

MENTAL RETARDATION FOLLOWING IN UTERO EXPOSURE TO
THE ATOMIC BOMBS, HIROSHIMA AND NAGASAKI

広島および長崎における原爆胎内被爆後の知能遅滞

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SUMMARY

The prevalence of mental retardation by 17 years of age in children exposed in utero to the atomic bombs of Hiroshima and Nagasaki was examined in relation to the most recent estimation of radiation dose received. Significant increases at doses of over 50 rad in Hiroshima and 200 rad in Nagasaki were found, with the risk of mental retardation generally increasing with increasing dose. The lower dose-effect in Hiroshima may have been due to neutrons, which were virtually absent in Nagasaki.

INTRODUCTION

Studies by ABCC in Hiroshima and Nagasaki have shown an increased prevalence of mental retardation in persons prenatally exposed at close distances to the hypocenters of the atomic bombs of August 1945.¹⁻⁵ In 1954 a group of 169 Hiroshima children, a group at that time thought to comprise all children born of mothers pregnant at the time of the bomb (ATB) exposed within 2200m was examined. An inordinately heavy concentration of mental retardation (and small head circumference) was noted to occur in those who were exposed within 1200m during the 7th to 15th week of gestation.³ Since that time information on additional persons who were in utero ATB has been obtained and careful estimates of radiation dosage have been made.⁶ A fixed sample cohort of 1613 Hiroshima and Nagasaki individuals, roughly one-third of whom were within 2000m from the hypocenters, has been established. Studies within this expanded sample have confirmed the early findings of increased mental retardation for those exposed at close proximity.¹⁻⁵

Recently individual radiation dose (in rad) estimates, based on shielding configurations as well as distance, have been calculated for the mothers of

要約

広島・長崎における原子爆弾胎内被爆者が17歳に達するまでの間に認められた知能遅滞の頻度と最も新しい被曝放射線線量推定値との関係を検討した。広島では50 rad以上、長崎では200 rad以上の被曝線量で知能遅滞の有意な増加が認められ、一般にその頻度は被曝線量の増加につれて増大した。広島では低線量で影響が認められたが、これは長崎にはほとんどなかった中性子によるものかもしれない。

緒言

広島と長崎のABCCの調査により、1945年8月に爆心地近くで胎内被爆した者に知能遅滞の頻度の増加していることが認められた。¹⁻⁵ 広島において2200 m以内の距離で胎内被爆した者全員と思われる169名の調査を1954年に行なった。そのうち、原爆時に妊娠7-15週で1200 m以内の距離で被爆した母親の子供には知能遅滞(および小頭囲)が特に多く認められた。³ その後、他の胎内被爆児が確認され、個人の被曝線量推定値が入念に求められた。⁶ このようにして、広島・長崎合計で1613名からなる固定集団が設けられた。そのうち約3分の1は爆心地から2000 m以内の胎内被爆者であった。この拡大群を対象にした調査で、以前に認められた近距離の胎内被爆者における知能遅滞の増加が確認された。¹⁻⁵

最近この固定集団のほとんどの母親について、遮蔽状態および距離を加味した線量推定値(rad)が算定された。⁶

almost all members of the fixed sample.⁶ Utilizing these assigned doses, the purpose of the study reported herein was to examine the relation between mental retardation and radiation dose, with emphasis on establishing at which doses prevalence was increased and on determining whether higher doses yielded higher rates of retardation.

METHODS

The fixed sample cohort of 1613 Hiroshima and Nagasaki children in utero ATB consists of a group of persons proximally exposed (within 2000 m) to the atomic bomb matched by gestational age and sex with two "controls": a group distally exposed (3000-4999 m) and a group not in city (NIC) ATB.⁷ The children in this sample were scheduled for yearly clinical examinations from 10-19 years of age at ABCC (from 1956-65), as described elsewhere.⁴

The determination of mental retardation for members of the sample has been previously reported by Wood et al,⁵ who listed all cases of mental retardation discovered by 17 years of age, providing a discussion of the criteria used in the diagnoses. A child was judged mentally retarded only if he were "unable to perform simple calculations, to make conversation, to care for himself, or if he was completely unmanageable or had been institutionalized".⁵

In the present analysis percentages of mental retardation within groups of individuals classified according to radiation dose intervals were computed. These percentages were tested for significance against the percentages of mentally retarded children in the combined distal exposed and NIC control groups. Since the control groups were comprised of substantially larger numbers of persons, the control percentages were considered as essentially constant. The tests were then one-sample statistical tests of whether the various dose-group percentages differed significantly from this constant.

