TECHNICAL REPORT
18-73
業 績 報 告 書

LATE EFFECTS IN CHILDREN EXPOSED TO THE ATOMIC BOMB WHILE IN UTERO

胎 内 被 爆 者 の 晩 発 障 害

HIROO KATO, M.D., M.P.H. 加藤寛夫

ABCC JNIH

ATOMIC BOMB CASUALTY COMMISSION

国立予防衛生研究所－原爆傷害調査委員会

JAPANESE NATIONAL INSTITUTE OF HEALTH OF THE MINISTRY OF HEALTH AND WELFARE

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LATE EFFECTS IN CHILDREN EXPOSED TO THE ATOMIC BOMB WHILE IN UTERO

胎内被爆者の晩発障害

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SUMMARY

A brief review was made of the findings of studies conducted to date at ABCC on the late effects observed in children exposed to the atomic bomb while in utero.

Radiation effects noted to date in children heavily exposed in utero include: (1) delay of growth and development including height and increased frequency of microcephaly; (2) increased mortality, especially infant mortality; (3) temporary supression of antibody production against influenza; and (4) an increase in the frequency of chromosomal aberration in peripheral lymphocytes. However, there has been no increase observed to date in the incidence of leukemia and cancers. Furthermore, no effect on reproductive potential nor on the sex ratio of their offspring was noted.

However, very careful and long-range follow-up observation should be continued since the in utero exposed subjects have recently reached the reproductive and cancer age.

INTRODUCTION

ABCC in collaboration with JNIH is conducting a long-term follow-up on fixed populations of atomic bomb survivors for late effects of A-bomb radiation. As shown in Figure 1, a sample of approximately 110,000 persons has been followed since 1950 in a mortality study of A-bomb survivors, and pathology studies are being made on autopsies obtained for deaths occurring in this sample (autopsy rate 20%-40%). Further, the ABCC-JNIH Adult Health

要 約

胎内被爆児に対する原爆放射線の影響について現在までにABCCで行なわれた研究業績について簡単なreviewを行なった.

現在までに原爆放射線の影響としては(1)身長・頭囲などの成長発育の遅延および小頭症の頻度の増加,(2)死亡率,特に乳児死亡率の増加,(3)インフルエンザ抗体産生能力の一時的低下,(4)末梢血リンパ球の染色体異常の頻度の増加,が強度の放射線胎内被曝児にみられる.しかし,白血病および癌の発生率の増加は現在までのところみられない.また,生殖能力およびその子供の性比の影響も認められない.

なお,胎内被爆児はこれから生殖年齢,癌年齢に達してくるので,今後長期にわたり,注意深いfollow-upが必要であろう.

緒 言

ABCCでは国立予防衛生研究所と共同で,原爆放射線の後影響を調べるために,被爆者の固定集団について長期間の追跡調査を行なっている.図1に示したように被爆者については約11万人を対象として1950年から死亡調査を行なっており,死亡者の剖検例(剖検率20%—40%)について病理学的調査をしている.またこの調査対象のうち2万人のsubsampleについて成人健康調査(2年に1回

Study, a program of detailed biennial examinations on a subsample of 20,000 members from this population was begun in 1958, and is presently in the 8th cycle of examinations. A brief summary of the main findings obtained to date on A-bomb survivors follows:

(1) The increased incidence of leukemia among A-bomb survivors is well known, and although the risk of leukemia has decreased with the lapse of time since the peak in around 1950-52, it is still higher in the group exposed to high doses of 200 rad or more as compared with the controls.

(2) The risk of cancers other than leukemia has shown an increase since about 1960-65. To date, an increased risk has been demonstrated for cancers of the thyroid, lung, breast, and salivary gland; and

(3) Except for cataracts, no disease besides leukemia or other cancers has been noted to be particularly related to A-bomb radiation, and there is in general no definite evidence of accelerated aging due to radiation.

Studies of in utero exposed children are also in progress. A fixed population of 2600 subjects is being followed for deaths as shown in Figure 1, and in addition, a program of detailed clinical examinations has been conducted. These are described in detail later. Children born to A-bomb survivors also are being investigated, and in addition to the mortality study on a fixed population of some 53,000 children born to A-bomb survivors, various genetic studies have been made, but so far no apparent genetic effects due to A-bomb radiation have been found. Among the various effects that A-bomb radiation have on man, this report deals specifically with the details of those in children exposed to the bomb while in utero.

STUDY SAMPLE

Children born to A-bomb survivors during a period of approximately 10 months after the bomb (August 1945 - May 1946) were defined as children exposed in utero. For the establishment of the study sample, ABCC investigators made field surveys on all children born in Hiroshima or Nagasaki City between August 1945 and May 1946, based on information from birth reports, to investigate the exposure status of thier parents, particularly their mother. All children proximally exposed in utero within 2000 m from the hypocenter were included in the study sample, and comparison groups with equal numbers of children as the proximal group were drawn at random from among those exposed in utero at greater distances and

の精密検診）を1958年に始めており，現在第８回目の検診を実施中である．被爆者についての現在までの主要な知見を簡単に要約すると，

(1) 被爆者に白血病の発生率が高いことはよく知られており，白血病発生の risk は1950－52年ごろを頂点として，年とともに減少はしているが，200 rad 以上の高線量を受けた群では現在でもまだ対照に比べて risk は高い．

