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SEVERE MENTAL RETARDATION AMONG THE PRENATALLY EXPOSED SURVIVORS OF THE ATOMIC BOMBING OF HIROSHIMA AND NAGASAKI: A COMPARISON OF THE T65DR AND DS86 DOSIMETRY SYSTEMS

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SUMMARY

In March 1986, as a result of a comprehensive re-evaluation of the exposures of the survivors of the A-bombing of Hiroshima and Nagasaki, a new method for the estimation of individual doses was introduced, termed the Dosimetry System 1986 (DS86). Important differences obtain between the estimation of organ-absorbed doses in this system and the one previously employed at RERF, the T65DR. The fetal absorbed doses associated with the latter are merely the estimates of maternal shielded kerma multiplied by average correction factors; whereas in the new system they are computed individually without the use generally of explicit, average correction factors and thus allow better for the scattering of radiant energy that occurs within tissues. Actual fetal absorbed doses, as such, are not yet available, and therefore, the comparisons described here rest on the computed dose to the mother's uterus. The DS86 sample itself consists of 1,544 individuals (96.6%) of the 1,598 belonging to the clinical sample on whom T65DR doses are available, including all of the 30 individuals diagnosed to be severely mentally retarded. A variety of models with and without a threshold have been fitted to the individual as well as grouped dose data to ascertain the most suitable dose-response relationship.

要　約

広島・長崎原爆被爆者の被曝状況が総合的に再評価され，その結果，1986年3月に，線量システム1986（DS86）と呼ばれる新しい個人線量推定方式が導入された．このDS86方式と従来から放影研で利用してきたT65DR方式の両臓器吸収線量推定には重要な違いがある．T65DR方式による胎児吸収線量は母親の遮蔽カーマ線量に平均修正因子を掛けて求めた推定値にすぎない．一方，新しい方式による線量推定値は，明確な平均修正因子を用いずに，個人別に計算し，組織内に生ずる放射エネルギーの散乱をより正当に考量したものである．実際の胎児吸収線量はまだ利用できない．したがって，本報の比較は母親の子宮推定線量に基づいている．T65DR線量が利用可能で，臨床集団に属する1,598例のうち，DS86集団は1,544例（96.6%）から成っており，重度精神遅滞であると臨床的に認められた30例全員が含まれている．最も妥当な線量反応関係を確認する目的で，閾値を含む場合と含まない場合の多様なモデルをグループ線量データに限らず個人線量データにも適用した．

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Briefly the findings of this comparison are as follows: The risk of severe mental retardation due to radiation exposure changes little from one dosimetric system to the other. The highest risk of radiation damage to the embryonic and fetal brain occurs 8-15 weeks after fertilization under both the T65DR and DS86 systems. Although other dose-response models will fit the data, damage to the 8-15 week old fetus expressed as the frequency of severe mental retardation appears adequately described by a simple linear model without a threshold. The risk at 1 Gy is about 46% with the T65DR system and 43% with the DS86 under a simple linear model, and 56% and 48%, for the T65DR and DS86 dosimetries, respectively, under an exponential linear model.

Somewhat more evidence exists under the DS86 system of a threshold to the dose-response relationship in the 8-15 week interval than existed with the T65DR doses. However, the location and reality of the threshold are difficult to assess. Without exclusion of five cases of probable nonradiation-related etiologies, and using a linear model, the grouped dose data suggest a threshold at about 0.20 Gy; whereas the individual dose data yield a threshold in the neighborhood of 0.40 Gy. The estimate of the threshold varies substantially with the model fitted and whether the five cases of mental retardation with probable nonradiation-related etiologies are or are not included.

Damage to the fetus 16-25 weeks after fertilization seems linear-quadratically or quadratically related to dose, especially in the DS86 sample, and suggests a threshold in the neighborhood of 0.70 Gy (DS86 dose), under a linear model using the individual dose data, with a lower 95% confidence bound of 0.21 Gy. Grouped dose data give the same lower bound, but an estimate of the threshold of 0.64 Gy.

INTRODUCTION

The human brain is arguably the most complex of all organs of the body. Its proper development and function depend upon an elaborate sequence of events including neural induction, neuronal proliferation, migration, and aggregation, cytodifferentiation, growth of specific connections, cell death, and neurite consolidation. These must be coordinated temporally and spatially. Any disturbance of this sequence, however transitory, can lead to abnormality, for proper neuronal function depends upon the proper situating of the neuronal cells. Abnormally

以下，この比較結果を簡単に述べる．放射線被曝による重度精神遅滞のリスクは線量推定方式によってほとんど差がない．胎芽及び胎児の脳への放射線障害の最も高いリスクは，T65DR 及び DS86 線量の両方式において，受胎後８～15週に起こる．ほかの線量反応モデルもデータに適合するが，重度精神遅滞頻度として現れる８～15週齢の胎児への障害は，閾値を含まない単純な線形モデルが適合するようである．1 Gy でのリスクは単純な線形モデルを用いた場合，T65DR 方式で約46%，DS86 方式で約43％であり，指数線形モデルを用いた場合，T65DR 方式で約56%，DS86 方式で約48%である．

DS86 方式では，T65DR 方式よりも８～15週齢の線量反応関係の閾値の存在が幾分強く現れる．しかし，その閾値の位置及び実在を評価するのは困難である．放射線に関連しない病因によると思われる５例を除外せず，線形モデルを用いると，グループ線量データは約 0.20 Gy の閾値を示唆する．一方個人線量データからは 0.40 Gy に近い閾値が得られる．閾値の推定値は当てはめたモデルによって，また放射線に関連しない病因によると思われる精神遅滞５例を含めるか否かによってかなり変動する．

受胎後16～25週の胎児の障害は，特に DS86 集団については，線形- 2 次線量反応関係，又は，２次線量反応関係にあり，個人線量データを用いた線形モデルでは，0.70 Gy（DS86 線量）の近傍の閾値と，0.21 Gy の95％下限推定値を示唆する．グループ線量データが示唆する下限推定値は同じであるが，閾値の推定値は 0.64 Gy である．

緒　言

ヒトの脳は人体の全臓器のうち恐らく最も複雑である．その適切な発達及び機能は，神経の誘導，ニューロンの増殖，移動，及び集合，細胞分化，特定の細胞間の線維連絡，細胞死，並びに神経突起の分枝の固質化などの精密な一連の事象に依存している．これらの事象は時間的に空間的に統合されていなければならない．ニューロンが十分に機能を発揮するためにはニューロン細胞が適切に配置されなければならない．この順序に変調が起こると，それが一過性であろうとも，異常が起こり得る．例えば，異常な

disposed neurons are, for example, a recognized focus of epileptogenic seizures.[1]

Epidemiologic and experimental evidence testify to the deleterious effects on the developing embryonic and fetal brain of a variety of agents, such as alcohol, methylmercury, and ionizing radiation, although the specific process or processes upon which any one impinges is still unclear. Documentation of the harmful effects of exposure to ionizing radiation rests largely, although not exclusively, on the many studies of those survivors exposed prenatally to the A-bombing of Hiroshima and Nagasaki.[2-8] Four of these early investigations suggested an increase in severe mental retardation and small head size with increasing exposure, and collectively identified the specific types of biological risk that follow exposure in utero. These studies occurred, however, at a time when it was not possible to assign individual absorbed doses to the embryo or fetus, and thus to provide acceptable quantitative insight into the absolute risks.

Several years ago a reexamination of these earlier findings was initiated; it was prompted primarily by the availability of data on the estimated absorbed dose in fetal tissue, given that the exposure in air is known,[9,10] and by recent developments in the understanding of the sequence and timing of the prenatal events culminating in the human brain.[11-13] This reevaluation was itself tentative, for the estimates of individual exposures used were based on the so-called T65DR dosimetry[14,15] which was then under extensive review. The latter reassessment was completed in 1986, and new estimates of fetal absorbed dose based on the dose to the mother's uterus are now available.[16]

The purposes of this report are twofold: first, to evaluate the absolute risks to the developing human embryonic and fetal brain using these newer doses, and second, to compare the estimates of risk so derived with those based on the earlier dosimetry. Attention will be limited to the data on clinically recognized severe mental retardation.

MATERIALS AND METHODS

Over the years, ABCC and its successor, RERF, have established at least three overlapping samples of individuals prenatally exposed to the A-bombing of Hiroshima and Nagasaki.[17] These have been termed the original PE-86 sample, the revised or

移動をしたニューロンは，癲癇発作を起こす原因と考えられている.[1]

アルコール，メチル水銀，電離放射線などの様々な因子が胎芽及び胎児の脳の成長に有害な影響を及ぼすことは疫学的及び実験的に実証されているが，それがどの発達段階に障害を与えるかは依然として不明である．電離放射線被曝の有害な影響に関する文献のうちすべてではないがほとんどが，広島・長崎の原爆胎内被爆者について実施された多くの調査結果を報告したものである.[2-8] 初期の四つの調査研究が，被曝線量の増加に伴う重度精神遅滞及び小頭症の増加を示唆し，また，これらの総合的結果から，胎内被爆後の特定の生物学的リスクを確認した．しかし，これらの研究調査の実施時期は，胎芽又は胎児の個人吸収線量を付与することが不可能な時期であり，その結果，絶対リスクを定量化することができなかった．

これら初期の所見の再検討が数年前に開始された．再検討の主な理由として，空中被曝線量が判明している場合の胎児組織の吸収線量推定値に関するデータの入手が可能になったこと,[9,10] 並びにヒトの脳の形成過程での事象の順序及び時期を理解する上で最近重要な進展があった点が挙げられる.[11-13] 使用された個人被曝線量推定値は，当時大規模な検討下にあったいわゆるT65DR線量推定方式[14,15]に基づいていたために，この再評価自体暫定的なものであった．線量推定方式の見直しは1986年に完了し，母親の子宮線量に基づく胎児の吸収線量の新しい推定値が現在利用可能になった.[16]

本報の目的は二つある．第一は，新線量推定値を用いてヒトの胎芽及び胎児の脳の発達に与える絶対リスクを評価すること，第二は，得られたリスク推定値をT65DR推定方式に基づく推定値と比較することである．ここでは臨床的に確認された重度精神遅滞に関するデータに限定する．

材料及び方法

ABCC及びその後身である放影研は，永年にわたり，広島・長崎の胎内被爆者について少なくとも三つの重複する集団を設定した.[17] これらは，最初のPE86集団，改定又は臨床検査PE86集団，及び胎内被爆

clinical PE-86 sample, and the in utero mortality cohort. Differences between these samples reflect the different purposes for which they were initially chosen, e.g., as the bases for clinical examinations, or mortality surveillance. The relationship of these samples one to another has been described in detail elsewhere.[7] Herein are related the results of analyses based on one of these, i.e., the clinical sample, where the observations on the occurrence of severe mental retardation are most complete.

Severe mental retardation. Of the 1,613 nonexposed and exposed children in the in utero clinical sample in Hiroshima and Nagasaki reported by Wood et al,[2] 10 cases with unknown dose and 5 cases outside the date of birth restriction were excluded; thus the sample we use is based on 1,598 individuals. (Note earlier publications have referred to nine unknown dose cases;[6-8] however the reassessment has revealed one further case where two sharply discrepant interviews could not be resolved. This case has been excluded from the T65DR and DS86 samples.) All of the 30 cases of severe mental retardation described in Appendix 1 were diagnosed before the age of 17 and these diagnoses have not been changed in any subsequent analysis of these data including the present report. Judgments of severe mental retardation were based upon clinical impressions and not on an IQ score, if such existed. A child was deemed to be severely mentally retarded if he or she was "unable to perform simple calculations, to make simple conversation, to care for himself or herself, or if he or she was completely unmanageable or had been institutionalized."[2]

Nine of the mentally retarded individuals have health problems, presumably nonradiation-related, which could account for their severe mental retardation. Since their disposition in the analyses to be described shortly could obscure efforts to assess the role of exposure to ionizing radiation, we describe the cases and our handling of them for analytical purposes. Three of these individuals are known to have, or have had Down's syndrome (MF [redacted] – now dead, [redacted], and [redacted]), a fourth, to have a retarded sibling (MF [redacted]), and a fifth had Japanese encephalitis in infancy (MF [redacted]). It is conceivable in these instances that the severe mental retardation was merely a part of the Down's syndrome, or genetic but apparently not chromosomal in origin, or secondary to the infection, but in any event not radiation-related. In

者死亡調査集団と呼ばれている．各集団間の差異は，標本抽出の異なる目的，例えば，臨床検査を基盤とするか，あるいは死亡調査を基盤とするかを反映している．これらの集団の相互関係はほかの報告書に詳細に述べている．[7] 本報ではこれらの集団のうち，重度精神遅滞発生に関して最も綿密に観察した臨床集団に基づく解析結果について述べる．

重度精神遅滞． Wood ら[2] が報告した広島・長崎の胎内被爆者臨床集団の非被爆者及び被爆者1,613人のうち，線量が不明な10例及び生年月日が設定範囲外である5例を除外した．したがって本調査の対象者は1,598人である．（前回の報告では線量の不明者は9例であったが，[6-8] 再評価で2回の面接結果が大きく矛盾する1例を追加したことを注意する．この1例はT65DR及びDS86集団から除外された．）付録1に示した重度精神遅滞30例はすべて17歳以前に診断されており，本報を含めその後のデータ解析の診断は変更されていない．重度精神遅滞の判定は，IQスコアが判明している場合でも，臨床的所感に基づいている．すなわち，“簡単な計算や会話ができない者，身の回りのことが自分でできない者，全く扱い難い者，あるいは施設に収容されていた者”を重度精神遅滞者とした．[2]

重度精神遅滞者9例は，恐らく放射線に関連のない健康上の問題があり，それが重度精神遅滞の原因である可能性があった．後述する解析で，これらの対象者のうち最初の3例（MF [redacted] 既に死亡，[redacted]，評価できなくなる可能性があるので，解析するこれらの対象者，及びこれらの扱いについて述べる．対象者のうち最初の3例（MF [redacted] 既に死亡，[redacted]，[redacted]）はDown症候群に過去及び現在において罹患しており，また第4例（MF [redacted]）は精神遅滞者の同胞をもち，第5例（MF [redacted]）は幼児期に日本脳炎に罹患していた．これらの例ではいずれも重度精神遅滞は放射線に関連しておらず，Down症候群の一部であるか，染色体性のものではないが遺伝的であるか，感染が原因である可能性がある．下記の結果の項では，これらの対象者を含めた場合と除外

the results to follow we shall exhibit analyses which both include and exclude these cases to illustrate the dependence of the results upon their disposition. Exclusion of these children does not, generally speaking, alter the findings appreciably for either the T65DR or the DS86 dosimetry.

There are in addition four other individuals with clinical diagnoses which might be functionally related to their mental retardation. Two of these, one stated to have had a birth injury (MF [redacted]) and one with congenital lues (MF [redacted]), received less than 0.01 Gy and were, moreover, exposed at prenatal ages outside either of the periods of apparent vulnerability. Furthermore, the diagnosis of "birth injury" is tenuous; it was not directly made, but rests on the mother's assertion that the child was dropped at five months of age, injuring the spine. The diagnosis of congenital lues was based on repeated strongly positive serological reactions on both the mother and child. They have not been excluded since they do not contribute to the estimate of the risk either in the 8-15 or 16-25 week periods when the "controls" are not combined, but do when these are combined.