RESULTS

Thirty children in the in utero sample, 21 of whom were proximally exposed to the A-bomb were classified as mentally retarded by Wood et al.⁵ The distribution of these persons according to radiation dose-category is shown in Table 1. In parentheses are given the number of cases which appeared to be due to causes other than radiation exposure.

In all groups which received 50 rad or more in Hiroshima, mentally retarded children occurred in a

本調査の目的はこれらの推定線量値を用いて知能遅滞と線量との関係を調べることにあった。特に、どの線量域でその頻度が増加するか、また被曝線量値が高くなるにつれて知能遅滞の頻度が増加するか否かを究明することに重点を置いた。

方 法

本調査の対象は広島・長崎合計で1613名からなる固定集団である。この集団は近距離(2000 m以内)で胎内被爆した群と、これと原爆時の妊娠期・性別構成が一致する二つの「対照群」すなわち遠距離胎内被爆群(3000-4999 m)と原爆時市内にいなかった群とによって構成されている。⁷ 別に報告されたように、この集団の子供を10-19歳の間にABCCで毎年(1956-65年)検診した。⁴

この群における知能遅滞については、さきに Wood ら⁵ が報告したが、その報告には17歳に達するまでに認められたすべての知能遅滞例が記載され、用いた診断基準について考察が加えられている。簡単な計算や簡単な会話のできない者、身の回りのことが自分でできない者、全く扱いようのない者、または精神薄弱児童施設に収容された者にかぎり知能遅滞とみなした。⁵

本解析では、被曝線量別に分類した群における知能遅滞の発生率を計算した。この率を遠距離胎内被爆群と市内不在者群とを併せた対照群における知能遅滞の発生率と比較して有意差を検定した。対照群が多数で構成されているので、対照群における発生率は実質上、一定であった。そこで各線量群における発生率と対照群におけるそれとの間に有意差があるか否かを統計的に検定した。

結 果

Wood ら⁵ は、21名の近距離胎内被爆例が含まれている胎内被爆群のうち30名に知能遅滞を認めた。⁵ 表1に知能遅滞例を被曝線量別に示した。かっこの内は放射線以外の原因によると思われる例である。

広島において50 rad以上の線量を受けた群では非被爆群

TABLE 1 NUMBER OF CASES AND RELATIVE RISK OF MENTAL RETARDATION
ACCORDING TO DOSE CATEGORY

表1 線量別群にみた知能遅滞例とその相対的危険率

Dose	Hiroshima			Nagasaki		
	Sample	Cases*	Relative Risk†	Sample	Cases*	Relative Risk†
NIC, distal	830	5 (2)	1.0(1.0)	246	4(2)	1.0(1.0)
0-9 rad	145	3(1)	3.4(3.8)	11	0	-
10-49	189	2(1)	1.8(1.5)	45	0	-
50-99	47	3(1)	10.6(11.8)	20	0	-
100-199	29	4(1)	22.9(28.6)	13	0	-
200-299	8	3	62.3(104)	5	1(1)	12.3
300+	6	2	55.3(92.2)	7	3	26.4(52.7)

* Numbers in parentheses refer to persons (included in the totals), whose mental retardation was apparently due to causes other than intrauterine irradiation (see text for details).

かつこ内の数値は、胎内被爆以外の原因によると思われる知能遅滞例である(合計に含まれる)(委細は本文を参照)。

† Numbers in parentheses are relative risks after exclusion of persons with mental retardation due to causes other than irradiation.

かつこ内の数値は、胎内被爆以外の原因によると思われる知能遅滞例を除いて算定した相対的危険率である。

very significantly larger percentage than among the nonexposed in Hiroshima ($P < .01$). The percentage for the nonexposed (.006) was based on a sample of 830 children of whom 5 were mentally retarded—3 NIC and 2 distally exposed. In Nagasaki the difference in percentages approached statistical significance when the group exposed to 200-299 rad was compared with the nonexposed ($P < .10$). (The percentage for the control group was based on a sample of 246 children of whom 4 were mentally retarded—2 each in the NIC and distally exposed groups.) When the dose was very high, 300 rad or more, the excess of mental retardation in these cases as compared with controls was very significant ($P < .01$). The statistical significance continued to hold when cases apparently due to causes other than radiation were excluded from the analysis, except in the Nagasaki category, 200-299 rad, where the one case with mental retardation had von Recklinghausen's disease.

To guard against the possibility that the Hiroshima percentages for the control group might be lower than normal, the tests in Hiroshima were repeated using the 0-49 rad percentage of .015 (5/334) for comparison with the higher dose-category percentages. Again the percentages for all groups that received 50 rad or more were significantly larger ($P < .05$).