(2) 白血病以外の癌の発生の risk は1960－65年ごろから高くなりつつあり，現在までに甲状腺癌，肺癌，乳癌，唾液腺癌の発生の risk が高いことが認められている．

(3) 白血病および癌以外の疾患で白内障以外は特に原爆放射線と関連のある疾患は認められず，放射線による加齢現象の促進も一般的には明らかでない．

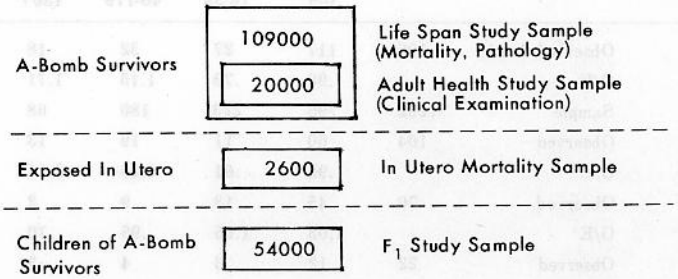
胎内被爆児については図１に示したように2600人の固定集団について死亡の追跡を行なっている．またこれとは別に精密検診も行なわれていたが，詳細については後述する．また被爆者の子供については約53,000人の固定集団について死亡調査の他，種々な遺伝学的調査を行なっているが，現在までのところ原爆放射線による遺伝的影響は認められない．このような原爆放射線の人体に及ぼす影響のうち今回は特に胎内被爆児について詳細に述べる．

調査対象

被爆後約10ヵ月間（1945年８月－1946年５月）に被爆者から生れた子供を胎内被爆児とした．調査対象を設定するために出生届を基にして，1945年８月－1946年５月に広島市または長崎市で生まれた子供の全数について，ABCC の調査員が野外調査によって両親特に母親の被爆状態を調べた．爆心地から2000ｍ以内で被爆した至近距離胎内被爆児の全員と，対照として遠距離胎内被爆児と非被爆者（被爆当時広島市または長崎市にいなかった者）からそれぞれ至近距離胎内被爆児と同数を random に選んで調

FIGURE 1 SAMPLE FOR THE STUDY

図1　調査対象群



those not exposed (not in Hiroshima City or Nagasaki City at the time of the bombs). A supplementary source of cases was the in utero exposed children born outside the city and seen at ABCC in the clinical medical program. The sample for the mortality study totals 2600 subjects as shown in Figure 1. Apart from this, ABCC had conducted since around 1952 a clinical medical study on in utero exposed children selected from various sources. Annual detailed examinations were made, particularly through the ages of 10 to 19 years. Approximately half of the subjects in the aforementioned mortality study sample were also included in the sample of this clinical medical study.

MORTALITY

An analysis limited to those in utero exposed children enumerated from birth records among the aforementioned 2600 subjects of the In Utero Mortality Study sample has been made.[1] The nonexposed children were excluded since a previous preliminary study had shown that the distribution of concominant socioeconomic factors which tend to markedly influence mortality, particularly infant mortality, differed between the in utero exposed and nonexposed children, but not between the various distance groups of in utero exposed children. The number of subjects in the analysis was 1073 in Hiroshima and 219 in Nagasaki. Ascertainment of death was considered to have been virtually complete through check of the koseki. In the event of death, the cause of death was transcribed from the vital statistics death schedule.

査対象とした．また市外で生まれた胎内被爆児でABCCの臨床調査にきた者などを補助的に調査対象に加え，図1に示したように合計2600名の調査対象について死亡調査を行なっている．これとは別にABCCでは種々な資料から胎内被爆児を選んで1952年ごろから臨床検査を行なっており，特に10歳から19歳まで毎年1回精密検診を行なってきた．前述の死亡調査対象のうち，約½はこの臨床調査の対象にもなっている．

死亡率

前述の胎内被爆児の死亡調査の対象2600名のうち出生届けのあるものに限定し，しかもこれまでの予備的調査の結果，原爆放射線以外に死亡，特に乳児死亡に強く影響する社会経済的要因などが，胎内被爆児と非被爆児との間には差があるが，胎内被爆児の間では被爆距離によってそのような要因の分布に差がないことが分かっているので，解析は非被爆児を除いて胎内被爆児に限定して行なった.[1] 解析に用いた対象数は広島1073名，長崎219名である．死亡の確認には戸籍を調べているので死亡の洩れはほとんどないと考えられる．死亡している場合には人口動態死亡票から死因を転記した．

TABLE 1 MORTALITY OF IN UTERO EXPOSED CHILDREN BY RADIATION DOSE AND AGE AT DEATH, 1945-69

表1　胎内被爆児の死亡率：被曝線量および死亡時年齢別，1945－69年

Age at death	Statistic	Total	Dose (rad)				
			0-9	10-39	40-179	180+	Unknown
All ages	Observed death	196	117	27	32	18	2
	O/E		.98	.79	1.15	1.71	.52
	Sample	1292	795	223	180	68	26
Under 1	Observed	104	60	11	19	13	1
	O/E		.95	.61	1.26	2.14	.52
1-9	Observed	70	45	13	9	2	1
	O/E		1.03	1.05	.95	.70	.68
10+	Observed	22	12	3	4	3	0
	O/E		.89	.74	1.45	2.89	-