Two other individuals, both exposed to more than 0.01 Gy in the 8-15 week interval, were stated to have neurofibromatosis (MF [redacted]) and neonatal jaundice (MF [redacted]). We have elected not to exclude these for the following reasons: First, although intelligence, on average, is diminished with neurofibromatosis (average IQ is 85-90), the individual in question had an IQ of 62 (Koga Test), a value associated with only a few percent of a random sample of individuals with neurofibromatosis. Moreover, the initial tentative diagnosis rested exclusively on the presence of café au lait pigmentation, and vitiliginous changes on the chest and back. At no subsequent examination, including one as late as 30 years of age, were actual tumors described. Ocular examinations failed to reveal the phacoma, common in this disease, but did disclose the polychromatic granular sheen which has been described as radiation-related. Second, insofar as the case of neonatal jaundice is concerned, this child subsequently died (at age 7) of a primary malignancy of the right lobe of the liver. The diagnosis of neonatal jaundice was anamnestic, and at no time while this child was under clinical surveillance by ABCC, including the six months immediately prior to death, was jaundice diagnosed. Accordingly, we do not

した場合の解析について述べ，それらの扱い方が結果をどのように左右するかを示す．一般的には，T65DR及びDS86線量推定方式のいずれも，これらの子供を除外することで所見が大きく変わることはない．

更に，臨床診断が精神遅滞と機能的に関連しているかもしれない対象者はほかに4例いた．そのうち1例（MF [redacted]）は出生時損傷があり，ほかの1例（MF [redacted]）は先天性梅毒に罹患していたが，これら2例は被曝線量が0.01 Gy未満である上，明らかに感受性が強い時期のいずれにも当てはまらない胎内週齢で被爆している．更に，“出生時損傷”の診断が不明確である．これは直接に診断されたものではなく，5か月のときに子供を落とし脊椎の損傷を招いたという母親の申し立てによるものである．先天性梅毒の診断は，母親及び子供の両方に繰り返し強い血清学的陽性反応を認めたことに基づく．これらの対象者は“対照者”を含めない場合には8～15週齢又は16～25週齢でのリスク推定値に影響しないので対照者を含めて除外せずに行った．

ほかの2人は8～15週齢で0.01 Gy以上に被曝したが，このうち1人（MF [redacted]）は神経線維腫症に，ほかの1人（MF [redacted]）は新生児黄疸に罹患していた．この2症例は次の理由で除外しなかった．まず，神経線維腫症に罹患すると一般的に知能は低下するが（平均知能指数85～90），ここで問題にしている患者の知能指数は62（古賀テスト）であり，神経線維腫症患者の無作為標本のうちわずか数パーセントがこの程度の指数を示す．その上，最初の仮診断は，淡褐色の色素沈着と胸部及び背の白斑変化のみによるものであった．その後30歳になるまでの検査では，実際の腫瘍の記述はない．眼科検査ではこの疾病で通常確認される水晶体腫は観察されなかったが，放射線に関連すると考えられる多色性顆粒性光輝が認められた．次に新生児黄疸の症例であるが，この子供は肝臓右葉の原発性悪性腫瘍のため死亡した（7歳）．新生児黄疸の診断は記憶によるもので，死亡直前の6か月間を含めABCCの臨床検査では黄疸は認められなかった．したがって，これらの

believe the clinical evidence to be sufficient to justify the exclusion of either of these cases. Lastly, it warrants note that the existence of another possible etiology does not preclude the fact that in those exposed, exposure worsened their situation.

Dosimetry: For comparative purposes, the results of two analyses are presented, one based on the estimates of fetal absorbed dose using the T65 dosimetry after relocation of the hypocenter in Nagasaki (commonly referred to as the T65DR),[15] and the other, the DS86 organ-absorbed dose (uterus). The fetal absorbed doses associated with the T65DR system are merely the estimates of maternal shielded kerma multiplied by correction factors averaged over all stages of fetal development and without regard to orientation or posture at the time of exposure.[10] These correction factors differed trivially from those associated with the uterus (see Table 9[10]).

The DS86 estimates are computed differently. Within 1,600 m in Hiroshima (2,000 m in Nagasaki) where detailed shielding histories exist on most survivors within the major study samples, exposures are individually modeled without the use of explicit average correction factors and take into account orientation and posture, where known; thus they allow better for the effects of the latter and the scattering of radiant energy that occurs within tissues.[16] Estimates made in this manner are customarily designated as direct DS86 doses.[18] For exposed individuals on whom complete shielding histories do not exist, regression functions are used to estimate free-in-air (FIA) kerma, and the latter values are then adjusted using average house and body transmission factors. Such estimates are said to be indirect. Appendix 2 gives the numbers of individuals within the clinical sample whose doses were directly and indirectly estimated by dose groups.

Actual DS86 fetal absorbed doses are not yet available, and may not be for some time. We use, therefore, the mother's uterus-absorbed dose (gamma rays and neutrons), and the expression "fetal" to emphasize the approximation involved. Phantom studies[10] have shown that the correspondence between the uterus dose and that to fetal tissues is high in the latter half of pregnancy, but may overestimate the energy absorbed by tissues in the first half when more fluid surrounds the embryo or fetus.

The correspondence in estimated doses in the two systems is illustrated in Table 1 and Figure 1. The

対象者を除外するだけの臨床的証拠はないと考えた．最後に，被爆がほかの病因の存在により被爆者の状態を悪化させたという事実が打ち消される訳ではないことに留意する必要がある．

線量推定：長崎の爆心地移動後の T65 線量推定方式（通常 T65DR と呼ばれる）[15] を用いた胎児吸収線量推定値に基づく解析結果と，DS86 臓器吸収線量（子宮）に基づく解析結果とを比較するために示す．T65DR 線量推定方式による胎児吸収線量は，被爆時の身体の方向及び姿勢は考慮に入れず，単に母親の遮蔽カーマ線量推定値に，胎児発育の全段階の平均をとった補正因子を掛けて求めたものである．[10] これらの補正因子は子宮の補正因子とはほとんど差異はなかった（表 9 参照[10]）．

DS86 推定値は異なる方法で算出される．主要調査標本の対象者の大部分について詳細な遮蔽歴が存在する広島の 1,600m 以内での被爆者（長崎では 2,000m 以内）については，明確な平均補正因子を用いず，身体の方向及び姿勢が判明している場合はそれらを考慮に入れて個人別にモデル化して行った．したがって，これらの推定値は身体の方向・姿勢及び組織内で起きる放射エネルギーの散乱の影響をより正確に評価した推定値である．[16] この方法で得られた推定値は通常 DS86 直接線量推定値と呼ばれている．[18] 完全な遮蔽歴が存在しない被爆者については，回帰関数を用いて自由空中（FIA）カーマ線量を推定し，その推定値を家屋及び身体の平均透過率を用いて補正した．これらは間接線量推定値と呼ばれている．付録 2 は，直接又は間接に線量を推定した臨床集団の被爆者数を線量群別に示す．

実際の DS86 胎児吸収線量はまだ算出されておらず，算出には時間を要するかもしれない．したがって，我々は母親の子宮吸収線量（ガンマ線及び中性子線）を使用し，近似値であることを強調するため“胎児”という表現を用いる．ファントム調査の結果によると，[10] 妊娠の後半期では子宮線量と胎児組織線量の相関関係が強いが，胎芽又は胎児を取り巻く羊水量が多い前半期では組織が吸収したエネルギーを過大評価するおそれがある．

二つの推定方法による線量推定値の関係を表 1 及び図 1 に示す．重度精神遅滞の解析に用いた DS86 標本

TABLE 1 RELATIONSHIP OF FETAL ABSORBED DOSES IN THE T65DR AND DS86 SYSTEMS OF DOSIMETRY IN THE STUDY SAMPLE

表1 T65DR及びDS86線量推定方式による胎児吸収線量の対象集団における関係

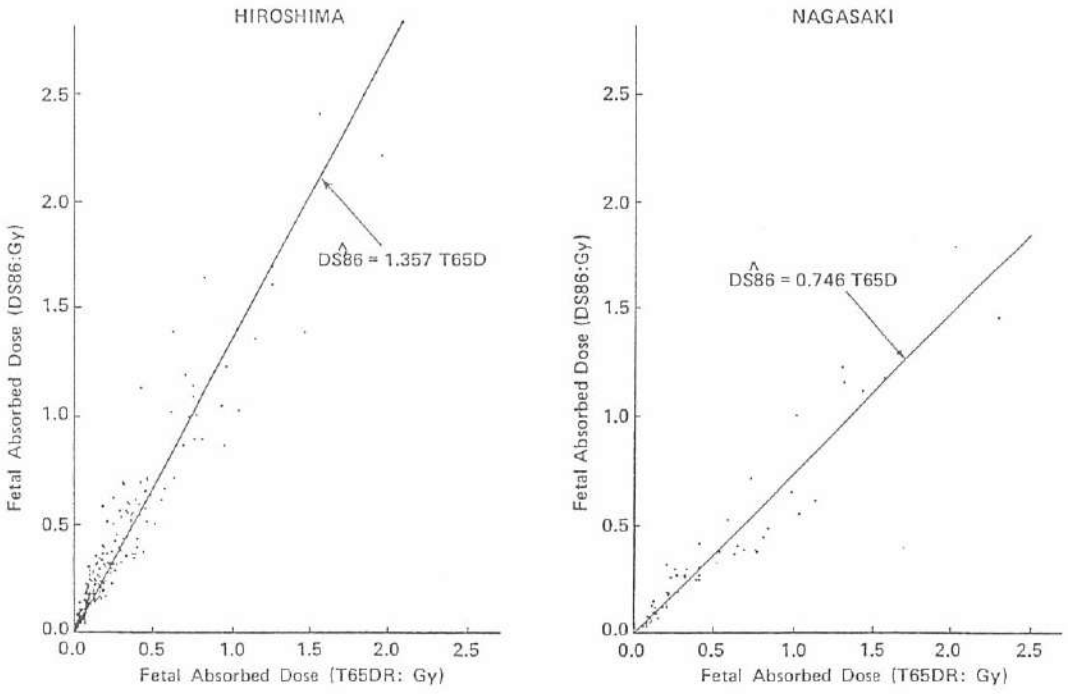
Fetal absorbed dose based on T65DR(Gy)	Fetal absorbed dose based on DS86(Gy)							
	<0.01	0.01-0.09	0.10-0.49	0.50-0.99	1.00+	Subsample	Unknown dose	Total
<0.01	1068	4	1			1073	12	1085
0.01-0.09		191	78			269	23	292
0.10-0.49		6	118	28	1	153	16	169
0.50-0.99			10	12	11	33	1	34
1.00+				2	14	16	2	18
Unknown dose [a]							1	1
Total	1068	201	207	42	26	1544	55	1599

[a] Note that one additional child (MF# [redacted]), exposed 15 weeks after fertilization, has been assigned to the unknown dose category. Two different interviews of the mother resulted in sharply discrepant unreconcilable statements about her position at the time of the bombing. Her stated distance varied by over 1,000 m on the two occasions.

[a] 受胎後15週齢で被爆した1例の子供(MF# [redacted])は線量区分不明に分類したことを注意する．母親との2回の面接の結果，被爆場所に解決し難い大きな矛盾があった．この母親の説明した二つの場所は1,000m以上の開きがあった．

FIGURE 1 RELATIONSHIP BETWEEN T65DR FETAL ABSORBED DOSE AND DS86 UTERUS ORGAN DOSE ESTIMATES FOR SAMPLE OF SEVERE MENTAL RETARDATION

図1 重度精神遅滞集団のT65DR胎児吸収線量とDS86子宮臓器線量推定値の関係



DS86 sample used in the analysis of severe mental retardation consists of 1,544 individuals (96.6%) of the 1,598 belonging to the clinical sample on whom T65DR doses are available, including all of the 30 diagnosed to be severely mentally retarded. The principal differences between the T65DR and DS86 samples are: 1) the shift of 78 (29%) of the 269 prenatally exposed survivors in the 0.01-0.09 Gy T65DR group to the 0.10-0.49 Gy DS86 group, and 2) an increase in the 1.00+ Gy group from 16 in the T65DR to 26 in the DS86. These changes reflect the higher transmission of gamma rays through tissue with the new dosimetry. In both instances, the control or comparison group consists of prenatally exposed survivors receiving doses of less than 0.01 Gy and those individuals not-in-city (NIC) at the time of the bombing (ATB).

は，臨床検査集団に属し，T65DR 線量が判明している1,598人のうち1,544人（96.6%）から成っており，その中には重度精神遅滞と診断された30人全員が含まれている．T65DR 標本と DS86 標本の主な違いは 1) T65DR 方式では 0.01～0.09 Gy 群に属していた胎内被爆者269人のうち78人（29%）が，DS86 方式では 0.10～0.49 Gy 群に移行したこと，並びに，2) 1.00＋Gy 群の対象者数が T65DR 方式では16人であったのに対し，DS86 方式では26人に増加したことである．これらの変更は，新線量推定方式ではガンマ線の組織透過率が高くなったことを反映している．いずれの場合でも，対照群は 0.01 Gy 未満の線量を受けた胎内被爆者と原爆時（ATB）に市内不在であった者（NIC）から成る．

Neither under the new system nor the old have neutrons been a significant contributor to most fetal exposures, and as a consequence, the effect of this source of radiation is a lesser problem in the analysis of the occurrence of severe mental retardation than in radiation carcinogenesis. Indeed, the DS86 FIA neutron kerma in Hiroshima at about 2,000 m was only 0.04 Gy, and in Nagasaki essentially 0. Thus, the DS86 "fetal" absorbed dose estimates to be discussed shortly include few neutrons in Hiroshima, and basically none in Nagasaki and, therefore, we have ignored the possible effect of their relative biological effectiveness (RBE, see Appendix 1).

新旧いずれの推定方式でも中性子線は胎児被曝線量に大きく寄与していないので，重度精神遅滞発生の解析では，放射線による発癌の解析ほど中性子線の影響は大きな問題にはならない．事実，約2,000m での DS86FIA 中性子カーマ線量は広島ではわずか 0.04 Gyであり，長崎では実質的には0であった．したがって後述する DS86“胎児”吸収線量推定値には中性子線量は広島ではほとんど，長崎では実質的に全く含まれていないので，中性子線の生物学的効果比（RBE，付録1参照）の影響は無視した．

Gestational age. The date of pregnancy ATB is based upon the inferred first day of the last menstrual period, and has been calculated with the following function:

胎内週齢． 原爆時の妊娠日数は最終月経の推定開始日に基づき，下記の方式により算出した．

$$\text{Days of pregnancy ATB} = 280 - (\text{Date of birth} - \text{6 or 9 August 1945})$$

妊娠日数（原爆時）　　生年月日　　又は

where the mean duration of pregnancy is taken to be 280 days, and the date of birth being obtained by interview with the individual or his or her mother. To obtain the gestational age, 14 days have been subtracted from the "days of pregnancy ATB". Age in days was changed to age in weeks by dividing by seven and the latter quotient was presumed to be zero if it was negative.

