	26	1947	34	36	B	〃 46,XX,t(5;17)(p13;q25)§	§*de novo* mutant
FH2210	F	26	1947	23	29	B	〃 46,XX,t(5;8)(q22;p11.2)pat	Paternal origin
FH2690	M	17	1957	23	27	Fa	〃 46,XY,t(5;8)(q22;p11.2)pat	Paternal origin
FH4493	M	29	1949	32	34	C	〃 46,XY,t(6;12)(q15;q22)	
FH4595	M	23	1955	27	30	C	〃 46,XY,t(1;6)(q21;p21)	
FH6611	F	29	1951	27	32	Mo	〃 46,XX,t(3;8)(q21;q24.1)	
FH6771	M	26	1954	30	35	Mo	〃 46,XY, 〃	Sibs; inherited, origin unknown (ND)
FH7342	F	32	1949	27	36	C	〃 46,XX,t(12;13)(q21.32;p12.3)§	§*de novo* mutant
FH9219	M	25	1957	25	31	C	B3. 46,XY,t(5;7)(q15;p21)pat	Paternal origin
FH9876	F	13	1970	29	30	C	〃 46,XX,t(5;8)(q22;p11.2)pat	Paternal origin
FH9922	M	13	1971	25	30	C	〃 46,XY,t(6;8)(q13;q22)	
FH1705	F	25	1946	34	35	C	B4. 46,XX,inv(2p+q−)	
FH5672	M	32	1947	27	32	C	〃 46,XY,inv(18)(p11.32q11.2)mat	Maternal origin
FH6099	M	27	1953	27	38	Mo	〃 46,XY,inv(2)(p11.2q13)	
FH7331	F	16	1964	27	33	C	〃 46,XX,inv(2)(p11.2q13)pat	
FH7333	F	14	1966	29	34	C	〃 46,XX, 〃	Sibs; inherited, origin unknown (ND)
FH9118	M	35	1948	39	45	C	〃 46,XY,inv(2)(p11.2q14.2)	
FH9254	M	34	1949	27	34	C	〃 46,XY,inv(5)(p15.3q13)	
FH7361	F	24	1957	24	25	Fa	B8. 47,XX,+mar*§ (*minute)	§*de novo* mutant. F_2:one (liveborn)
FH6169	F	23	1956	28	28	Mo	B9. 46,XX/47,XX,+mar* (*minute)	46:9 cells, 47:91 cells
FH8980	M	14	1969	25	28	Fa	〃 46,XY,del(18)(p11.1)/46,XY,i(18q)	del(18p):181 cells, i(18q):7 cells (ND)
FH7594	M	15	1966	25	25	Fa	C1. 47,XY,+21§	§*de novo* mutant

(Continued 続く)

APPENDIX TABLE 1 Continued 付表1 続き

Case No.	Sex	Age ATE	Year of birth	Age at birth Mo	Age at birth Fa	Exposure status	Type of abnormality	Remarks
			Nagasaki					
FN0217	M	13	1956	37	33	Mo	A1. 47,XYY	
FN0486	M	21	1948	30	35	Fa	" "	
FN0970	M	19	1951	26	28	Fa	" "	
FN1717	M	26	1948	31	39	C	A2. 47,XXY	
FN2696	M	18	1957	27	27	C	" "	
FN4025	M	30	1948	27	31	Mo	" "	
FN4171	M	25	1953	22	19	C	" "	
FN4317	M	28	1951	40	45	C	" "	
FN6865	M	14	1970	25	29	C	" "	
FN3338	M	21	1956	25	30	Mo	A4. 46,XX	XX male (ND)
FN3252	F	22	1955	24	27	Fa	A6. 47,XXX	
FN4237	F	31	1947	20	24	C	" "	
FN2120	F	18	1956	26	24	Mo	A7. 46,XX/47,XXX	46:3 cells, 47:96 cells
FN3202	F	21	1956	33	37	C	A8. 46,XXq−	
FN4935	F	32	1948	32	46	C	B1. 45,XX,t(13q14q)pat	Sibs; paternal origin
FN4936	F	28	1952	36	50	C	" 45,XX, "	
FN5837	M	13	1969	32	34	Fa	" 45,XY,t(13q14q)pat	Sibs; paternal origin
FN5859	F	17	1965	29	31	Fa	" 45,XX, "	
FN0870	M	18	1952	23	31	B	B2. 45,XY,t(DqGq)	
FN6530	F	14	1969	29	36	Fa	" 45,XX,t(14q21q)	
FN1638	M	24	1950	21	22	C	B3. 46,XY,t(Cq−;17q+)pat	Paternal origin
FN3068	F	28	1948	40	44	C	" 46,XX,t(18q+;20q−)	
FN3948	M	21	1957	33	41	C	" 46,XY,t(1p−;12q+)mat	Maternal origin
FN4419	F	32	1947	22	28	C	" 46,XX,t(2p−;8p+)	Sibs; inherited, origin unknown (ND)
FN4891	F	31	1949	24	30	C	" 46,XX, "	
FN4724	M	29	1951	24	29	C	" 46,XY,t(Bq−;Cq+)pat	Paternal origin
FN5049	F	29	1951	28	35	C	" 46,XX,t(2q−;13q+)	
FN2357	F	26	1949	23	46	Fa	B8. 47,XX,+mar* mat (*minute)	Maternal origin
FN3990	M	22	1957	40	37	C	B9. 46,XY/47,XY,+mar*§ (*minute)	§*de novo* mutant. 46:18 cells, 47:31 cells
FN4121	M	30	1948	20	29	Mo	" 46,XY/47,XY,+mar*§ (*minute)	§*de novo* mutant. 46:21 cells, 47:9 cells
FN6023	M	31	1951	23	24	C	" 46,XY/47,XY,+mar/48,XY,+mar x2§	§*de novo* mutant. Complex mosaic consisting of cell lines with 2 or 3 different minute markers of varying combinations.

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