A total of 196 deaths was found during the period to December 1969. These subjects were divided, as shown in Table 1, into four groups by the dose received by their mothers, and the expected number of deaths, standardized for sex and age, was calculated based on the assumption that there is no difference in mortality by dose. The ratio of observed to expected deaths represents, therefore, a kind of relative risk. As shown in Table 1, the mortality increased with dose throughout the entire study period from 1945 to 1969. This increase in mortality with increasing dose is marked in infants under 1 year of age, but is not observed at ages 1 to 9, and is again observed at ages 10 and over. Analysis of mortality by cause of death showed no cause to be particularly increased, except for perinatal deaths. There was only one death due to leukemia and two deaths from neoplasms other than leukemia. This is very close to the mortality for all Japan, and shows no relation to maternal exposure dose.

By trimester of gestation at time of exposure, there is, as shown in Table 2, a remarkable increase in mortality with dose only in the group exposed to A-bomb radiation in the third trimester in utero.

It might have been expected from the viewpoint of radiation biology that radiation effects on mortality, if any, would appear more strongly among those exposed in the early stage of gestation. Actually, however, the effects are stronger in the third trimester (Table 2). The following two major reasons can be considered for this. First, this may have been due to the process of selection, resulting from the high rates of spontaneous abortions and stillbirths following exposure of fetuses at early developmental stages. Second, the body of the mother provided shielding, and it is possible that the penetration

1969年12月までに196名の死亡者が確認されたが，これを表1に示すように母親の被曝線量によって4群に分けて，被曝線量によって死亡率に差がないと仮定した場合の性，年齢訂正期待死亡数を計算した．したがって観察死亡数と期待死亡数の比は一種の relative risk を表わしている．表1に示したように，1945－69年までの全調査期間の死亡率は被曝線量が増加するにつれて高くなっている．この被曝線量の増加に伴う死亡率の上昇は1歳未満の乳児死亡率に顕著にみられるが，その後1－9歳時ではみられず，ついで10歳以上に達した後再びみられる．死亡原因別では周産期死亡を除いては特に増加のみられた死因はなく，白血病は1名のみ，また白血病以外の癌による死亡者は2名で，いずれも全国死亡率と同程度で母親の被曝線量との関連は認められない．

被爆時における母親の妊娠時期別にみると表2に示したように，被曝線量に伴う死亡率の増加は妊娠後期に被曝した群にのみ著明にみられる．

放射線生物学的には死亡に対して放射線の影響があるならば，妊娠前期に特に影響が強く表われてくることが期待されるが，実際には表2に示したように，むしろ妊娠後期に影響が強く表われている．その主な理由としては次の二つが考えられる．その第1は妊娠初期に胎児が放射線を受けた場合は，自然流産，死産の率が高く，それによる selection のためかもしれない．その第2は，母体が放射線を遮蔽する役目をしているが，母体組織による

TABLE 2 MORTALITY OF IN UTERO EXPOSED CHILDREN BY RADIATION DOSE AND TRIMESTER, 1945-69

表2 胎内被爆児の死亡率：被曝線量および妊娠3か月期別，1945－69年

Trimester	Statistic	Total	Dose (rad)				
			0-9	10-39	40-179	180+	Unknown
I	Observed death	53	35	4	11	3	0
	O/E		1.05	.47	1.54	1.23	-
II	Observed	78	50	11	10	5	2
	O/E		1.09	.85	.79	1.09	1.15
III	Observed	65	32	12	11	10	0
	O/E		.79	.96	1.38	2.88	-

factor for maternal tissue differs by the trimester of gestation. A more definite answer must await progress in methodology of dosimetry.[12]

Mortality, especially infant mortality, can be strongly affected by factors other than radiation exposure, such as birth order, maternal age and socioeconomic conditions. Hence, infomation on these factors was obtained from birth records and from a mail questionnaire survey to see whether these factors were dissimilarly distributed among the dose groups. However, no differences were found in any of these factors except birth weight.

Accordingly, the increase in mortality with increasing maternal exposure dose is not due to these concomitant variables. An association between mortality and dose was seen again at ages 10 and over, but the number of cases is small so that further follow-up is needed to determine the association with causes of death and other factors.

LEUKEMIA AND CANCER

Of the 1292 children exposed to the bomb while in utero, there was one death from infantile cancer during the first 10 years of life. This is very close to the expected value of 0.75 calculated from the infant cancer mortality for all Japan (Table 3).[2]

Stewart et al reported a high incidence of infant cancer in children whose mothers received X-ray irradiation during pregnancy, and state that 572 extra deaths from cancer can be expected per million person-rad. In calculations using their value, there should be 36.9 deaths from cancer in this sample, but this is not consistent with the actual data. Further, only one death from leukemia was found during the first 24 years of life in this sample, and this is nearly the same as the average rate for all Japan. Thus, so far there has been no apparent tendency for cancer or leukemia to be increased in the children who were exposed to the bomb while in utero.

放射線量の透過係数が妊娠時期によって異なることが十分考えられるので，今後の線量の測定法の進歩をまたなければ，正確なことは分らないと考えられる.[12]

また死亡率特に乳児死亡率は被爆以外の他の因子，たとえば出生順位，母親の年齢，社会経済的因子などに強く影響されることが考えられる．そこで出生票，および郵送調査などからこれらの因子に関する情報を入手し，各被曝線量群間のこれらの因子の分布に差があるかないかを検討したが，出生時体重以外の因子では差は認められなかった.