ただし，平均妊娠期間を280日とし，生年月日は子供又は母親との面接によって得られたものを用いた．“原爆時の妊娠日数”から14日を引き受胎後日数を求めた．その日数を7で割り週齢を求め，後者の商が負になる場合は週齢を0と仮定した．

Statistical considerations and methods. Gestational age is the most important single factor in determining the nature of the insult to the developing embryo or fetus resulting from exposure to ionizing radiation. Accordingly, since different functions in

統計的検討及び方法． 胎内週齢は，電離放射線被曝が発達過程の胎芽又は胎児へ与える障害の特徴を知る上で最も重要な因子である．ヒトの脳の種々の

the human brain are localized into different structures, and since the differentiation of these takes place at different stages of gestation and over different periods of time, gestational ages have been grouped so as to reflect these known phases in normal development. Four categories measured from the presumed moment of fertilization have been used: 0-7, 8-15, 16-25, and 26 or more weeks. In the first period, the precursors of the neurons and neuroglia, the two principal types of cells that give rise to the cerebrum, have emerged and are mitotically active.[19] In the second, a rapid increase in the number of neurons occurs; they migrate to their ultimate developmental sites and lose their capacity to divide, becoming perennial cells.[12,13] In the third, differentiation in situ accelerates, synaptogenesis that began about the eighth week increases, and the definitive cytoarchitecture of the brain unfolds. The fourth period is largely one of continued architectural and cellular differentiation and synaptogenesis.

機能は異なる組織に局在しており，各組織の分化は受胎後の様々な段階及び時期に起こるので，正常な発達における既知の段階を反映するよう胎内週齢を区分した．すなわち，推定受胎日から計算して０～７週，８～15週，16～25週及び26週以上の四つに区分した．第１期では，大脳を形成する２種類の主な細胞であるニューロンとニューログリアの前駆体が発生し，両者は活発に有糸分裂する．[19] 第２期では，ニューロンの産出が活発に行われる．未熟なニューロンは脳芽壁の増殖層から大脳表層へ移動し，細胞分裂の特性を失い非分裂細胞になる．[12,13] 第３期では，潜在的分化が促進され，第８週ごろに始まるシナプス形成が増加し，脳の最終的な細胞構築が進む．第４期では主として，構築，細胞分化，及びシナプス形成が継続する．

Given the number of different developmental processes which are proceeding simultaneously and whose relative susceptibilities to radiation-related effects are unknown, a variety of models have been fitted to the individual as well as the grouped dose data (six groups have been used). As simple statistical approximations to the events which culminate in severe mental retardation, the following binomial models have been fitted: a linear one (L), a linear-quadratic one (L-Q), and a quadratic one (Q) dependent on the "fetal" absorbed doses. Since it has been suggested that the model proposed by Lea[20] might be a more suitable descriptor of the dose-response relationship than a simple linear model,[21] a variety of exponential models (exponential linear, exponential linear-quadratic, and exponential quadratic) have also been fitted to these same data. To avoid confusion in subsequent paragraphs, the terms linear, linear-quadratic or quadratic alone will always refer to the binomial model; when the exponential has been fitted, the model will be described as exponential linear, exponential linear-quadratic or exponential quadratic.

放射線に対する相対的感受性が未知の同時に進行する様々な発達段階を仮定し，種々のモデルをグループ線量データ（六つの線量群を使用）と同様に個人線量データに適用した．重度精神遅滞を起こす事象への単純な統計的近似として，次の二項モデル，すなわち，“胎児”吸収線量に依存する線形モデル（L），線形-２次モデル（L-Q），及び２次モデル（Q）などの二項モデルを当てはめた．Lea[20] が提案したモデルは単純な線形モデルより線量反応関係を適切に表すことが示唆されているので，[21] 種々の指数モデル（指数線形，指数線形-２次，指数２次）も同一のデータに適用した．混乱しないよう以下の説明を付け加えておく．線形，線形-２次，又は２次という語を単独に用いる場合は，常に二項モデルを意味する．指数モデルを当てはめる場合は，指数線形，指数線形-２次，指数２次として表す．

In addition to the models without thresholds just described, we have fitted to the individual and the dose-grouped data variations of the binomial and exponential models which assume the existence of a dose threshold, T, in the occurrence of the severely mentally retarded. These models are of the following general forms: In the binomial case,

上記の閾値のないモデルに加えて，重度精神遅滞が起こった場合の線量閾値Ｔの存在を仮定した様々な二項モデル及び指数モデルを個人及びグループ線量データに当てはめた．これらのモデルは下記のような一般的形式，すなわち，二項モデルの場合には，

$$P_i = a + b\,(D_i - T) \qquad (A)$$

and in the exponential one,

指数モデルの場合には，次のようになる．

$$P_i = 1 - \exp\,[-\{a + b\,(D_i - T)\}] \qquad (B)$$

where D_i denotes the i-th fetal absorbed dose, i= 1,2, ..., 6 for grouped data, and i= 1,2, ..., n for binary response data (1,0), i.e., 1 for a severely retarded individual and 0 for others, and (A) and (B) hold only if $(D_i - T) \geq 0$.

ただし，D_i は第 i 番目の胎児吸収線量を示し，i=1, 2,..., 6 のグループデータ及び i=1, 2,..., n の二値反応データ(1, 0)，すなわち重度精神遅滞者に対して1，そうでない者に対して0を表し，(A)及び(B)は$(D_i - T) \geq 0$の場合にのみ成立する．

To assign a threshold the smallest chi-square (χ^2) or largest log likelihood value was selected from a number of χ^2 or log likelihood values obtained through using a succession of arbitrarily fixed values of T, e.g., T = 0, 0.05, 0.10, ..., Gy. The 95% or 90% confidence limits were also determined from the same likelihood ratio χ^2 statistic,[22,23] namely,

閾値を割り当てるために，任意に固定した一連のT値，例えば T=0, 0.05, 0.10,..., Gy を用いて求めた多くのカイ2乗(χ^2)値又は対数尤度値から，最小の χ^2 値又は最大対数尤度値を選択する．95%又は90%信頼限界も，同様の尤度比 χ^2 統計量,[22,23] すなわち，

$$\chi^2_\alpha = -\,2 \log\,[L(X\,|T^*)/L(X\,|T)]$$

where T* = L(a 95% or 90% lower bound) or U(a 95% or 90% upper bound) and T is the maximum likelihood estimate, i.e.,

から求める．ただし，T^*=L(95%又は90%下限)又はU(95%又は90%上限)及び，Tは最大尤度推定値，すなわち，次式として用いる．

$$-\log L(X\,|T^*) = -\log L(X\,|T) + \chi^2_\alpha/2 \quad .$$

RESULTS

The occurrence of severe mental retardation in children exposed in utero is given by gestational ages (weeks) and city for "fetal" absorbed doses based on the T65DR dosimetry in Table 2a and on the DS86 in Table 2b (see also Figure 2). The average "fetal" absorbed dose in the successive dose groups is 0, 0.04, 0.23, 0.72, 1.31, and 2.19 Gy for all cases based on the T65DR, and 0, 0.05, 0.23, 0.64, 1.25, and 2.91 Gy for the DS86 sample. Observe too that the frequency of severely mentally retarded individuals in the 1.00+ Gy group in the DS86 sample is 12/26 (46.2%) which is higher than the 7/18 (38.9%) in the same T65DR dose group for all gestational ages, but the frequency in the 0.50-0.99 Gy DS86 dose group decreases from the 6/34 (17.6%) in the T65DR to 4/42 (9.5%). The number at the top of each histogram in Figure 2 is the number of cases with severe mental retardation.

結　果

表2a と表2b は各々T65DR と DS86 に基づく“胎児”吸収線量について，胎内被爆者の重度精神遅滞発生状況を胎内週齢別及び都市別に示した(図2も参照)．全症例を一連の線量群に分類した場合の平均“胎児”吸収線量は，T65DR では 0, 0.04, 0.23, 0.72, 1.31, 2.19 Gy であり，DS86 では 0, 0.05, 0.23, 0.64, 1.25, 2.91 Gy である．全胎内週齢についてみると，DS86 標本の 1.00＋Gy 群に属する重度精神遅滞者の頻度は 12/26(46.2%)で T65DR の 1.00＋Gy 群の 7/18(38.9%)より高いが，0.50-0.99 Gy 群の頻度は T65DR で 6/34(17.6%)であるのに対し，DS86 では 4/42(9.5%)と低くなっていることにも留意する必要がある．図2のヒストグラムでは各列の上の数字は重度精神遅滞症例数を示す．

TABLE 2a SEVERE MENTAL RETARDATION IN CHILDREN EXPOSED IN UTERO TO THE ATOMIC BOMB BY CITY AND FETAL ABSORBED DOSE, BASED ON THE T65 REVISED DOSIMETRY, FOR DIFFERENT GESTATIONAL AGES. THE ABSORBED DOSES ARE BASED ON KERR'S BODY SHIELDING FACTORS

表2a 原爆胎内被爆者の重度精神遅滞，T65改定線量推定方式に基づく異なる胎内週齢別，都市別及び胎児吸収線量別．吸収線量はKerrの遮蔽率に基づく

Dose category Gy	Fetal absorbed dose (Gy)	All gestational ages			0-7 weeks			8-15 weeks			16-25 weeks			26 weeks or more		
		Subjects	Retarded	Percent	Subjects	Retarded	Percent	Subjects	Retarded	Percent	Subjects	Retarded	Percent	Subjects	Retarded	Percent
Both cities combined																
Control	0	1085(-2)	9(-2)	0.8(0.6)	210	1	0.5	257	2	0.8	312(-1)	2(-1)	0.6(0.3)	306(-1)	4(-1)	1.3(1.0)
0.01-0.09	0.04	292(-1)	4(-1)	1.4(1.0)	55	0	0.0	69	3	4.3	86(-1)	1(-1)	1.2(0.0)	82	0	0.0
0.10-0.49	0.23	169(-2)	4(-2)	2.4(1.2)	26	0	0.0	50(-2)	4(-2)	8.0(4.2)	45	0	0.0	48	0	0.0
0.50-0.99	0.72	34	6	17.6	2	0	0.0	13	4	30.8	15	2	13.3	4	0	0.0
1.00-1.99	1.31	15	5	38.9	2	0	0.0	6	5	75.0	4	0	20.0	3	0	0.0
2.00+	2.19	3	2		0	0		2	1		1	1		0	0	
Total	-	1598(-5)	30(-5)	1.9(1.6)	295	1	0.3	397(-2)	19(-2)	4.8(4.3)	463(-2)	6(-2)	1.3(0.9)	443(-1)	4(-1)	0.9(0.7)
Hiroshima																
Control	0	832(-2)	5(-2)	0.6(0.4)	149	0	0.0	210	0	0.0	244(-1)	2(-1)	0.8(0.4)	229(-1)	3(-1)	1.3(0.9)
0.01-0.09	0.04	269(-1)	4(-1)	1.5(1.1)	50	0	0.0	65	3	4.6	75(-1)	1(-1)	1.3(0.0)	79	0	0.0
0.10-0.49	0.23	120(-2)	4(-2)	3.3(1.7)	15	0	0.0	38(-2)	4(-2)	10.5(5.6)	36	0	0.0	31	0	0.0
0.50-0.99	0.72	22	6	27.3	0	0	0.0	11	4	36.4	9	2	22.2	2	0	0.0
1.00-1.99	1.37	7	3	42.9	1	0	0.0	3	3	100.0	3	0	0.0	0	0	-
2.00+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total	-	1250(-5)	22(-5)	1.8(1.4)	215	0	0.0	327(-2)	14(-2)	4.3(3.7)	367(-2)	5(-2)	1.4(0.8)	341(-1)	3(-1)	0.9(0.6)
Nagasaki																
Control	0	253	4	1.6	61	1	1.6	47	2	4.3	68	0	0.0	77	1	1.3
0.01-0.09	0.07	23	0	0.0	5	0	0.0	4	0	0.0	11	0	0.0	3	0	0.0
0.10-0.49	0.22	49	0	0.0	11	0	0.0	12	0	0.0	9	0	0.0	17	0	0.0
0.50-0.99	0.71	12	0	0.0	2	0	0.0	2	0	0.0	6	0	0.0	2	0	0.0
1.00-1.99	1.26	8	2	36.4	1	0	0.0	3	2	60.0	1	0	50.0	3	0	0.0
2.00+	2.19	3	2		0	0		2	1		1	1		0	0	
Total	-	348	8	2.3	80	1	1.3	70	5	7.1	96	1	1.0	102	1	1.0

Numbers and percents in parentheses reveal the results after the exclusion of five severely retarded cases with probable nonradiation-related etiologies; one case with a retarded sibling, three with Down's syndrome, and one with Japanese B encephalitis.

括弧内の数値及び百分率は，放射線に関連しない病因が考えられる重度精神遅滞5例を除外した結果を示す．1例は精神遅滞者の同胞をもち，3例はDown症候群，1例は日本脳炎に罹患していた．

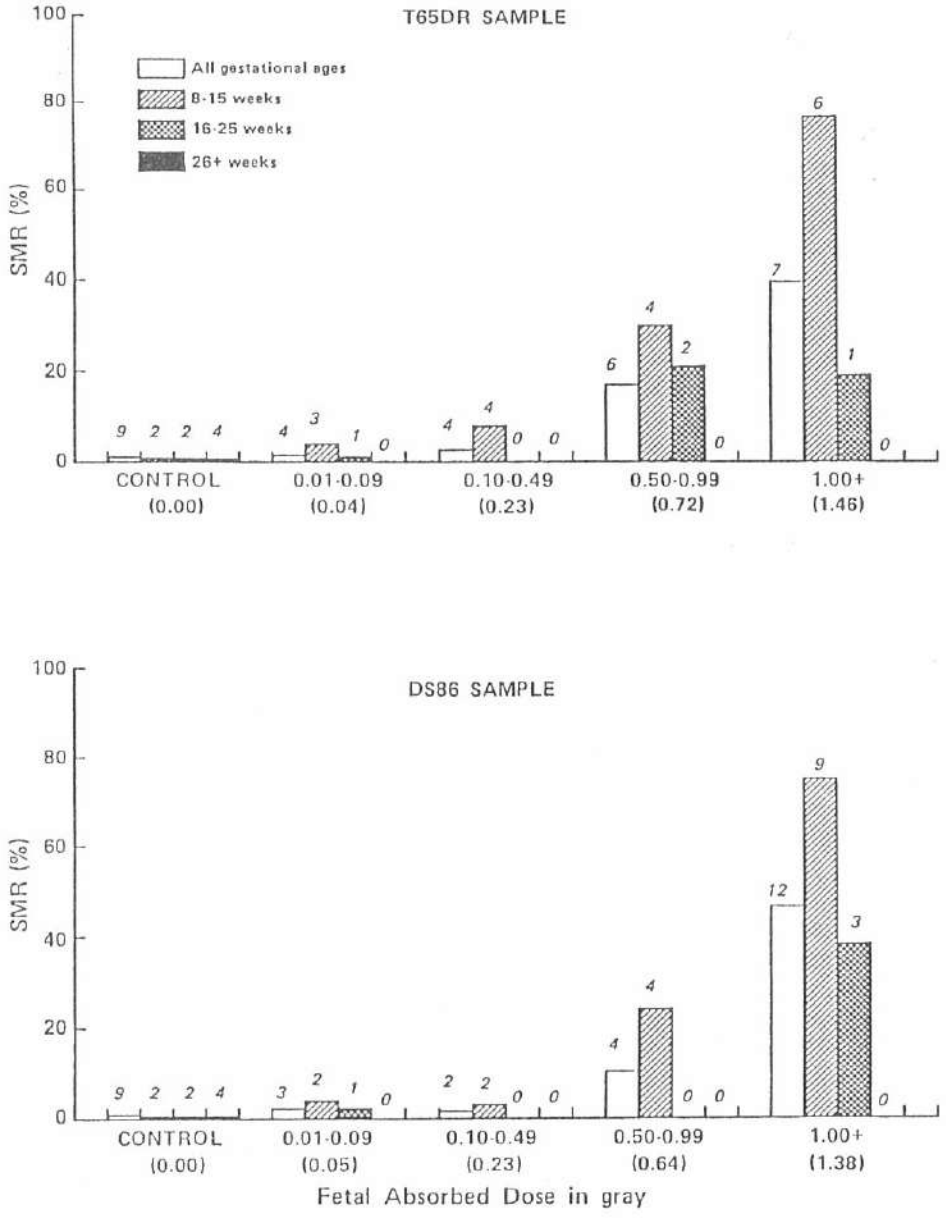
TABLE 2b SEVERE MENTAL RETARDATION IN CHILDREN EXPOSED IN UTERO TO THE ATOMIC BOMBS BY CITY AND FETAL ABSORBED DOSE, BASED ON THE DS86 DOSIMETRY, FOR DIFFERENT GESTATIONAL AGES