Also listed in Table 1 is the relative risk for mental retardation in each dose group; that is, the ratio of the percentage of mentally retarded individuals in a

に比較して有意に高率な知能遅滞がみられた($P < .01$). 非被爆群における発生率は.006であった。すなわち、830名の子供のうち知能遅滞は市内不在者に3名、遠距離胎内被爆者に2名、計5名に認められた。一方、長崎では200-299 rad被爆群と非被爆群とを比較した場合に統計的に有意な差が示唆された($P < .10$)。(対照群における発生率は246名によって構成されている群を用いて計算したが、知能遅滞は市内不在者群および遠距離被爆群にそれぞれ2名、計4名に認められた。) 300 rad以上の高線量群と対照群とを比較した場合、知能遅滞についてきわめて大きな有意差が認められた($P < .01$)。放射線以外の原因による者を解析から除外しても統計的有意性は存続した。ただし、長崎の200-299 rad群における1例の知能遅滞者には von Recklinghausen 病が認められた。

広島の対照群における発生率が一般より低いという可能性を除外するために、広島では0-49 rad群における発生率である.015 (5/334)を用いてあらためて高線量群と比較検定したが、やはり、50 rad以上の全群に有意な高率($P < .05$)を認めた。

表1に各線量群の知能遅滞の相対的危険率をも示した。すなわち、各線量群における知能遅滞発現率と非被爆群

dose category to the percentage in the nonexposed group. Values of relative risk were consistently greater than 10 for doses 50 rad or more in Hiroshima and doses 200 rad or more in Nagasaki. The relative risk of mental retardation surpassed 50 for the group that had received 200 rad or more in Hiroshima. The risks were generally increased when adjustment was made for those cases attributed to causes other than radiation. The adjusted risks are given in parentheses.

Mental retardation attributed to other causes may have been made worse by intrauterine radiation exposure. The diagnosis of other causes in Hiroshima were congenital jaundice (175 rad); two Down's syndrome (27 and 95 rad); Japanese B encephalitis (5 rad); Down's syndrome (NIC); and mental retardation in a sibling, suggesting a familial trait (distal exposed group). In Nagasaki the other causes were von Recklinghausen's disease (274 rad); congenital syphilis and difficult delivery (both cases in distal exposed group).

におけるそれとの比を相対的危険率とした。相対的危険率は広島では50 rad以上の群と、長崎では200 rad以上の群とにおいて10以上という高い値を示した。広島では200 rad以上の被曝群において相対的危険率は50を越えた。放射線以外のものに起因する例について補正を行なった場合、相対的危険率は一般に上昇した。補正後の相対的危険率をカッコ内に示した。

放射線以外の原因による知能遅滞も胎内被爆によっていっそう悪化させられたかもしれない。広島におけるその他の原因として診断されたものは、先天性黄疸1例(175 rad)、Down症候群2例(27 radおよび95 rad)、日本脳炎1例(5 rad)、Down症候群1例(市内不在者)および兄弟に知能遅滞が認められ遺伝が考えられる1例(遠距離胎内被爆者)、一方長崎では、他の原因として、von Recklinghausen病1例(274 rad)ならびに先天性梅毒および難産のそれぞれ1例(両者とも遠距離胎内被爆者)であった。

TABLE 2 PROPORTIONS OF CASES OF MENTAL RETARDATION ACCORDING TO GESTATIONAL AGE AND DOSE CATEGORY

表2 原爆時の妊娠期別および線量群別にみた知能遅滞例の割合

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

* Gestational age ATB was based on the date of conception, as estimated by subtracting 38 weeks from child's birth date, and adjusting for pre- or post-maturity.

原爆時の妊娠期間は、子供の誕生日より38週を引き、早産と遅産に対して補正を行なったうえ、推定した受胎日に基づいて算定した。

As noted by Wood et al⁵ the gestational age of those with mental retardation spanned the range 6-27 weeks with the concentration especially heavy in the first half of this gestational age period. In Table 2 are listed proportions of cases of mental retardation according to gestational age (adjusted for pre- or post-maturity) and dose. The proportions are expressed as the number of cases of retardation divided by the number of persons observed in the particular city-dose-gestational age classification. Numbers of cases with possibly explained cause are given in parentheses. Prevalence rates for the 6-15 week gestational age group are generally higher than the age-specific rates for other gestational ages.

Woodら⁵が指摘しているように、知能遅滞例の原爆時妊娠期は6-27週で、この期間の前半にあった者が特に多い。表2は知能遅滞発現の割合を妊娠期別(早産と遅産について補正)および線量別に示した。この割合は知能遅滞例をその特定都市・線量・妊娠期の各別群の構成数で除して得た数値である。知能遅滞の原因が判明している例数はカッコ内に示した。原爆時の妊娠期が6-15週間であった者における頻度は他の妊娠期にあった者に比較して一般に高い値を示した。

No significant differences in average maternal age according to dose category were noted. The total proximal sample average age ATB was 28.9. The 50-99 rad dose group average was 28.8, the 100+ rad dose group average was 27.9.