したがって前述の母親の被曝線量に伴う死亡率の増加は，これらの付随因子によるものではない．また10歳以上の死亡率に再び線量との関係がみられたが，これについては例数も少ないので，今後さらに観察を続けて死因との関係などについて研究する必要があると考えられる.

白血病，癌

1292名の胎内被爆児のうち，生後10年以内に小児癌で死亡した者は1名で，日本全国の小児癌による死亡率から計算した期待値0.75名と非常によく一致している（表3）.[2]

Stewartらは母親が妊娠中にX線照射を受けた子供からの小児癌の発生が多く，Million person-rad 当たり572名の癌による過剰死亡数が期待されると述べている．その値を用いて計算してみると，このsampleでは36.9人の癌死亡者があることになるので実際のdataと一致しない．また白血病もこのsampleの中から出生後24年間に1名しかみられず，全国の平均値とほぼ同じ値を示している．このように現在までのところ胎内被爆児に癌または白血病が増加している傾向はみられない.

TABLE 3 OBSERVED AND EXPECTED DEATHS FROM CANCER IN 10 YEARS FOR IN UTERO EXPOSED CHILDREN

表3 胎内被爆児の生後10年間の癌による死亡の観察値と期待値

Maternal Dose (rad)	No. of Children	Maternal Person-rad	Cancer Deaths Under 10 Yr.		
			Observed	Japanese National Rates	Extra at 572 Per Million Person-rad
<1	551		0	0.32	-
1-39	467	5495	0	0.27	3.1
40-299	215	22699	1	0.12	13.0
300-499	17	6739	0	0.01	3.9
500+	16	29557	0	0.01	16.9
Unknown	26		0	0.02	-
Total	1292		1	0.75	36.9

On the other hand, however, the risk of leukemia and cancer has been found to be especially high among those A-bomb survivors who were exposed at younger ages of 20 and under.[3] In view of this fact, careful follow-up should be continued hereafter because the in utero exposed children are now 26 years old and will be entering the so-called cancer age.

しかし一方，被爆者の中では原爆時年齢が20歳以下の若年であったものに白血病および癌の発生のriskが特に高くなっている事実[3]を考慮すると，胎内被爆児は現在26歳でこれからいわゆる癌年齢になってくるので，今後注意深く観察を続ける必要がある．

GROWTH AND DEVELOPMENT

A medical sample of in utero exposed children were examined annually through the ages of 10 to 19. There was no remarkable increase in the frequency of diseases except for disturbances of growth and development such as small head circumference.

The frequency of small head circumference at examinations through 1956-65 (i.e., ages 10-19) and the number of persons who also had mental retardation are shown by maternal dose in Table 4.[4] Head circumference was defined to be small if, on one or more examinations, it was at least 2 standard deviations below the average for the age and sex of

成長発育

胎内被爆児の臨床調査対象について10－19歳時まで毎年精密検診が行なわれていたが，小頭症など成長発育に関する以外は特に注目すべき疾患の頻度の増加はみられない．

1956－65年すなわち，10歳から19歳の診察時における小頭症の頻度を母親の線量別に表4に示した．[4] なお( )内の数字は知能の遅滞を伴ったものの数である．小頭症の定義としては，少なくとも1回の診察で頭囲が同一の性・年齢の非被爆者群についての平均値よりも標準偏差の

TABLE 4 FREQUENCY OF SMALL HEAD CIRCUMFERENCE BY GESTATIONAL AGE AND EXPOSURE

表4 小頭症の頻度：妊娠時期および被曝線量別

Dose (rad)	Gestational Age							
	Hiroshima				Nagasaki			
	0-17 wks		18+		0-17		18+	
0-9	4(1)*/63	6%	4/65	6%	0/1	-%	0/9	-%
10-19	6(1)*/54	11	0/44	-	0/7	-	0/6	-
20-29	6/24	25	1/14	7	0/5	-	2/7	29
30-39	4/8	50	0/10	-	2/4	50	0/6	-
40-49	3/11	27	0/6	-	0/6	-	0/3	-
50-99	9(2)*/20	45	2/24	8	0/9	-	0/11	-
100-149	2/4	50	0/10	-	0/2	-	1/5	20
150+	5(5)*/13	38	1(1)*/8	13	8(3)*/9	89	2(1)*/9	22

** Also had mental retardation*

the subject, and was on all previous and subsequent examinations at least 1 standard deviation below the average. Mental retardation was judged by clinical examination and history, and was diagnosed only if so severe that the subject was unable to perform simple functions.

Although the number of cases is small, the subjects were separated by city and by gestational age at the time of the bomb, that is, whether under or over 18 weeks of gestation, and especially marked effects are seen in the group exposed at under 18 weeks of gestation in both Hiroshima and Nagasaki. The Hiroshima data show an excess in the frequency of small head circumference even in the group whose mothers were exposed to comparatively small doses of 10-19 rad. On the other hand, in Nagasaki an excess becomes apparent from the group exposed to 150 rad or more. In both Hiroshima and Nagasaki, many cases in the group exposed to high doses of 150 rad or more also had mental retardation. Particularly, in Hiroshima, all cases with small head circumference in this dose group had mental retardation. Radiation apparently causes general cell depletion of the brain in the developing fetus, with secondary small head circumference. When depletion is great enough, mental retardation occurs. With less depletion intelligence is within normal range.