表2b 原爆胎内被爆者の重度精神遅滞，DS86 線量推定方式に基づく異なる胎内週齢別，都市別及び胎児吸収線量別

Dose category Gy	Fetal absorbed dose (Gy)	All gestational ages			0-7 weeks			8-15 weeks			16-25 weeks			26 weeks or more		
		Subjects	Retarded	Percent	Subjects	Retarded	Percent	Subjects	Retarded	Percent	Subjects	Retarded	Percent	Subjects	Retarded	Percent
Both cities combined																
Control	0	1068(-2)	9(-2)	0.8(0.7)	205	1	0.5	255	2	0.8	308(-1)	2(-1)	0.6(0.3)	300(-1)	4(-1)	1.3(1.0)
0.01-0.09	0.05	201(-1)	3(-1)	1.5(1.0)	41	0	0.0	44	2	4.5	55(-1)	1(-1)	1.8(0.0)	61	0	0.0
0.10-0.49	0.23	207(-1)	2(-1)	1.0(0.5)	31	0	0.0	58(-1)	2(-1)	3.4(1.8)	57	0	0.0	61	0	0.0
0.50-0.99	0.64	42(-1)	4(-1)	9.5(7.3)	5	0	0.0	16(-1)	4(-1)	25.0(20.0)	16	0	0.0	5	0	0.0
1.00-1.99	1.25	24	11	46.2	1	0	0.0	11	8	75.0	8	3	37.5	4	0	0.0
2.00+	2.91	2	1		1	0		1	1		0	0		0	0	
Total	-	1544(-5)	30(-5)	1.9(1.6)	284	1	0.4	385(-2)	19(-2)	4.9(4.4)	444(-2)	6(-2)	1.4(0.9)	431(-1)	4(-1)	0.9(0.7)
Hiroshima																
Control	0	825(-2)	5(-2)	0.6(0.4)	145	0	0.0	209	0	0.0	243(-1)	2(-1)	0.8(0.4)	228(-1)	3(-1)	1.3(0.9)
0.01-0.09	0.05	180(-1)	3(-1)	1.7(1.1)	35	0	0.0	41	2	4.9	47(-1)	1(-1)	2.1(0.0)	57	0	0.0
0.10-0.49	0.22	168(-1)	2(-1)	1.2(0.6)	24	0	0.0	51(-1)	2(-1)	3.9(2.0)	46	0	0.0	47	0	0.0
0.50-0.99	0.64	37(-1)	4(-1)	10.8(8.3)	5	0	0.0	14(-1)	4(-1)	28.6(23.1)	14	0	0.0	4	0	0.0
1.00-1.99	1.23	17	7	42.1	0	0	0.0	8	5	6.7	7	2	28.6	2	0	0.0
2.00+	2.91	2	1		1	0		1	1		0	0		0	0	
Total	-	1229(-5)	22(-5)	1.8(1.4)	210	0	0.0	324(-2)	14(-2)	4.3(3.7)	357(-2)	5(-2)	1.4(0.8)	338(-1)	3(-1)	0.9(0.6)
Nagasaki																
Control	0	243	4	1.6	60	1	1.7	46	2	4.3	65	0	0.0	72	1	1.4
0.01-0.09	0.05	21	0	0.0	6	0	0.0	3	0	0.0	8	0	0.0	4	0	0.0
0.10-0.49	0.26	39	0	0.0	7	0	0.0	7	0	0.0	11	0	0.0	14	0	0.0
0.50-0.99	0.62	5	0	0.0	0	0	-	2	0	0.0	2	0	0.0	1	0	0.0
1.00-1.99	1.28	7	4	57.1	1	0	0.0	3	3	100.0	1	1	100.0	2	0	0.0
2.00+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total	-	315	8	2.5	74	1	1.4	61	5	8.2	87	1	1.1	93	1	1.1

See the description in Table 2a. 表2a の注を参照.

FIGURE 2 SEVERE MENTAL RETARDATION FREQUENCY AND ABSORBED DOSE
BOTH CITIES COMBINED
図2 重度精神遅滞頻度と吸収線量，両市合計



The number of cases on the top of histogram expresses severe mental retardation.
棒グラフの上の数字は重度精神遅滞症例数を示す.

An increased risk of severe mental retardation is observed with an increase in dose for the gestational age-group 8-15 weeks after fertilization and also, but to a lesser extent, in the gestational age-group 16-25 weeks. No mentally retarded subjects of less than 8 weeks of gestational age nor 26 weeks and over were seen in the exposed groups although one was seen in the numerically much larger control group. Most of the retarded subjects are in Hiroshima (22 of 30) and were exposed at 8-15 weeks of intrauterine life, i.e., measured from the supposed day of fertilization; indeed, the relative risk for exposures at these weeks is four times or more greater than that for exposure at 16-25 weeks after fertilization.

受胎後８～15週の胎内週齢群では，線量の増加に伴う重度精神遅滞リスクの増加が認められ，16～25週の群でもこの傾向を認めるが，顕著ではない．胎内週齢８週未満又は26週以上の被爆群では精神遅滞例は認められなかったが，対象者が被爆群より多い対照群に１例を認めた．精神遅滞例のほとんどは広島（30人中22人）で，推定受胎日から計算して８～15週目に被爆している．事実，この時期の被爆による相対リスクは，受胎後16～25週目の被爆の４倍強である．

Dose-response models without a threshold. The regression coefficients based on a no-threshold linear dose-response relationship, using the grouped data in Tables 2a and 2b, are summarized by gestational age for all individuals included in the T65DR and DS86 samples in Table 3a and after exclusion of the five aforementioned clinically diagnosed cases of mental retardation in Table 3b. The maximum likelihood estimates (MLE) of these regression coefficients were obtained by a conventional Newton-Raphson iterative procedure. As is evident from the estimates, the risk of severe mental retardation changes little from one dosimetric system to the other. The highest risk of severe mental retardation due to radiation exposure occurs between 8 and 15 weeks after fertilization, and within this critical period, the occurrence of severe mental retardation can be linearly related to the absorbed dose received by the fetus. There is a highly significant increase in the occurrence of severe mental retardation with dose in Hiroshima and in the data for the cities combined in all gestational ages and at 8-15 weeks, and a suggestive increase at 16-25 weeks. The ratio of the slope of frequency of occurrence on dose for 8-15 weeks and for 16-25 weeks varies by a factor of 4 to 5 for both the T65DR and DS86 samples.

閾値を含まない線量反応モデル． 表2a及び2bのグループ線量データを用いて，閾値を含まない線形線量反応関係に基づく胎内週齢別の回帰係数を，T65DR及びDS86標本に属する全対象者について要約し，表3aに示し，前記の精神遅滞臨床診断例５例を除外した対象者についての要約を，表3bに示した．通常のNewton-Raphson反復法によりこれらの回帰係数の最大尤度推定値（MLE）を求めた．これらの推定値から明らかであるように，重度精神遅滞のリスクはいずれの線量推定方式でもほとんど同じである．放射線被曝による重度精神遅滞のリスクが最も高いのは，受胎後８～15週であり，この危険期間の重度精神遅滞の発生は胎児が受けた吸収線量と線形関係にある．広島及び両市合計データで，全胎内週齢及び８～15週齢について，線量と共に重度精神遅滞発生の高い有意な増加が認められ，16～25週齢については示唆的増加が認められる．T65DR及びDS86の両標本とも，８～15週齢の線量に対する発生頻度の勾配比率は，16～25週齢の４～５倍である．

In the "both cities" data, without exception, the variation in frequency of occurrence with dose, when exposure occurred 8-15 weeks after fertilization, is largely accounted for by a linear model in both samples. Somewhat differently put, the residual chi-square is never significantly large under a linear model when the T65DR estimates are used (Tables 3a and 3b). However, with the DS86 sample, there is the suggestion that a nonlinear element or a linear

"両市"のデータでは，受胎後８～15週齢に被爆した場合，線量に伴う発生頻度の変化が両標本とも線形モデルにほぼ適合する．幾分異なる見方をすると，T65DR推定値を用いると線形モデルでは残差カイ２乗が有意に大きくなることはない（表3a及び3b）．しかしDS86標本では，非線形要素又は線量反応

TABLE 3a LINEAR-RESPONSE RELATIONSHIP OF SEVERE MENTAL RETARDATION TO GROUPED FETAL ABSORBED DOSES FOR ALL INDIVIDUALS INCLUDED IN THE T65DR AND DS86 SAMPLES DESCRIBED IN TABLES 2a AND b

表3a 表2a及び2bに示したT65DR標本及びDS86標本に含まれる全対象者に関する重度精神遅滞とグループ胎児吸収線量の線形反応関係

Gestational age	Cities combined						Hiroshima only					
	a	b	s_b	χ^2_{Reg}	χ^2_{Res}	P_{Res}	a	b	s_b	χ^2_{Reg}	χ^2_{Res}	P_{Res}
T65DR Sample												
A. Relationship to fetal absorbed dose.												
All gestational ages	0.762	0.183	0.043	17.89**	4.08	0.25	0.567	0.242	0.062	15.14**	3.20	0.36
8 - 15 weeks	0.866	0.462	0.091	26.70**	1.55	0.67	0.264	0.554	0.124	19.82**	2.02	0.36
16 - 25 weeks	0.603	0.101	0.058	3.03 Sug	2.04	0.56	0.783	0.098	0.069	2.02	4.37	0.22
B. Relationship to fetal absorbed dose when the "controls" are excluded.												
8 - 15 weeks	1.297	0.443	0.092	22.92**	1.30	0.73	1.989	0.501	0.150	11.14**	0.49	0.48
16 - 25 weeks	0.410	0.106	0.064	2.74 Sug	2.03	0.36	0.619	0.103	0.077	1.81	4.31	0.12
C. Relationship to fetal absorbed dose when all "controls" are combined.												
Pooled control (8-15 weeks)	0.850	0.462	0.090	26.37**	1.55	0.67	0.625	0.560	0.128	19.11	1.02	0.60
DS86 Sample												
A. Relationship to fetal absorbed dose.												
All gestational ages	0.736	0.166	0.038	19.01**	13.74	< 0.01	0.558	0.166	0.043	15.24**	7.38	0.06
8 - 15 weeks	0.747	0.429	0.088	24.17**	4.78	0.19	0.214	0.360	0.076	22.58**	4.47	0.21
16 - 25 weeks	0.608	0.095	0.054	3.12 Sug	6.90	0.08	0.794	0.073	0.053	1.92	4.48	0.21
B. Relationship to fetal absorbed dose when the "controls" are excluded.												
8 - 15 weeks	0.239	0.441	0.097	20.50**	4.89	0.09	0.921	0.398	0.104	14.53**	2.87	0.24
16 - 25 weeks	0.375	0.100	0.060	2.83 Sug	6.86	0.03	0.670	0.076	0.057	1.74	4.51	0.10
C. Relationship to fetal absorbed dose when all "controls" are combined.												
Pooled control (8-15 weeks)	0.832	0.427	0.087	24.02**	4.78	0.19	0.611	0.406	0.091	19.78**	2.98	0.39

χ^2_{Reg} has one degree of freedom; χ^2_{Res} has three (A & C) or two (B) degrees of freedom and two (A & C) or one (B) for only 8-15 weeks in the T65DR sample in Hiroshima. P_{Res} is the probability (two-tailed) of exceeding the χ^2_{Res} by chance under the null hypothesis. a is the estimated number (intercept) of cases of mental retardation (per 100 individuals) in the 0 Gy group. b is the increase in the frequency of severe mental retardation with dose (D) expressed in gray (100 rad) and s_b its standard error.

χ^2_{Reg}は自由度1である．χ^2_{Res}は自由度3（AとC）又は自由度2（B），広島のT65DR標本の8～15週齢については自由度2（AとC）又は自由度1（B）である．P_{Res}は帰無仮説の下でχ^2_{Res}を超える確率（両側検定）を示す．aは0 Gy（100例当たり）での精神遅滞症例推定数（切片）．bは単位gray（100rad）線量（D）に対する重度精神遅滞頻度増加，S_bはその標準誤差．

Sug Significant at the 10% level. 10%水準で有意.

* Significant at the 5% level. 5%水準で有意.

** Significant at the 1% level. 1%水準で有意.

A linear (L) model $P_i = a + bD_i$ (i=1,2, ... , 5 or 4) was used in all of the analyses above.

上記のすべての解析は線形（L）モデル$P_i = a + bD_i$（i=1, 2,..., 5又は4）を適用した.