DISCUSSION

Previously reported findings of increased prevalence of mental retardation among children exposed in utero at close distances to the atomic bombs of Hiroshima and Nagasaki suggested that the cause of the higher prevalence was ionizing radiation. When the relationship of mental retardation to radiation dose was examined, this conclusion was strengthened. The risk of mental retardation was increased at doses as low as 50-99 rad (in Hiroshima), and became progressively greater with increasing dose. These findings, in conjunction with those from animal experiments⁸ and with mental retardation observed in children prenatally exposed to therapeutic maternal pelvic irradiation,⁹⁻¹¹ indicate that radiation can be an etiologic factor in mental retardation.

In Hiroshima the risk of mental retardation was significantly increased among children whose mothers were exposed to doses of more than 50 rad, as compared with a minimum dose-effect at 200 rad in Nagasaki. Similar differences have been found between the two cities with regard to small head circumference among those exposed in utero,¹² and for leukemia and other cancer among those exposed later in life.^{13,14} Mental retardation presumably due to radiation exposure affected 5 of 76 children in Hiroshima whose mothers were exposed to doses of 50-199 rad as compared with none among 33 persons in Nagasaki.

The quality of radiation released by the atomic bombs was different in Hiroshima and Nagasaki. Fission neutrons accounted for more than 20% of the total radiation (gamma+neutron) in Hiroshima, but only a negligible percent in Nagasaki.⁶ A possible explanation for the difference in effects at low doses in the two cities would therefore be the greater relative biological effectiveness (RBE) of neutrons as compared to gamma rays.

Twenty-eight of the 30 mentally retarded subjects had head circumferences smaller than the mean for their age and sex. In Hiroshima, the occurrence of small head circumference (more than 2 standard deviations below the mean) was significantly increased though intelligence was normal at doses as low as 10-19 rad in those exposed before the 18th

線量別にみた場合、母親の平均年齢に有意な差は認められなかった。近距離被爆群の原爆時平均年齢は28.9歳、50-99 rad 群の平均年齢は28.8歳および100+ rad 群では27.9歳であった。

考 察

広島・長崎の爆心地近くで胎内被爆した子供に知能遅滞例が多いという以前の報告は、電離放射線が原因であることを示唆した。知能遅滞と線量との関係を検討したところ、この結論がいつそうよく裏づけられた。広島では、知能遅滞の危険は50-99 rad という低い線量でも増加し、さらに線量の増加に伴って増大した。動物実験の結果⁸ および母親が骨盤の治療用放射線を受けた時胎内にあった子供における知能遅滞⁹⁻¹¹ をあわせて考察すると、前記の所見は放射線が知能遅滞の原因でありうることを示すものである。

広島においては、50 rad 以上の線量を受けた母親の胎内にあった子供に知能遅滞の危険率が有意に増加したが、長崎では200 rad 以上ではじめてその増加がみられた。同じような都市別差異は胎内被爆者における小頭囲¹² および被爆者における白血病その他の癌にみられる。^{13,14} 放射線被曝に起因すると思われる知能遅滞が、広島では50-199 rad を受けた母親の胎内にあった子供76名中5名に認められたが、長崎では33名中1例もなかった。

広島の前爆が放出した放射線質は長崎のそれと異なっている。広島の前爆放射線(ガンマ線+中性子)における核分裂の際放出される中性子の占める割合は20%以上であったが、長崎ではそれは無視できる割合にすぎなかった。⁶ 低線量域における影響にみられる両市間の相違は、中性子の生物学的効果比がガンマ線のそれより高いことによって説明できるかもしれない。

知能遅滞が認められた30名中28名の頭囲は、同年齢・性別群の平均より小さかった。広島では、妊娠18週以前に10-19 rad の低い線量を受けた場合、小頭囲(平均値より2標準偏差以上小さい)が有意に増加していたが、知

week of gestation. The effect became more pronounced with increasing dose.¹² Hence it appears radiation may cause cell depletion of the developing brain, resulting in mental retardation at substantial doses, and in reduced head size with possible (subclinical) lessening of intelligence at lower doses.

能は正常であった。線量の増加に伴ってその影響は顕著となった。¹² したがって、放射線は発育中の脳細胞の減少をもたらす、その結果、高線量では知能遅滞、低線量では、知能低下(準臨床的)をもたらす可能性のある小頭をひきおこすと思われる。

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