The difference in the dose effect between Hiroshima and Nagasaki may be ascribed to the following two reasons. First, the quality of radiation differed in the two cities. That is, aside from gamma rays, neutrons accounted for more of the radiation in Hiroshima than in Nagasaki. Moreover, the biological effectiveness of neutrons is greater than that of gamma rays. In other words, the difference between the two cities may have occurred because the RBE is greater than 1. Second, although many other factors besides radiation can affect the growth of children, such as malnutrition or severe illness, one can easily imagine that factors accompanying the socioeconomic confusion immediately after the bombs would have had greater effect in Hiroshima because the bomb was dropped in the center of the city in Hiroshima, whereas it was in the suburban valley of Urakami in Nagasaki. The effects of low dose in the in utero exposed children of Hiroshima seen in these data may not be directly applicable to medical irradiation of mothers during pregnancy. This is because in A-bomb exposure the neutron influence mentioned earlier cannot be excluded and the influence of environmental destruction may have been present.

Due to the small number of cases, estimation of the RBE of neutrons is difficult from these data, but the

2倍以上小さい場合，またはすべての診察で標準偏差以上小さい場合を小頭症と定義した．また知能遅滞は検診および病歴調査に基づいて判定し，単純な行動が果たされないなど重篤であった場合にのみ知能遅滞とみなした．

例数は少ないが広島・長崎別に，また母親の被爆時の妊娠時期によって18週未満と18週以上に分けてみると，広島・長崎とも18週未満の時期に被爆した群に特に顕著な影響がみられ，広島では母親の被曝線量が10—19 radの比較的少ない線量を受けた群でも小頭症の頻度の増加がみられる．これに反して長崎では150 rad以上の高線量を受けた群で初めて小頭症の頻度の増加がみられる．また広島・長崎とも150 rad以上の高線量を受けた群で知能遅滞を伴う例が多く，特に広島ではこの線量群の小頭症の全例が知能遅滞を伴っている．つまり放射線は発育中の胎児に対して，一般に脳の細胞の減少をもたらし二次的に小頭症を起こしており，その際細胞の減少が強い場合に知能遅滞がみられるが，細胞の減少が少ない場合には知能は正常範囲内にとどまるものと考えられている．

広島と長崎とで線量効果に差があることには次の二つの理由が考えられる．その第1は広島と長崎における原爆放射線の線質に差があることである．すなわちγ線以外に広島では長崎よりも中性子が多く含まれており，しかも中性子の方がγ線よりも生物学的効果が強い．すなわちRBEが1より大きいためにこのように両市で差が出てきたものと考えられる．その第2は子供の発育に影響を及ぼす因子としては放射線以外に栄養・重篤な疾病など他の多くの要因が考えられるが，原爆は広島の場合には市の中心部に落とされ，長崎では浦上の一つの谷間に落とされたために，被爆直後の社会経済状態の混乱に伴うこうした要因は，広島の方により大きく影響したであろうことは容易に想像できる．したがって，このdataの示す広島の胎内被爆児に認められた低線量の影響は，医療用放射線を母親が妊娠中に受けた場合には直接適用できない．それは原爆被爆の場合は，前述のように中性子の影響もあり得るし，また被爆直後の環境の破壊による影響も考えられるからである．

なおこの例の場合には例数が少なく，このdataから中性子のRBEの値を推定することは困難であるが，原爆被爆

estimated RBE of neutrons for leukemia and malignancies other than leukemia has been suggested to be approximately in the neighborhood of 5 in A-bomb survivors.[3]

Next, the relationship between frequency of mental retardation in the in utero exposed children and exposure dose will be described.[5] In this case, a child was judged mentally retarded only if he was unable to perform simple calculation, to make conversation, to care for himself, or if he had been institutionalized. The frequency of mental retardation is shown by dose in Table 5. The frequency of mental retardation among the various dose groups was examined using the proportion to cases with mental retardation (0.6%) among 830 Hiroshima children and 246 Nagasaki children in the nonexposed and distal group, and it was found that the risk is increased at doses of over 50 rad in Hiroshima. In Nagasaki, on the other hand, an elevation in risk becomes apparent from the high dose group exposed to 200 rad or more.

者における白血病，および白血病以外の悪性腫瘍の場合の中性子のRBEの推定値としてはおおよそ5に近い値であると考えられている.[3]

次に，胎内被爆児における知能遅滞に示したものの頻度と被曝線量との関係について述べる.[5] この場合の知能遅滞の定義は簡単な計算や会話ができないもの，身の回りのことが自分でできないもの，また施設に収容された者に限定した．知能遅滞の頻度を線量別に表5に示した．非被爆者および遠距離胎内被爆児，広島830名，長崎246名中の知能遅滞の割合（0.6%）を基準として，各線量群中の知能遅滞の頻度をみると，広島では50 rad以上の群からriskの上昇がみられる．これに反して長崎では200 rad以上の高線量群で初めてriskの上昇がみられる．