TABLE 3b LINEAR-RESPONSE RELATIONSHIP OF SEVERE MENTAL RETARDATION TO GROUPED FETAL ABSORBED DOSES AFTER THE EXCLUSION OF FIVE SEVERELY RETARDED CASES WITH PROBABLE NONRADIATION-RELATED ETIOLOGIES IN THE T65DR AND DS86 SAMPLES DESCRIBED IN TABLE 2a AND b

表3b 表2a及び2bに示したT65DR標本及びDS86標本から放射線に関連しない病因と考えられる重度精神遅滞5例を除外した後の重度精神遅滞とグループ胎児吸収線量の線形反応関係

Gestational age	Cities combined						Hiroshima only					
	a	b	s_b	χ^2_{Reg}	χ^2_{Res}	p_{Res}	a	b	s_b	χ^2_{Reg}	χ^2_{Res}	p_{Res}
T65DR Sample												
A. Relationship to fetal absorbed dose.												
All gestational ages	0.570	0.166	0.041	16.21**	6.98	0.07	0.331	0.213	0.059	13.29**	5.84	0.12
8 - 15 weeks	0.845	0.427	0.095	20.24**	3.52	0.32	0.253	0.436	0.112	15.07**	4.57	0.10
16 - 25 weeks	0.236	0.093	0.053	3.05 Sug	2.76	0.43	0.300	0.090	0.062	2.15	5.42	0.14
B. Relationship to fetal absorbed dose when the "controls" are excluded.												
8 - 15 weeks	1.444	0.412	0.105	15.39**	3.22	0.20	1.232	0.403	0.144	7.88**	2.88	0.09
16 - 25 weeks	-	-	-	-	-	-	-	-	-	-	-	-
C. Relationship to fetal absorbed dose when all "controls" are combined.												
Pooled control (8-15 weeks)	0.664	0.433	0.093	1.47**	3.67	0.30	0.380	0.512	0.129	15.82**	2.97	0.23
DS86 Sample												
A. Relationship to fetal absorbed dose.												
All gestational ages	0.550	0.149	0.036	17.13**	17.04	<0.01	0.321	0.146	0.040	13.45**	9.53	0.02
8 - 15 weeks	0.738	0.394	0.089	19.54**	6.95	0.07	0.180	0.258	0.066	15.38**	8.90	0.03
16 - 25 weeks	0.241	0.086	0.048	3.13 Sug	7.60	0.06	0.302	0.067	0.047	2.01	4.74	0.19
B. Relationship to fetal absorbed dose when the "controls" are excluded.												
8 - 15 weeks	0.185	0.407	0.099	17.03**	7.10	0.03	0.794	0.359	0.105	11.73**	4.51	0.10
16 - 25 weeks	-	-	-	-	-	-	-	-	-	-	-	-
C. Relationship to fetal absorbed dose when all "controls" are combined.												
Pooled control (8-15 weeks)	0.648	0.396	0.088	20.02**	6.95	0.07	0.370	0.371	0.092	16.08**	4.78	0.19

See footnote on five cases with probable nonradiation-related etiologies in Table 2a and description in Table 3a.

放射線に関連しない病因と考えられる5例については表2aの脚注及び表3aの注を参照.

model with a threshold in the dose-response function might fit the data better. Certainly, a linear model based on the DS86 exposures fits poorly the data for all gestational ages, for 16-25 weeks after fertilization in both cities combined, and also the data for 8-15 and 16-25 weeks when the "control" is excluded in both cities. Inspection of the DS86 data also suggests the existence of a threshold in the low dose region for damage in the period 16-25 weeks (Figure 3). Note that the foregoing findings are not materially altered when the five mentally retarded individuals with other possible etiologies are excluded (Table 3b).

The results obtained from fitting an exponential linear model to the dose-grouped data are essentially the same as those with the linear model as is shown in Tables 4a and 4b, but the absolute risk is slightly greater than that of the linear model. The results of regression analyses based on fitting a linear-quadratic (L-Q) model and a quadratic (Q) model and their exponential counterparts to the data in Tables 2a and 2b are given in Table 5. As is obvious from this table, the simple L-Q and the Q models as well as their exponential variants give acceptable fits to the data on all gestational ages, 8-15 weeks, and 16-25 weeks after fertilization. The probabilities associated with the goodness of fit of the Q model are generally higher than those of the L-Q model. A significant increase in mental retardation with dose is observed only for the quadratic and not for the linear term in the L-Q model.

To explore the dose-response relationship further, the linear and the exponential linear models described above under "Statistical considerations and methods" were fitted to the individual binary (1,0) response data. Analytic approaches based on individual dose estimates are more powerful in the statistical sense than regression analyses derived from mean dose estimates of grouped data. The results of such fitting to the individual binary data based on the T65DR and DS86 samples are shown in Tables 6 and 7 for the linear and exponential linear models without a threshold, respectively. It should be noted that the regression coefficients that emerge from fitting to the individual doses do not differ markedly from those found with the grouped data (Tables 3 and 4).

Dose-response models with a threshold. To examine the issue of a threshold in the dose-response relationship both the individual and the dose-

関数で閾値をもつ線形モデルの方がデータによく適合することが示唆されている．確かに，DS86 被曝線量に基づく線形モデルは，両市合計の全胎内週齢及び16～25週齢データ，また両市合計で"対照者"を除外した場合の８～15週齢及び16～25週齢のデータの適合度はよくない．また，DS86 データを検討すると，16～25週齢で障害を受けた場合には，低い線量域に閾値の存在を示唆する（図３）．ほかの病因と考えられる精神遅滞者５例を除外しても，これらの所見は実質的に変化しないことに留意する必要がある（表3b）．

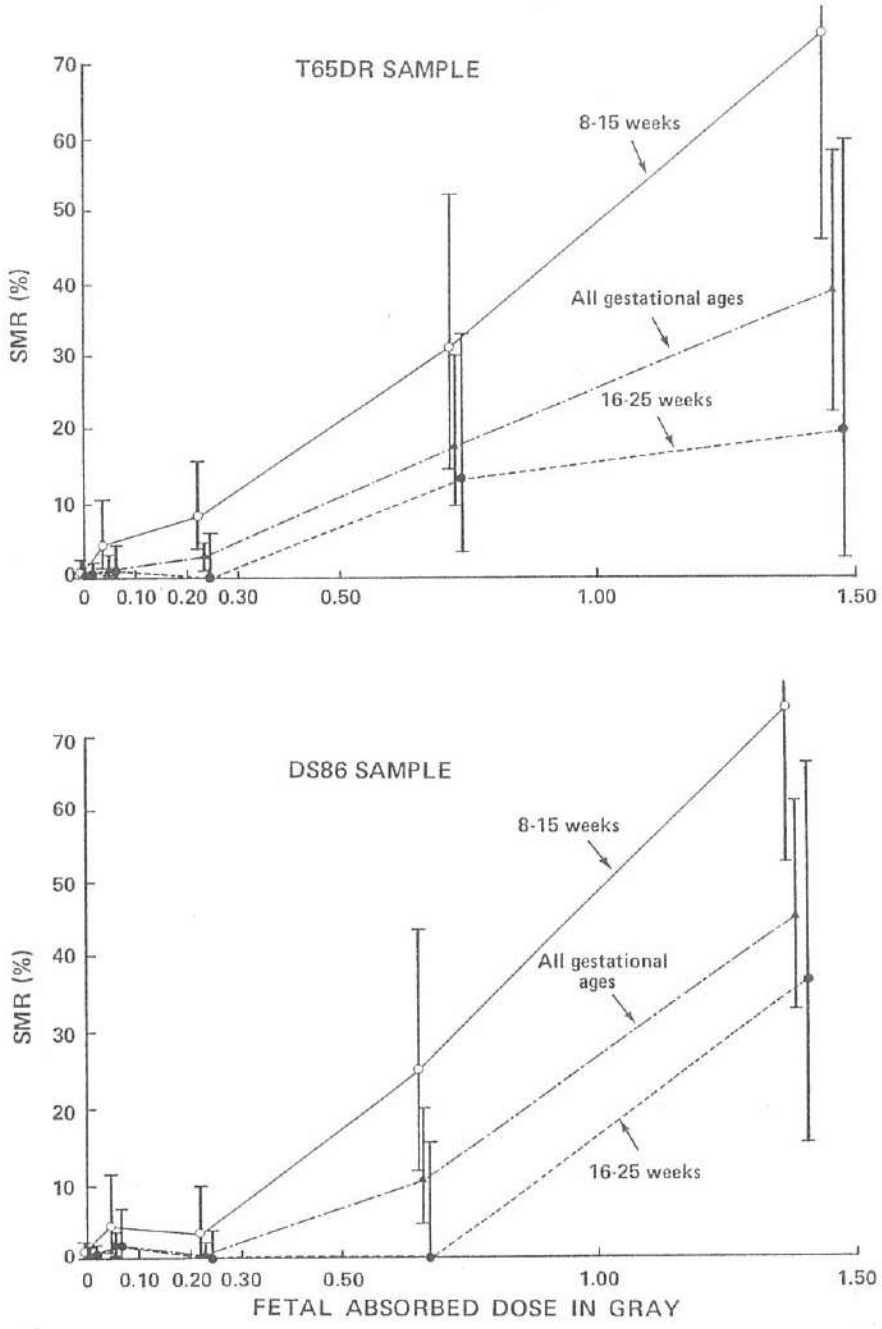
表4a 及び4b に示すように，グループ線量データに指数線形モデルを当てはめた結果は，線形モデルを用いた結果と本質的に同じであるが，絶対リスクは線形モデルを当てはめたときより若干大きい．線形-２次（L-Q）モデル，２次（Q）モデル，指数線形-２次モデル，指数２次モデルを表2a 及び2b のデータに当てはめた回帰解析の結果を表５に示す．この表から明らかなように，単純なL-Q モデル，Qモデル，指数L-Q 及び指数Q モデルは，全胎内週齢，受胎後８～15週齢，16～25週齢のデータに満足な適合を示す．Qモデルの適合度の確率は全体的にL-Q モデルより高い．線量と共に起こる精神遅滞の有意な増加はL-Q モデルの２次の項についてのみ認められ，線形の項については認められない．

線量反応関係を更に検討するために，"統計的検討及び方法"で述べた線形及び指数線形モデルを個人二値（1，0）反応データに当てはめた．統計学的な意味では，個人線量推定値に基づく解析方法は，グループデータの平均線量推定値を用いた回帰解析より強力である．T65DR 及びDS86 標本に基づく個人二値データに，閾値を含まない線形モデル及び指数線形モデルを当てはめた結果を各々表６，７に示す．個人線量モデルを当てはめたときの回帰係数は，グループデータの場合と大きく異ならないことに留意する必要がある（表３及び４）．

閾値を含む線量反応モデル．線量反応関係における閾値の問題を検討するために，個人線量データ及び

FIGURE 3 THE FREQUENCY OF SEVERE MENTAL RETARDATION AMONG THOSE EXPOSED IN UTERO BY DOSE AND GESTATIONAL AGE, BOTH CITIES COMBINED

図 3 胎内被爆者の重度精神遅滞頻度，線量別及び胎内週齢別，両市合計



The vertical lines indicate the 90% confidence intervals.
縦線は90%信頼限界を示す.

TABLE 4a EXPONENTIAL LINEAR-RESPONSE RELATIONSHIP OF SEVERE MENTAL RETARDATION TO GROUPED FETAL ABSORBED DOSES FOR ALL INDIVIDUALS INCLUDED IN THE T65DR AND DS86 SAMPLES DESCRIBED IN TABLES 2a AND b

表4a 表2a及び2bに示したT65DR標本及びDS86標本に含まれる全対象者に関する重度精神遅滞とグループ胎児吸収線量の指数線形反応関係

Gestational age	Cities combined						Hiroshima only					
	a	b	s_b	χ^2_{Res}	χ^2_{Res}	P_{Res}	a	b	s_b	χ^2_{Reg}	χ^2_{Res}	P_{Res}
T65DR Sample												
A. Relationship to fetal absorbed dose.												
All gestational ages	0.763	0.194	0.049	15.50**	4.97	0.17	0.566	0.255	0.070	13.10**	3.87	0.28
8 - 15 weeks	0.824	0.560	0.149	14.07**	2.66	0.45	0.247	0.706	0.124	32.27**	1.83	0.40
16 - 25 weeks	0.604	0.104	0.063	2.73 Sug	2.10	0.55	0.783	0.104	0.076	1.85	4.32	0.23
B. Relationship to fetal absorbed dose when the "controls" are excluded.												
8 - 15 weeks	1.419	0.535	0.168	10.13**	2.53	0.28	1.691	0.621	0.226	7.54**	0.92	0.34
16 - 25 weeks	0.401	0.110	0.070	2.47	2.08	0.35	0.595	0.110	0.085	1.65	4.25	0.12
C. Relationship to fetal absorbed dose when all "controls" are combined.												
Pooled control (8-15 weeks)	0.843	0.556	0.148	14.34**	2.65	0.45	0.616	0.676	0.193	12.26**	1.13	0.57
DS86 Sample												
A. Relationship to fetal absorbed dose.												
All gestational ages	0.742	0.169	0.041	16.71**	15.78	< 0.01	0.561	0.171	0.046	13.52**	8.53	0.04
8 - 15 weeks	0.746	0.479	0.124	14.97**	7.09	0.07	0.164	0.516	0.076	46.28**	4.42	0.22
16 - 25 weeks	0.612	0.095	0.056	2.90 Sug	7.35	0.06	0.800	0.074	0.055	1.81	4.68	0.20
B. Relationship to fetal absorbed dose when the "controls" are excluded.												
8 - 15 weeks	0.053	0.501	0.144	12.18**	7.13	0.03	0.667	0.464	0.154	9.10	4.03	0.13
16 - 25 weeks	0.039	0.101	0.062	2.63	7.30	0.03	0.683	0.076	0.060	1.64	4.70	0.10
C. Relationship to fetal absorbed dose when all "controls" are combined.												
Pooled control (8-15 weeks)	0.834	0.477	0.123	14.98**	7.10	0.07	0.609	0.466	0.132	12.47**	4.04	0.26

See the descriptions and significance levels in Table 3a.

表3aの注及び有意水準を参照.

An exponential linear model $P_i = 1 - \exp[-(a + bD_i)]$ (i=1, 2, ... , 5 or 4) was used in all of the analyses above.

上記のすべての解析は指数線形モデル: $P_i = 1 - \exp\{-(a + bD_i)\}$ (i=1,2,..., 5又は4)を用いた.

TABLE 4b EXPONENTIAL LINEAR-RESPONSE RELATIONSHIP OF SEVERE MENTAL RETARDATION TO GROUPED FETAL ABSORBED DOSES AFTER THE EXCLUSION OF FIVE SEVERELY RETARDED CASES WITH PROBABLE NONRADIATION-RELATED ETIOLOGIES IN THE T65DR AND DS86 SAMPLES DESCRIBED IN TABLES 2a AND b

表4b 表2a及び2bに示したT65DR標本及びDS86標本から放射線に関連しない病因と考えられる重度精神遅滞5例を除外した後の重度精神遅滞とグループ胎児吸収線量の指数線形反応関係

Gestational age	Cities combined						Hiroshima only					
	a	b	s_b	χ^2_{Reg}	χ^2_{Res}	p_{Res}	a	b	s_b	χ^2_{Reg}	χ^2_{Res}	p_{Res}
T65DR Sample												
A. Relationship to fetal absorbed dose.												
All gestational ages	0.572	0.172	0.045	14.31**	8.02	0.05	0.332	0.220	0.064	11.77**	6.67	0.08
8 - 15 weeks	0.824	0.492	0.140	12.26**	4.91	0.18	0.233	0.557	0.112	24.57**	4.11	0.13
16 - 25 weeks	0.237	0.094	0.056	2.84 Sug	2.86	0.41	0.301	0.094	0.066	2.00	5.42	0.14
B. Relationship to fetal absorbed dose when the "controls" are excluded.												
8 - 15 weeks	1.310	0.473	0.155	9.32**	4.77	0.09	1.691	0.524	0.204	6.60**	2.81	0.09
16 - 25 weeks	-	-	-	-	-	-	-	-	-	-	-	-
C. Relationship to fetal absorbed dose when all "controls" are combined.												
Pooled control (8-15 weeks)	0.660	0.499	0.139	12.84**	4.99	0.17	0.375	0.593	0.180	10.81 *	3.25	0.06
DS86 Sample												
A. Relationship to fetal absorbed dose.												
All gestational ages	0.554	0.151	0.039	15.28**	19.26	<0.01	0.324	0.145	0.042	12.15**	11.21	<0.01
8 - 15 weeks	0.744	0.425	0.117	13.12**	9.36	0.02	0.116	0.372	0.066	31.85**	7.00	0.07
16 - 25 weeks	0.242	0.085	0.050	2.91 Sug	8.13	0.04	0.303	0.067	0.048	1.91	4.99	0.17
B. Relationship to fetal absorbed dose when the "controls" are excluded.												
8 - 15 weeks	0.132	0.444	0.134	10.92**	9.44	<0.01	0.714	0.398	0.141	7.95**	5.78	0.06
16 - 25 weeks	-	-	-	-	-	-	-	-	-	-	-	-
C. Relationship to fetal absorbed dose when all "controls" are combined.												
Pooled control (8-15 weeks)	0.651	0.427	0.118	13.40**	9.36	0.02	0.369	0.410	0.124	10.97**	5.92	0.12

See footnote on the five cases with probable nonradiation-related etiologies in Table 2a and the description of the exponential model in Table 4a.

放射線に関連しない病因が考えられる5例に関する表2aの脚注及び指数モデルに関する表4aの注を参照.

TABLE 5 LINEAR-QUADRATIC AND QUADRATIC RESPONSE RELATIONSHIPS OF SEVERE MENTAL RETARDATION TO GROUPED FETAL ABSORBED DOSES FOR ALL INDIVIDUALS INCLUDED IN THE DS86 SAMPLE

表5 DS86 標本に含まれる全対象者に関する重度精神遅滞とグループ胎児吸収線量の線形-2次及び2次反応関係

Gestational Age	MLE of Regression Coefficients						Goodness of fit	
	a	s_a	b (Gy^{-1})	s_b (Gy^{-1})	c (Gy^{-2})	s_c (Gy^{-2})	χ^2_{Res}	P_{Res}
Model: (Q) $P_i = a + cD_i^2$ or (L-Q) $P_i = a + bD_i + cD_i^2$								
All gestational ages:								
Q	0.858	0.247			0.221**	0.046	2.04	0.56
L-Q	0.962	0.287	-0.048	0.049	0.270**	0.069	1.62	0.44
8-15 weeks:								
Q	1.318	0.654			0.401**	0.058	4.26	0.10
L-Q	0.981	0.644	0.136	0.152	0.291*	0.136	2.78	0.25
16-15 weeks:								
Q	0.685	0.400			0.131 Sug	0.070	3.36	0.34
L-Q	0.734	0.448	-0.038	0.110	0.182	0.141	2.85	0.24
Relationship of severe mental retardation to dose: "controls" excluded								
8-15 weeks:								
Q	3.274	1.967			0.383**	0.063	0.97	0.62
16-25 weeks:								
Q	0.779	0.809			0.130 Sug	0.070	3.19	0.20
Model: (Q) $P_i = 1-\exp(-(a + cD_i^2))$ or (L-Q) $P_i = 1-\exp(-(a + bD_i + cD_i^2))$								
All gestational ages:								
Q	0.854	0.248			0.261**	0.066	2.76	0.43
L-Q	0.993	0.295	-0.068	0.053	0.343**	0.101	2.02	0.36
8-15 weeks:								
Q	1.202	0.632			0.681**	0.194	3.91	0.27
L-Q	1.073	0.704	0.058	0.177	0.612**	0.282	3.48	0.18
16-25 weeks:								
Q	0.689	0.404			0.137 Sug	0.081	3.66	0.30
L-Q	0.752	0.448	-0.064	0.071	0.241*	0.113	3.55	0.17
Relationship of severe mental retardation to dose: "controls" excluded								
8-15 weeks:								
Q	2.823	1.930			0.636**	0.193	1.16	0.56
16-25 weeks:								
Q	0.788	0.822			0.136 Sug	0.081	3.48	0.18

See the descriptions and significance level in Table 3a.

表3a の注及び有意水準を参照.

TABLE 6 RELATIONSHIP OF SEVERE MENTAL RETARDATION TO INDIVIDUAL FETAL ABSORBED DOSES FOR ALL MEMBERS OF THE T65DR AND DS86 SAMPLES BASED ON A LINEAR-RESPONSE MODEL WITHOUT A THRESHOLD

表6　閾値を含まない線形反応モデルに基づく T65DR 標本及び DS86 標本の全対象者に関する重度精神遅滞と個人胎児吸収線量の関係

Gestational age	T65DR sample					DS86 sample				
	a	S_a	b	S_b	χ^2_{Reg}	a	S_a	b	S_b	χ^2_{Reg}
All individuals included in T65DR and DS86 samples										
All gestational ages	0.789	0.242	0.184	0.044	-17.64^{**}	0.745	0.238	0.168	0.039	18.88^{**}
8-15 weeks	1.063	0.630	0.369	0.057	42.00^{**}	0.724	0.499	0.466	0.098	$22{\cdot}74^{**\dagger}$
16-25 weeks	0.631	0.395	0.104	0.061	2.89^{Sug}	0.645	0.410	0.090	0.053	2.91^{Sug}
8-15 weeks (pooled control)	0.897	0.287	0.372	0.055	45.64^{**}	0.825	0.272	0.463	0.097	$22.70^{**\dagger}$
After the exclusion of the five cases with probable nonradiation-related etiologies in the T65DR and DS86 samples										
All gestational ages	0.580	0.206	0.169	0.042	16.26^{**}	0.550	0.203	0.152	0.037	17.08^{**}
8-15 weeks	0.989	0.593	0.353	0.065	29.92^{**}	0.722	0.496	0.424	0.098	18.71^{**}
16-25 weeks	0.231	0.231	0.099	0.057	3.05^{Sug}	0.241	0.241	0.085	0.049	3.03^{Sug}
8-15 weeks (pooled control)	0.699	0.254	0.358	0.062	33.10^{**}	0.644	0.241	0.426	0.097	19.11^{**}

See the descriptions and significance levels in Table 3a.

表3a の注及び有意水準を参照.

A linear model $P_i = a + bD_i$ (i=1, 2, ... , n) was applied for individual binary response data (1,0).

線形モデル $P_i = a + bD_i$ (i=1, 2, ..., n)を個人二値反応データ(1, 0)に適用した.

†When the expected values for a few cases were larger than 1.0, the Newton-Raphson iterative values and the log likelihood were adjusted to 0.999.

数例の期待値が1.0を超える場合は, Newton-Raphson 反復値及び対数尤度を0.999に補正した.

TABLE 7 RELATIONSHIP OF SEVERE MENTAL RETARDATION TO INDIVIDUAL FETAL ABSORBED DOSES FOR ALL MEMBERS OF THE T65DR AND DS86 SAMPLES BASED ON AN EXPONENTIAL LINEAR-RESPONSE MODEL WITHOUT A THRESHOLD

表7 閾値を含まない指数線形反応モデルに基づくT65DR標本及びDS86標本の全対象者に関する重度精神遅滞と個人胎児吸収線量の関係

Gestational age	T65DR sample					DS86 sample				
	a	S_a	b	S_b	χ^2_{Reg}	a	S_a	b	S_b	χ^2_{Reg}
	All individuals included in T65DR and DS86 samples									
All gestational ages	0.793	0.245	0.190	0.049	15.22**	0.751	0.241	0.172	0.042	16.57**
8-15 weeks	0.939	0.601	0.526	0.144	13.39**	0.733	0.509	0.500	0.129	15.00**
16-25 weeks	0.635	0.399	0.104	0.063	2.68	0.650	0.414	0.090	0.055	2.72Sug
8-15 weeks (poolded control)	0.870	0.284	0.529	0.142	13.87**	0.831	0.275	0.497	0.128	14.99**
	After the exclusion of the five cases with probable nonradiation-related etiologies in the T65DR and DS86 samples									
All gestational ages	0.583	0.208	0.173	0.046	14.26**	0.554	0.205	0.154	0.039	15.25**
8-15 weeks	0.920	0.583	0.463	0.135	11.78**	0.735	0.508	0.443	0.122	13.12**
16-25 weeks	0.233	0.233	0.099	0.059	2.86Sug	0.242	0.242	0.085	0.050	2.86Sug
8-15 weeks (poolded control)	0.682	0.252	0.473	0.134	12.45**	0.649	0.244	0.445	0.122	13.38**

See the descriptions in Table 6.

表6の注を参照.

An exponential linear model $P_i = 1 - \exp[-(a + bD_i)]$ (i=1, 2, ... , n) has been fitted to individual binary response data (1,0).

指数線形モデル $P_i = 1 - \exp[-(a + bD_i)]$ (i=1, 2, ... , n)を個人二値反応データ(1, 0)に適用した.

grouped data have been used. The thresholds that are estimated are set forth in Tables 8a (grouped) and 8b (individual) for the simple linear model, and in Tables 9a (grouped) and 9b (individual) for the exponential linear model. It should be noted that irrespective of the method of analysis there is little or no evidence of a threshold when the T65DR dosimetry is used except within the 16-25 week period, but this is not true with regard to the DS86 doses. The estimated lower bound of the threshold for the most sensitive critical period of 8-15 weeks after fertilization for the DS86 sample and also for 8-15 weeks with the pooled control is zero dose for both the grouped and ungrouped data with the simple linear model (Table 8). With the exclusion of the five cases with probable nonradiation-related etiologies, a threshold emerges; it is 0.39 Gy (lower bound 0.12 Gy) with the grouped data, and 0.46 (lower bound 0.23) with the ungrouped, both significantly different from zero.

Under an exponential linear model, using all of the cases, a significant threshold emerges with or without exclusion of the questionable cases; within the 8-15 weeks group, the lower bound of the estimated threshold is 0.09 Gy for the grouped data and 0.15 Gy for the individual within the 8-15 week interval (Table 9). However, as Figure 4 illustrates, the log likelihood does not change markedly over a substantial range of possible threshold values, suggesting that the threshold itself is not well-estimated. This is, of course, also suggested by the large variances of the estimates themselves.

For the 16-25 weeks period, with and without inclusion of the two individuals alluded to previously, a threshold above 0.20 Gy seems to be present. Using the DS86 doses, the lower 95% bound of the threshold appears to be 0.21 Gy based on a linear model with either the individual or the dose-grouped data (Table 8) and to be 0.22-0.25 Gy with the exponential linear model (Table 9). If the results from the linear model may be considered conservative, the threshold for 16-25 weeks after fertilization is not less than 0.20 Gy but for the period 8-15 weeks after fertilization a threshold, if one exists, appears to be lower.

Uncertainties

A number of uncertainties are associated with these estimates of risk. These include the limited nature of the data, the appropriateness of the compari-

グループ線量データの両方を用いた．単純な線形モデルについては表8a（グループデータ）と8b（個人データ），指数線形モデルについては表9a（グループデータ）と9b（個人データ）に，推定した閾値を示した．T65DR線量推定方式では，いずれの解析方法を用いても16～25週齢の期間を除き閾値の存在はほとんど又は全く認めないが，DS86線量方式については状況が異なることに留意しなければならない．DS86標本及び全対照群によるいずれも最も感受性が高い危険期間の受胎後８～15週齢の閾値の下限推定値は，単純な線形モデルを用いたグループデータ及び個人データの両方に線量ゼロを含む（表８）．恐らく病因が放射線に関連していないと思われる５例を除外すると，閾値が存在する．グループデータについては 0.39 Gy（下限値は 0.12 Gy），個人データについては 0.46 Gy（下限値は 0.23 Gy）であり，両方共にゼロから有意に異なる．

指数線形モデルでは，全症例を用いると，疑わしい症例を除外するか否かにかかわらず有意な閾値が存在する．８～15週齢群では，閾値の下限推定値はグループデータの場合 0.09 Gy，個人データの場合 0.15 Gy である（表９）．しかし，図４に示すように，可能な閾値の実質的範囲内の対数尤度値は著しく変化しないために，閾値自体が正確に推定されないことを示唆する．もちろん，これは，推定値自体の大きな分散からも示唆される．

16～25週の期間については，前述した２例を含むか否かにかかわらず，0.20 Gy を超える閾値が存在すると思われる．DS86 線量を用いると，閾値の95％下限推定値は，個人又はグループ線量データに線形モデルを当てはめた場合 0.21 Gy（表８），指数線形モデルを当てはめた場合 0.22～0.25 Gy（表９）であるようである．線形モデルを用いた結果が控え目であるとすれば，受胎後16～25週齢の閾値は 0.20 Gy を下がることはないが，受胎後８～15週齢については，もし閾値が存在するならば，それ以下になると思われる．

不確定要素

これらのリスク推定値は多くの不確定要素と関係している．その中には，データに制限があること，

TABLE 8a ESTIMATED THRESHOLDS WITH THEIR 95% LOWER AND UPPER BOUNDS AND THE RELATIONSHIP OF SEVERE MENTAL RETARDATION TO GROUPED FETAL ABSORBED DOSES FOR ALL MEBERS OF THE T65DR AND DS86 SAMPLES BASED ON A LINEAR-RESPONSE MODEL

表8a 線形反応モデルに基づく T65DR 標本及び DS86 標本の全対象者の閾値とその95%下限・上限推定値，及び重度精神遅滞とグループ胎児吸収線量の関係

Gestational age	T65DR sample						DS86 sample					
	a	S_a	b	S_b	χ^2_{Res}	T	a	S_a	b	S_b	χ^2_{Res}	T
All individuals included in T65DR and DS86 samples												
All gestational ages	0.941	0.255	0.300**	0.069	0.73	0.18 (L=0, U=0.51)	0.949	0.252	0.498**	0.100	0.76	0.47* (L=0.18, U=0.61)
8-15 weeks	0.866	0.571	0.462**	0.091	1.55	0 (L=0, U=0.20)	1.352	0.644	0.613**	0.101	4.09	0.20 (L=0, U=0.55)
16-25 weeks	0.683	0.392	0.206 Sug	0.113	0.81	0.23 (L=0, U=0.68)	0.697	0.398	0.497*	0.231	1.52	0.64* (L=0.21, U≧0.64)†
8-15 weeks (Pooled control)	0.850	0.278	0.462**	0.090	1.55	0 (L=0, U=0.16)	0.988	0.294	0.608**	0.099	6.03	0.19 (L=0, U=0.52)
After the exclusion of the five cases with probable nonradiation-related etiologies in the T65DR and DS86 samples												
All gestational ages	0.719	0.221	0.312**	0.073	0.53	0.21* (L=0.11, U=0.58)	0.679	0.214	0.521**	0.106	0.43	0.51* (L=0.21, U=0.63)
8-15 weeks	1.522	0.661	0.566**	0.108	4.64	0.18 (L=0, U=0.59)	1.405	0.623	0.743**	0.121	3.89	0.39* (L=0.12, U=0.60)
16-25 weeks	0.232	0.230	0.213 Sug	0.113	0.63	0.23 (L=0, U=0.67)	0.697	0.398	0.497*	0.231	1.52	0.64* (L=0.21, U≧0.64)†
8-15 weeks (Pooled control)	0.664	0.246	0.433**	0.093	3.67	0 (L=0, U=0.23)	0.857	0.270	0.741**	0.119	8.09*	0.38* (L=0.10, U=0.60)

Threshold (T) and its 95% lower (L) and upper (U) bounds are expressed in grays.