TABLE 5 PROPORTIONS OF CASES OF MENTAL RETARDATION BY GESTATIONAL AGE AND EXPOSURE

表5 知能遅滞例の割合：妊娠時期および被曝線量別

Dose (rad)	Gestational Age							
	Hiroshima*				Nagasaki			
	<15		15+		<15		15+	
0-9	1/36	3%	2(1)*/109	2%	0/1	-%	0/10	-%
10-49	2(1)*/64	3	0/125	-	0/16	-	0/29	-
50-99	3(1)*/16	19	0/31	-	0/3	-	0/17	-
100-199	3(1)*/11	27	1/18	6	0/3	-	0/10	-
200-299	2/4	50	1/4	25	1(1)*/2	50	0/3	-
300+	2/2	100	0/4	-	1/3	33	2/4	50

**Mental retardation apparently not due to in utero exposure*

Further examination by gestational age under or over 15 weeks clearly shows, though the number of cases is small, a greater effect at under 15 weeks of gestation.

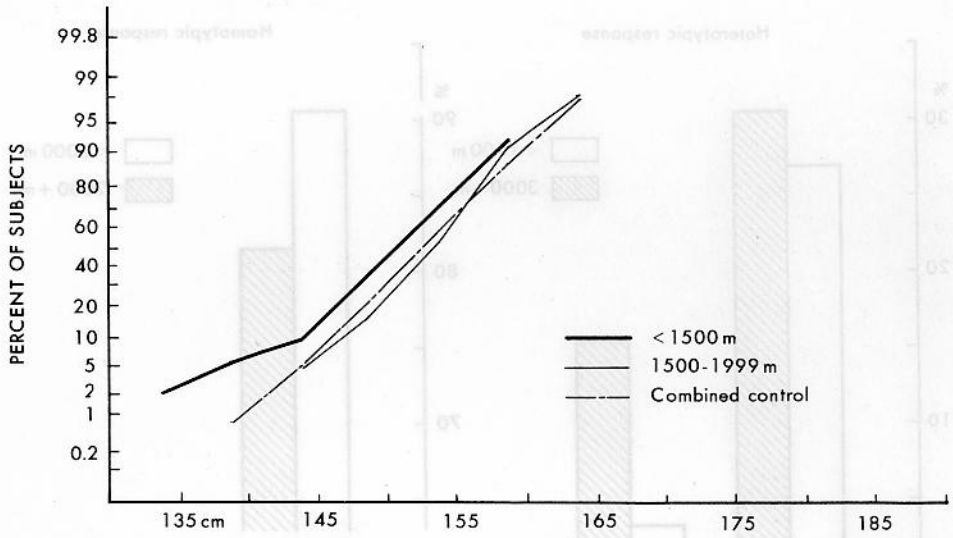
これをさらに妊娠時期別に15週以前と以後に分けてみると，例数は少ないが15週以前の方により影響が明らかにみられる．

The development status in height and weight will be described next. The cumulative percentages of height of the in utero exposed children of Hiroshima at age 17 years have been plotted on normal probability paper by dose in Figure 2.[6] The standing height measurements of the proximal exposed in utero subjects are distributed in the lower range as compared with the controls. The results of measurements at age 10 years likewise had shown lower values for these subjects than for the controls. However, neither the difference in the measurements between ages 10 to 17 for the same subject (i.e., the absolute value of the development attained in 7 years) nor the annual optimal growth rate show any relation to exposure distance. That is, a child exposed

次に身長，体重の発育状態について述べる．広島における胎内被爆児の17歳時の身長の累積百分率を正規確率紙の上に被爆距離別に示した（図2）が，至近距離胎内被爆児は対照に比べて身長が低い方に分布している.[6] また10歳の時に測定した結果も同様に，至近距離胎内被爆児は対照に比べて低い値を示している．しかし同一人についての10歳と17歳の測定値の差，すなわち7年間の発育した絶対値そのもの，および年間最大成長率をみても，被爆距離との関係はみられない．すなわち至近距離被爆児は10歳の時にすでに対照に比べて小さいが，その後7年

FIGURE 2 STANDING HEIGHT AT 17 YEARS OF AGE BY EXPOSURE DISTANCE, FEMALE

図2　17歳時の身長：被爆距離別，女



proximally in utero is smaller than his control at the age of 10, but the rate of his growth in the subsequent 7 years is normal and shows no difference as compared with his control. Hence, the subject in consequence shows a lower value for height than his control at the age of 17 years when growth has been practically completed. However, since no systematic measurements were made before these subjects attained the age of 10, it is unknown at what age the difference in development by exposure status had occurred.