閾値(T)とその95%下限(L)及び上限(U)推定値を gray 単位で示す.

See the descriptions in Table 6.

表6の注を参照.

A linear model $P_i = a + b(D_i - T)$ (i=1, 2, ... , 5) was used in all of the analyses above.

上記のすべての解析は線形モデル $P_i = a + b(D_i - T)$ (i=1, 2,..., 5)を適用した.

† The upper bound was not determined because the log likelihood values above 0.64 Gy are almost constant.

0.64 Gy を超える対数尤度値はほとんど一定であるので，上限は推定されない.

TABLE 8b ESTIMATED THRESHOLDS WITH THEIR 95% LOWER AND UPPER BOUNDS AND THE RELATIONSHIP OF SEVERE MENTAL RETARDATION TO INDIVIDUAL FETAL ABSORBED DOSES FOR ALL MEMBERS OF THE T65DR AND DS86 SAMPLES BASED ON A LINEAR-RESPONSE MODEL

表8b 線形反応モデルに基づくT65DR標本及びDS86標本の全対象者の閾値とその95%下限・上限推定値，及び重度精神遅滞と個人胎児吸収線量の関係

Gestational age	T65DR sample					DS86 sample				
	a	S_a	b	S_b	T	a	S_a	b	S_b	T
All individuals included in T65DR and DS86 samples										
All gestational ages	0.947	0.251	0.330**	0.070	0.23* (L=0.08, U=0.33)	0.952	0.253	0.419**	0.062	0.43* (L=0.23, U=0.56)
8-15 weeks	1.063	0.630	0.369**	0.057	0 (L=0, U=0.24)	1.664	0.673	0.996**	0.146	0.40 (L=0, U=0.56)†
16-25 weeks	0.674	0.388	0.464Sug	0.237	0.54* (L=0.04, U=0.71)	0.693	0.399	0.532*	0.234	0.70* (L=0.21, U=0.99)
8-15 weeks (pooled control)	0.897	0.287	0.372**	0.055	0 (L=0, U=0.11)	1.039	0.298	0.763**	0.131	0.24 (L=0, U=0.55)†
After the exclusion of the five cases with probable nonradiation-related etiologies in the T65DR and DS86 samples										
All gestational ages	0.678	0.213	0.335**	0.072	0.25* (L=0.11, U=0.53)	0.680	0.214	0.445**	0.061	0.50* (L=0.30, U=0.61)
8-15 weeks	1.467	0.646	0.409**	0.057	0.17 (L=0, U=0.31)	1.378	0.612	1.095**	0.158	0.46* (L=0.23, U=0.62)†
16-25 weeks	0.226	0.226	0.463*	0.231	0.53* (L=0.04, U=0.71)	0.232	0.232	0.539*	0.233	0.70* (L=0.21, U=0.99)
8-15 weeks (pooled control)	0.699	0.254	0.358**	0.062	0 (L=0, U=0.28)	0.852	0.268	1.104**	0.157	0.46* (L=0.23, U=0.61)†

Threshold (T) and its 95% lower (L) and upper (U) bounds are expressed in grays.

閾値(T)とその95%下限(L)及び上限(U)推定値をgray単位で示す.

See the descriptions in Table 6.

表6の注を参照.

A linear model $P_i = a + b(D_i - T)$ (i=1, 2, ..., n) has been fitted to individual binary response data (1,0).

線形モデル $P_i = a + b(D_i - T)$ (i=1, 2, ..., n)を個人二値反応データ(1, 0)に適用した.

TABLE 9a ESTIMATED THRESHOLDS WITH THEIR 95% LOWER AND UPPER BOUNDS AND THE RELATIONSHIP OF SEVERE MENTAL RETARDATION TO GROUPED FETAL ABSORBED DOSES FOR ALL MEMBERS OF THE T65DR AND DS86 SAMPLES BASED ON AN EXPONENTIAL LINEAR-RESPONSE MODEL

表9a 指数線形反応モデルに基づくT65DR標本及びDS86標本の全対象者の閾値とその95%下限・上限推定値，及び重度精神遅滞とグループ胎児吸収線量の関係

Gestational age	T65DR sample						DS86 sample					
	a	S_a	b	S_b	χ^2Res	T	a	S_a	b	S_b	χ^2Res	T
All individuals included in T65DR and DS86 samples												
All gestational ages	0.948	0.258	0.365^{**}	0.100	0.74	0.19^{*} (L=0.05, U=0.57)	0.679	0.215	0.665^{**}	0.178	0.59	0.51^{*} (L=0.20, U=0.62)
8-15 weeks	0.824	0.559	0.560^{**}	0.149	2.66	0 (L=0, U=0.22)	1.695	0.692	1.493^{**}	0.450	4.52	0.66^{*} (L=0.09, U=0.61)
16-25 weeks	0.684	0.394	0.232	0.141	0.74	0.23 (L=0, U=0.69)	0.700	0.401	0.626^{Sug}	0.370	1.52	0.64^{*} (L=0.22, U≥0.64)
8-15 weeks (Pooled control)	0.843	0.278	0.559^{**}	0.148	2.65	0 (L=0, U=0.20)	0.812	0.269	0.916^{**}	0.254	8.92^{*}	0.20^{*} (L=0.09, U=0.60)
After the exclusion of the five cases with probable nonradiation-related etiologies in the T65DR and DS86 samples												
All gestational ages	0.737	0.224	0.384^{**}	0.109	0.48	0.22^{*} (L=0.12, U=0.62)	0.682	0.216	0.743^{**}	0.200	0.43	0.55^{*} (L=0.22, U=0.63)
8-15 weeks	1.544	0.675	0.872^{**}	0.281	5.06	0.20 (L=0, U=0.67)	1.415	0.632	1.585^{**}	0.498	3.89	0.51^{*} (L=0.17, U=0.62)
16-25 weeks	0.232	0.230	0.239^{Sug}	0.140	0.56	0.23 (L=0, U=0.68)	0.242	0.236	0.632^{Sug}	0.370	0.40	0.64^{*} (L=0.22, U≥0.64)†
8-15 weeks (Pooled control)	0.877	0.276	0.901^{**}	0.282	10.78^{*}	0.20 (L=0, U=0.67)	0.861	0.272	1.557^{**}	0.483	8.09^{*}	0.50^{*} (L=0.16, U=0.62)

Threshold (T) and its 95% lower (L) and upper (U) bounds are expressed in grays.

閾値(T)とその95%下限(L)及び上限(U)推定値をgray単位で示す.

See the descriptions in Table 6.

表6の注を参照.

An exponential linear model $P_i = 1 - \exp[-\{a + b(D_i - T)\}]$ (i=1, 2, ... , 5) was used in all of the analyses above.

上記のすべての解析は指数線形モデル $P_i = 1 - \exp[-\{a + b(D_i - T)\}]$ (i=1, 2,..., 5)を適用した.

† The upper bound was not determined because the log likelihood values above 0.64 Gy are almost constant.

0.64 Gyを超える対数尤度値はほとんど一定であるので，上限は推定されない.

TABLE 9b ESTIMATED THRESHOLDS WITH THEIR 95% LOWER AND UPPER BOUNDS AND THE RELATIONSHIP OF SEVERE MENTAL RETARDATION TO INDIVIDUAL FETAL ABSORBED DOSES FOR ALL MEMBERS OF THE T65DR AND DS86 SAMPLES BASED ON AN EXPONENTIAL LINEAR-RESPONSE MODEL

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Gestational age	T65DR sample					DS86 sample				
	a	S_a	b	S_b	T	a	S_a	b	S_b	T
All individuals included in T65DR and DS86 samples										
All gestational ages	0.949	0.253	0.405**	0.109	0.24* (L=0.11, U=0.33)	0.953	0.254	0.742**	0.195	0.50* (L=0.33, U=0.60)
8-15 weeks	1.720	0.700	0.845**	0.255	0.20 (L=0, U=0.31)	1.694	0.691	1.584**	0.486	0.46* (L=0.15, U=0.59)
16-25 weeks	0.676	0.390	0.511Sug	0.309	0.53* (L=0.04, U=0.71)	0.694	0.400	0.733Sug	0.437	0.71* (L=0.25, U=1.00)
8-15 weeks (pooled control)	0.870	0.284	0.529**	0.142	0 (L=0, U=0.29)	1.105	0.302	0.965**	0.276	0.25* (L=0.16, U=0.59)
After the exclusion of the five cases with probable nonradiation-related etiologies in the T65DR and DS86 samples										
All gestational ages	0.677	0.213	0.398**	0.108	0.25* (L=0.12, U=0.58)	0.677	0.214	0.811**	0.218	0.55* (L=0.37, U=0.67)
8-15 weeks	1.425	0.635	0.810**	0.252	0.21 (L=0, U=0.31)	1.411	0.630	1.926**	0.624	0.55* (L=0.30, U=0.67)
16-25 weeks	0.226	0.226	0.539Sug	0.318	0.54* (L=0.04, U=0.71)	0.232	0.232	0.743Sug	0.437	0.71* (L=0.25, U=0.99)
8-15 weeks (pooled control)	0.853	0.270	0.845**	0.259	0.22 (L=0, U=0.31)	0.860	0.272	1.945**	0.625	0.55* (L=0.30, U=0.61)

Threshold (T) and its 95% lower (L) and upper (U) bounds are expressed in grays.

閾値(T)とその95%下限(L)及び上限(U)推定値をgray単位で示す.

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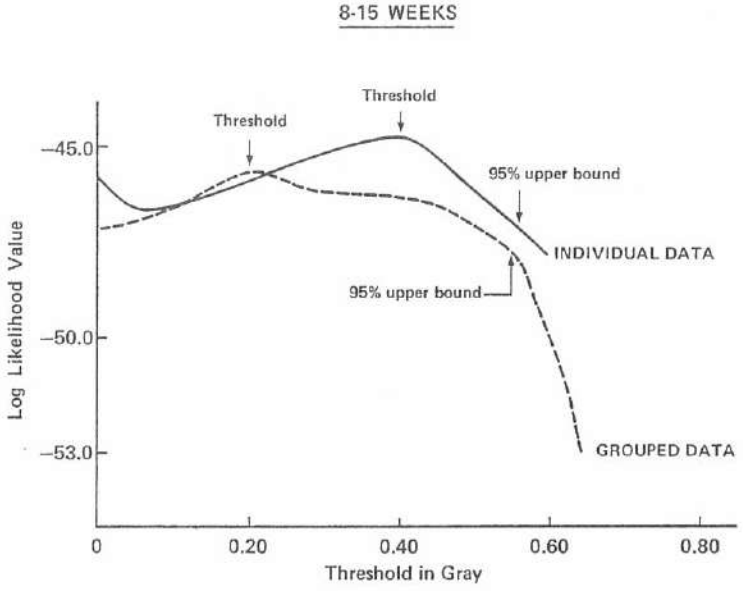
表6の注を参照.

An exponential linear model $P_i = 1 - \exp[-\{a + b(D_i - T)\}]$ (i=1, 2, ..., n) was fitted to the individual binary response data (1, 0).

指数線形モデル $P_i = 1 - \exp[-\{a + b(D_i - T)\}]$ (i=1, 2, ..., n)を個人二値反応データ(1, 0)に適用した.

FIGURE 4 THE LOG LIKELIHOODS OF VARIOUS THRESHOLDS AND THE 95% UPPER AND LOWER BOUNDS FOR THE THRESHOLD WITH THE HIGHEST LIKELIHOOD BASED ON INDIVIDUAL AND GROUPED DATA USING THE DS86 SAMPLE AND THE PERIOD 8-15 WEEKS AFTER FERTILIZATION

図 4　DS 86 標本の受胎後 8 ～15週齢の個人データ及びグループデータに基づいた種々の閾値に対する対数尤度値，及び最大尤度値をもつ閾値の95%上限・下限推定値



group, errors in the estimation of the tissue-absorbed doses and the prenatal ages at exposure, the variation in severity of mental retardation, and other confounding factors in the postbomb period, including nutrition and disease.

The limited data and the appropriateness of the comparison group. Only 21 of the 30 severely mentally retarded individuals in the revised clinical sample received "fetal" absorbed doses of 0.01 Gy or more, and 3 of these had health problems which could account for their retardation and not be radiation-related (2 cases of Down's syndrome and 1 case of Japanese encephalitis in infancy). As earlier noted, their exclusion does not alter the slope of the dose-response relationship materially; however, with their removal, there are only 18 cases without known cause for the retardation other than exposure to ionizing radiation.

It is important to bear in mind that the clinical observations are based on a sample, and not a full birth cohort in the usual sense. We know the cases and numbers of individuals at risk to be incomplete for at least three reasons. First, the primary source of

比較群の妥当性，組織吸収線量推定及び胎児の被爆時週齢の誤差，精神遅滞の重篤度の差異，栄養及び疾病などの原爆被爆後の交絡因子が含まれる．

データの制限及び比較群の妥当性． 改定臨床標本に含まれる重度精神遅滞30例のうちわずかに21例が0.01 Gy 以上の"胎児"吸収線量を受けており，それらのうち 3 例に精神遅滞の原因と思われるが放射線に関連しない健康上の問題があった（2 例は Down 症候群，1 例は幼児期の日本脳炎罹患）．前述したように，これらの症例を除外しても線量反応関係の勾配は実質的には変化しない．しかしこれらを除外すると，電離放射線被曝以外に精神遅滞の原因が考えられない症例はわずか18例である．

臨床的観察が通常の意味での出生児集団全体ではなく，標本に基づくことに留意する必要がある．観察集団及びその対象者数が不完全であることは少なくとも三つの理由により明らかである．第一に，標本

ascertainment of the sample was through births registered in Hiroshima and Nagasaki. Prenatally exposed survivors whose births were registered elsewhere are not included. Second, presence in the clinical sample entailed residence within contact areas (essentially the limits of the two cities), and thus migrants from the contact area after birth are not included. Finally, limited clinical space and personnel were determiners of the size of the sample. For example, it does not include survivors exposed at distances of 2,000-2,499 m, since at the time of the definition of the sample, these individuals were presumed to have received little or no irradiation.

While it is impracticable, if not impossible, to estimate the incompleteness of the clinical sample, through a comparison of our roster of cases with those of a variety of special survivor societies in Hiroshima, we have identified five exposed mentally retarded individuals not within the clinical sample. Four of these five were exposed in the 8-15 week interval, and all within 1,000 m or so of the hypocenter. While these cases cannot be factored into the dose-response relationship, since the number of individuals at risk from which they are drawn is unknown, they do provide information on the sensitive period, for gestational age at exposure is not a criterion for enrollment in the groups whose rosters are available.

As to the comparison group, the A-bombings resulted in exceptional circumstances that could have altered the normal frequency of severe mental retardation or have interacted with exposure nonadditively. However, as has previously been seen, exclusion of the comparison population does not generally alter the regression coefficient appreciably.