間の成長率は対照に比べてなんら変わりなく発育は正常であり，したがって17歳でのほとんど成長が終わった時点で，身長が対照に比べて低い値を示す結果になっている．しかしながら，10歳以前には Systematic な測定が行なわれていないので，何歳の時に被爆状態によって発育に差が出てきたかは分かっていない．

IMMUNE ANTIBODY

It has been demonstrated in animal experiments that there is a suppression of immune antibody production by irradiation. Studies have been made concerning influenza to determine the effects of radiation exposure on immune antibody production in children exposed to the atomic bomb while in utero.[7]

The antigenic composition of the strain of influenza A virus varies by time, the PR_8 and Weiss strains of Type A virus being prevalent before 1946, and FM_1 strain of Type A_1 virus between 1946 and 1956, and Type A_2 virus (Asian type) from 1957. Based on the doctrine of original antigenic sin proposed by Francis et al (i.e., the theory that man continues to

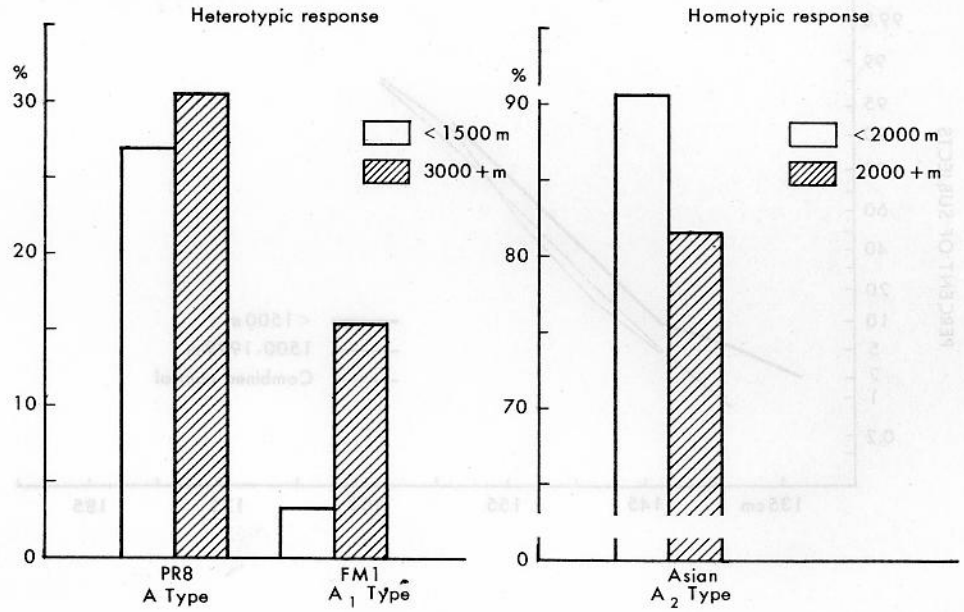
免疫抗体

動物実験では放射線照射によって免疫抗体の産生能力が抑制されることが知られている．胎内被爆児について，こうした免疫抗体の産生能力が阻害されたかどうかを調べるために influenza について調査がなされた．[7]

Influenza A 型の中でも strain の抗原構造が時とともに変わり，A 型（PR_8 株，Weiss 株）が1946年以前，A 1 型（FM_1 株）が1946—56年，次いで A 2 型（Asia 型）が1957年以降，というように抗原構造が変わってきている．Francis らの提唱している抗原原罪説，すなわち，人間は生まれ

FIGURE 3 ANTIBODY RESPONSE FOLLOWING ASIAN INFLUENZA VACCINATION

図3　Asia 型インフルエンザワクチン接種後の抗体反応



harbor antibodies against the virus of primary infection) an attempt was made to determine how high the antibody level was to Type A1 virus (FM1 strain), which had been the virus of primary infection in the in utero exposed subjects, by inoculation with Type A2 virus vaccine, that is, a heterotypic antigenic stimulation. As shown in Figure 3, the antibody response to Type A1 virus (FM1 strain), the virus of primary infection, is lower in the proximally exposed in utero subjects than in the controls. However, the antibody production against Type A2 virus does not differ significantly by exposure distance. That is, although antibody production against influenza may have been temporarily suppressed in the proximally exposed in utero subjects, it is apparent that, after the lapse of some 10 years following exposure, the antibody production has completely recovered with no difference from the controls.

CHROMOSOMAL ABERRATIONS

The frequency of chromosomal aberrations found in the peripheral lymphocytes of in utero exposed subjects is shown in Table 6.[8] Examination of 100 lymphocytes of each subject had been made. Comparison of the group exposed to moderate doses (24-85 rad) and the group exposed to high doses (104-477 rad) with the control group (nonexposed

て最初に感染した Virus に対する抗体をその後もずっと持ち続けるという説を利用して，胎内被爆児について A 2 型株に対する Vaccine すなわち，異種の抗原刺激を与えることによって，初感染 Virus である A 1 型（FM_1株）に対する抗体の上昇の程度を測定しようと試みた．図3に示したように，初感染 Virus である A 1 型（FM_1株）に対する抗体は，至近距離被爆胎児の方が Control に比べて response が低い．しかし A 2 型に対する抗体の産生状態は被爆距離によって差はない．すなわち，至近距離被爆児では influenza 抗体の産生能力が被爆後一時的に抑制されていたが，被爆後約10年を経てすっかり回復して対照と差異がなくなったということがいえる．

染色体異常

胎内被爆児について末梢リンパ球にみられた染色体異常の頻度を表6に示した．[8]　1人について100個のリンパ細胞について測定した．被曝線量によって中等度の線量（24－85 rad）を受けた群と，高線量（104 － 477 rad）を受けた群に分け対照群（非被爆群）と比較してみると，染

TABLE 6 CYTOGENETIC FINDINGS AMONG THE IN UTERO EXPOSED CHILDREN

表6 胎内被爆児における細胞遺伝学的所見

	Estimated Dose (rad)	Survivors	Total Cells Examined	Survivors with Aberrant Cells*	No. of Aberrant Cells*
Control	-	48	4678	2(4%)	2(0.04%)
Exposed	24-85	20	2000	3(15%)	3(0.15%)
	104-477	38	3643	15(39%)	19(0.52%)

*Including dicentrics, rings, fragments, and translocations.

group) revealed that the frequency of subjects with chromosomal aberrations (dicentrics, rings, fragments, translocations) increased with dose as compared with the rate of 4% in the control group. The frequency of cells with chromosomal aberrations was likewise increased in the higher dose group as compared with the frequency of 0.04% in the control group. Thus, although they have no clinical abnormalities, some in utero exposed subjects show abnormalities at the level of chromosomes in somatic cells. However, the clinical significance of this finding is unknown.

色体異常(dicentric, rings, fragments, translocation)を示すものの頻度は，対照群の4%に比較して線量が多くなるにつれて高くなっている．また染色体異常を示す細胞の頻度についてみても同様に，対照群の0.04%に比べて高線量の群では頻度が高くなっている．このように臨床的には異常はないが，体細胞の染色体levelでは異常を示すものが胎内被爆児にある．しかし，この臨床的な意味は不明である．

REPRODUCTIVE POTENTIAL AND EFFECTS IN THE OFFSPRING

生殖能力およびその子供に現われる影響

In animal experiments sterility has been observed among male mice exposed to radiation during fetal life, and total sterility (all animals incapable of reproduction) has occurred after doses of 600 rad or more.

動物実験では胎仔期に放射線に被曝した雄マウスに不妊がみられ，600 rad以上の線量では完全不妊(まったく子供ができない)がみられている．

Persons exposed in utero to the A-bomb in Hiroshima and Nagasaki have now reached the ages of 26-27 years, so that a study could be made to determine whether such effects are present or not.

広島，長崎の胎内被爆児も現在26－27歳に達しているので，このような影響があるかどうかをみる必要がある．

The marital status of the subjects in the mortality study sample described earlier and the sex ratio of their offspring[9] are shown in Table 7. Approximately 15% of males and 45% of females are married, and 4%-8% of males and 20%-30% of females in the groups exposed to 10 rad or more have children. There is no total sterility in the 10 rad or over groups, for children have been born to even those exposed to high doses of 100-199 rad, 200-599 rad, and 600 rad or more.[10] However, further observations should be made because data are still insufficient to evaluate whether or not there is any difference in the frequency of sterility by exposure dose.

前述の死亡調査対象について，結婚状態およびその子供のsex ratio（性比）を表7に示した．[9] 男の約15%，女の約45%が結婚しており，10 rad以上の被曝線量を受けた群でも男の4%－8%，女の20%－30%は子供がある．10 rad以上の群のうちさらに100－199 rad，200－599 rad，600 rad以上の高線量群においても子供が生まれており，完全不妊ということはない．[10] しかし不妊の頻度が被曝線量によって差があるかないかを調べるにはまだ資料が不足なので，さらに観察を続ける必要がある．

Meyer et al reported a higher rate of male births from mothers who received prenatal medical X-ray exposure within 30 weeks of gestation,[11] but there seems to be no difference in the sex ratio of offspring

またMeyerらは妊娠30週以内に母親の胎内で医療用X線照射を受けた女の子供には男が生まれる割合が多いことを報告しているが，[11] 女の胎内被爆児の場合には被曝線

TABLE 7 MARRIAGES AND OFFSPRING OF IN UTERO SAMPLE BY RADIATION DOSE AND GESTATIONAL AGE AT EXPOSURE

表7　胎内被爆対象群の結婚状態および子供：被曝線量および妊娠時期別

Sex	Statistics	Gestational Age					
		T65 Dose <10 rad			T65 Dose 10+ rad		
		0-14	15-26	27+	0-14	15-26	27+
Male	Number of Subjects	183	183	126	99	103	63
	Married %	13.7	18.6	17.5	8.1	12.6	12.7
	With Children %	7.1	11.5	10.3	4.0	6.8	7.9
	Children Male	8	15	11	2	8	2
	Female	8	10	6	3	1	3
Female	Number of Subjects	205	207	169	86	100	90
	Married %	45.9	45.9	43.8	31.4	41.0	52.2
	With Children %	24.9	24.2	21.3	20.9	23.0	31.1
	Children Male	28	32	22	14	11	18
	Female	30	25	19	9	15	15

of children born to pregnant mothers exposed to 10 rad or more as compared with those exposed to less than 10 rad (Table 7). That is, the in utero exposed children seem to show no change in reproductive potential nor any genetic effects as represented by sex ratio of their offspring. However, very careful observations should be continued since the subjects have only recently reached the reproductive age.

The above is a brief description of the findings obtained in studies made to date at ABCC on children exposed to the A-bomb while in utero.

量が10 rad 以上の場合も，それ未満の場合と比べて，生まれてきた子供の sex ratio には差はないようである（表7）．つまり，胎内被爆児についてはその生殖能力および遺伝的影響としての子供の sex ratio の変化は現在のところないようであるが，まだ対象は reproductive age に入って間もないので，今後も十分注意して観察を行なう必要があると考えられる．

以上，現在までに ABCC で行なわれた胎内被爆児についての調査結果について簡単に紹介した．

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