Errors in the estimation of fetal absorbed dose. All estimates of the doses to survivors of the A-bombing are subject to at least three sources of error, namely those that stem from: a) the air dose curves themselves, b) the attenuation factors for tissues, materials, positions, and the like, and c) the assertions of the survivors as to their locations. Some of these, notably the assertions of the survivors, can never be evaluated rigorously for all of the individuals concerned. Errors of this nature can affect inferences on the overall shape of the dose-response relationship as well as parameter values defining that shape.

確認の主な情報源は広島・長崎の出産登録である．それ以外の場所で出産が登録されている胎内被爆者は含まれていない．第二に，連絡区域内(基本的には両市内)に居住していなければ臨床標本には含まれないので，出生後連絡区域外へ転出した者は除外されている．最後に，臨床検査のためのスペースと人員が標本の大きさを制限する．例えば，2,000～2,499m での被爆者は，標本を決定する時期にはほとんど又は全く放射線を受けていないと考えられたため，対象から除外されている．

臨床集団の不完全性を推定することは不可能でなくとも困難であるが，本調査の対象としている症例のリストを広島にある様々な特別の被爆者団体のリストと比較することにより，臨床集団に含まれていない5例の精神遅滞者を確認している．この5例のうち4例は8～15週齢に被爆しており，5例全員が爆心地から1,000m以内で被爆している母集団である．観察対象者の数が判明していないためにこれらの症例は線量反応関係を検討する因数としては扱うことができないが，被爆時の胎内週齢が現在利用している集団への登録の基準になっていないために，これらの症例は感受性の高い時期に関する情報を与える．

比較群についてであるが，原爆は通常の重度精神遅滞頻度を変化させるか，又は非相加的に被爆と相互作用するような例外的状況をもたらした．しかし，前述したように，一般的には比較集団を除外しても回帰係数はあまり変化しない．

胎児吸収線量推定の誤差． 原爆被爆者の線量推定値にはすべて，少なくとも三つの誤差原因がある．すなわち，a) 空中線量曲線自体，b) 組織，遮蔽材料，位置関係などによる減衰率，c) 被爆者の位置に関する被爆者自身の発言に誤差があると考えられる．これらの幾つかのうち，特に被爆者発言については，関係者全員に対して厳密に評価することはできない．この種の誤差は，線量反応関係の全体的形状並びにそれを決定するパラメターの推定値に影響を及ぼす．

Errors in the estimation of prenatal age at exposure. The apparent timing of vulnerable events in development can be affected by errors in the determination of prenatal age, and possibly seriously so in specific cases. Postovulatory age is usually estimated from the onset of the last menstrual period, and adjustment is then made for the difference between that date and the probable date of fertilization (usually taken to be two weeks later). Women with irregular menstrual cycles or who miss a menstrual period for any of several reasons, notably lactational amenorrhea, illness or malnutrition, could erroneously identify the onset of their last cycle. All of these possible sources of error were present immediately prior to the cessation of hostilities in Japan. Women nursed their infants longer then than now prevails, so lactational amenorrhea may have been more common. Some were undernourished due to the economic stringencies that obtained during and following the war, and infectious diseases were more frequent in the surviving populations. The impact of these factors on the estimated ages we use is impossible to assess. No less important than these sources of error in the age after fertilization is the normal variability in developmental age, the critical measure of vulnerability, for fixed intervals of time after fertilization. Conceivably, some, possibly much, of the effect seen in the 16-25 week interval could be ascribable to individuals whose developmental ages were less than their chronological ages.

DISCUSSION

Two substantial observations previously made on the basis of the T65DR dosimetry[6] are not changed by the reassessment based on the DS86 sample: First, significant harmful effects of radiation on the developing brain of children exposed in utero in Hiroshima and Nagasaki are observed only for the periods 8-15 and 16-25 weeks after fertilization under both dosimetries. In the 8-15 week period, the one of maximum sensitivity, the dose-response relationship appears distinctly different from that at subsequent gestational ages, which suggests that the mechanism(s) through which radiation impinges on cerebral growth and development may vary with the gestational age at exposure. This period of maximum radiation sensitivity is also a time at which fundamentally important aspects of normal cerebral histogenesis occur. The neurons which will populate the cerebral cortex are generated exclusively in proliferative zones that are situated close to the ven-

被爆時胎内週齢推定の誤差. 発達過程において影響を受けやすい事象が起こる時期は，胎内週齢推定の誤差により，誤って推定される可能性があり，恐らく特定の症例についてはその可能性が大である．胎内週齢は通常最終月経の開始日から推定されるが，その日と推定受胎日（普通２週間後）の差異について補正する．月経周期が不規則な女性又は授乳性無月経，疾病，栄養失調などの理由により月経が飛んでいる女性の場合，最終周期の開始日を確認する際に誤りが生じやすい．日本では終戦直前までこのような誤差の原因となりうる要素が多く存在していた．当時の女性は一般的に現在より長期間にわたり授乳していたので，授乳性無月経はより高い頻度で認められたかもしれない．戦中戦後の経済的逼迫のために栄養失調になった者もいたし，伝染病が生存者集団の多くの人々に発生した．本報で用いる推定週齢へのこれらの要因の影響を評価するのは不可能である．胎内週齢推定上のこれらの誤差の原因と同程度に重要なのは，受胎後の一定の期間において，感受性の重要な尺度である発達週齢が通常多様性をもつことである．16～25週齢での影響の幾つか，あるいは恐らくその多くは，発達週齢が実際の週齢を下回る者について認められたのではないかと思われる．

考　察

T65DR 線量推定方式に基づく前回の二つの基本的観察結果[6]に，DS86 標本に基づく再評価でも変化は見られなかった．まず，いずれの線量推定方式においても，広島・長崎の胎内被爆者の脳の発達に及ぼす放射線の有意な悪影響は，受胎後８～15週齢及び16～25週齢についてのみ認められる．最も感受性が高い８～15週の線量反応関係はその後の胎内週齢におけるものとは明らかに異なると思われる．その点は，放射線が大脳の成長及び発達に影響を及ぼす機序が被爆時胎内週齢によって変化することを示唆している．この放射線感受性が最も高い時期は，通常の大脳組織発生の基本的に重要な事象が起こる時期である．大脳皮質を形成するニューロンは，発達中の脳の脳室表面付近に位置する増殖帯でのみ

tricular surfaces of the developing brain. Their most rapid proliferation and all or nearly all of the immature neurons migrate to the cerebral cortex from the ventricular and subventricular proliferative layers in these weeks and become perennial cells.[11-13] Radiation exposure at this period could induce neuronal abnormality and misarrangement of neurons or decrease the number of normal neurons and thus appear as brain damage.

Although it is difficult, from the data presently available, to be categorical about the best dose-response relationship or to derive risk coefficients with reasonably small sampling errors because the risks at low doses are low and the sample sizes are small, nevertheless the data are consistent with a linear or exponential linear dose-response relationship without threshold in the 8-15 week period with both the T65DR and DS86 doses. If there is a threshold in this period, it is difficult to estimate, and depends critically upon the model and the data which are actually used. Elsewhere we have set forth reasons why we believe it is unwise to perceive the increased risk of mental retardation from prenatal exposure as a phenomenon distinct from a more broadly expressed impairment of brain function. Mental retardation is a clinical judgment which dichotomizes a continuous distribution of qualities of brain function. If, as we believe, exposure to ionizing radiation moves this distribution downwards in proportion to dose, then the frequency of individuals with levels of intellectual function below the diagnostic threshold must necessarily increase as dose increases. However, the change in this frequency will be functionally dependent upon where the threshold of clinical judgement lies with respect to the distribution of qualities, and the dose-response relationship could appear linear or curvilinear, to have a threshold or not have one without being inconsistent with the basic biological hypothesis. Moreover this will hold true whether the actual change in the continuum is itself linear or curvilinear with dose.

At 16-25 weeks after fertilization, differentiation in situ accelerates, synaptogenesis that begins about the eighth week increases and the definitive cytoarchitecture of the brain unfolds. During this period radiation could presumably impair synaptogenesis, producing a functional deficit in brain connectedness. Whatever the mechanism, the effect seen in the period 16-25 weeks after fertilization suggests the existence of a threshold.

生成される．この時期にニューロンは最も急激に増殖し，未成熟なニューロンのすべて，又はほとんどすべてが脳室及び脳室下の増殖層から大脳皮質へ移動し非分裂細胞になる．[11-13] この期間の放射線被曝はニューロン異常及びニューロンの誤った構築をもたらすか，又は正常ニューロン数を減少させ，脳障害を発現させる可能性がある．

低線量でのリスクは低く，対象集団は小さいので，現在あるデータを用いて最適の線量反応関係を明確にしたり，標本抽出上の誤差のかなり小さいリスク係数を算出することは困難であるが，それにもかかわらず，T65DR及びDS86線量のいずれでも，8～15週齢のデータは閾値のない線形又は指数線形線量反応関係に適合する．この時期に閾値があったとしても，その推定は困難で，モデルと実際に用いるデータに大きく左右される．胎内被爆による精神遅滞リスクの増加を，一般的な脳の機能障害とは別個の現象としてとらえるべきでないと考える理由は別報に示した．精神遅滞の診断は，連続的な脳機能の分布を二分する臨症的判断である．我々が考えているように電離放射線被曝がこの分布を線量に比例して下方に移行させるならば，知的機能のレベルが診断上の閾値を下回る者の頻度は線量の増加に伴い必然的に増加する．しかし，この頻度の変化は属性の分布に関して臨床的判断の閾値がどこに存在するかに関数的に依存しており，基本的な生物学的仮定に矛盾しないで，線量反応関係が直線的とも曲線的とも考えられるし，また，閾値をもつともたないとも判断できる．更に，このことは，連続的事象の実際の変化そのものが線量に対して直線的であるか曲線的であるかにかかわらず起こる問題である．

受胎後16～25週齢では，潜在的分化が促進され，第8週ごろ始まるシナプス形成が増加し，脳の最終的な細胞構築が進む．この時期に放射線は恐らくシナプス形成に障害を与え，一連の脳機能に欠損をもたらす．受胎後16～25週に認められる影響は，その機序がいかなるものであれ，閾値の存在を示唆している．

Second, no evidence of a radiation-related increase in mental retardation is observed either in those survivors exposed 0-7 weeks after fertilization or 26 weeks or over. Certainly, no cases followed irradiation in these two periods of intrauterine life. The absence of an effect prior to the eighth week suggests that either the cells killed or inactivated at this stage of development are more readily replaced than those damaged later, or the embryo fails to develop further. The final weeks of gestation are largely a time of continued architectural and cellular differentiation and synaptogenesis; the basic neuronal structure of the cerebrum is nearing completion. Since differentiated cells are less radiosensitive generally than undifferentiated ones, measurable damage may require much higher doses and given the small number of survivors at these doses, more difficult to detect.

第二に，受胎後０～７週又は26週以降の被爆者については，放射線に関連する精神遅滞増加の証拠は認められない．事実，これら二つの時期の被爆者の中に精神遅滞症例はいない．第８週以前の影響が認められないことは，この発達段階で死亡又は不活性化した細胞は後の発達段階に比べ容易に補われること，又は胎芽がそれ以上発達しないことを示唆している．妊娠後期では，主として構築，細胞分化，シナプス形成が継続し，大脳の基本的ニューロン構築が完了に近くなる．分化した細胞は一般的に未分化細胞より放射線感受性が低いので，線量がかなり高くなければ測定可能な障害は発生せず，高線量の被爆者は少ないので，障害の確認が困難である．

Alternative nonradiation-related explanations of the effects to the embryonic and fetal central nervous system, possibly confounded here, could impinge on these findings. They include a) genetic variation, b) nutritional deprivation, c) bacterial and viral infections in the course of pregnancy, and d) embryonic or fetal hypoxemia, for there is substantial evidence to suggest that the cerebrum and its adnexa are especially sensitive to oxygen deprivation.[7,24,25] The possible roles these may play in the present context have been explored elsewhere[7]; suffice it here to state that no fully satisfactory assessment of their contribution can be made at this late date. Given the present uncertainties, since most of these extraneous sources of variation would have a greater impact at high than low doses, and thus produce a concave upwards dose-response function, the prudent course would be to assume that the dose-response relationship is not materially altered other than additively by these potential confounders.[7] This would have the effect of overestimating the risk at low doses where greatest regulatory concern exists.

胎芽及び胎児の中枢神経系へ影響を及ぼすような放射線に関連しない要因は，恐らくこの場合交絡因子となり，これらの所見に影響を与えるであろう．それらの要因としては，a) 遺伝的変異，b) 栄養不足，c) 妊娠中の細菌及びウイルス感染，d) 胎芽又は胎児の低酸素血症（大脳及びその付属器は特に酸素欠乏に対し感受性が強いことを示唆するかなりの証拠がある）が挙げられる．[7,24,25] これらの要因が本調査のような場合に果たす役割についてはほかで報告した．[7] それらの寄与を今日になっては充分な評価ができない点についてのみここで述べる．本解析における不確定性を考えると，放射線に関連しないこれらの変異の原因はほとんど低線量より高線量に大きな影響を与え，上に凹な線量反応曲線が得られるので，これらの交絡因子が線量反応関係を変化させることはあっても，実質的には相加的にのみ変化させると仮定するのが賢明であろう．[7] その場合，基準値に関する関心が最も高い低線量でのリスクを過大評価する恐れがある．

It appears commonly presumed that radiation-related damage to the developing brain must stem largely, if not solely from neuronal death. This assumption, in part at least, rests on the relatively large proportion of the retarded who have small heads. However, a small-for-date brain could result from circumstances having nothing to do with cell proliferation, such as a failure in the normal pattern of cell loss resulting in too many cells that are too small, or a failure of cells to migrate from the dense pro-

脳の発達に対する放射線関連障害はすべてでなくともほとんどがニューロン細胞死によると一般的に考えられているようである．この仮定は少なくとも部分的には，精神遅滞者中に占める小頭症患者の割合が比較的大きいことに起因する．しかし，細胞欠損が正常なパターンでなくなり小さ過ぎる細胞が過剰に産生されたり，高密度な増殖帯からかなり密度の低い皮質へ細胞が移動しないなど，細胞増殖とは関係のない状況からも，週齢の割に小さな脳が

liferative zones to the far less dense cortex. There is a need, therefore, to document what role, if any, these other possible causes of a small-for-date brain may play in radiation-related risk of mental retardation. The paragraphs that follow focus on one of these possible causes, namely, abnormal neuronal migration.

発生し得る．したがって，これらの週齢の割に小さな脳の原因となり得る要素が精神遅滞の放射線関連リスクにどのような影響を及ぼすかについて記述する必要がある．以下の説明では，これらの要素の一つ，すなわちニューロン移動の異常に焦点を当てる．

It is now clear that each cortical neuron has not only a designated date of birth, but a definite functional address. Since all proliferation of neuronal cells occurs in specific circumventricular zones, proper function implies migration. Although the latter process extends over weeks, individual cells move and reach their destinations in a matter of days at the most. The process by which undifferentiated neuronal cells move from the proliferative zones to their ultimate normal sites of function is an active, timed phenomenon dependent largely on an interaction between cell surfaces. Any damage to the cell surface, however transitory, could impair the timing of migration. While there is as yet no direct evidence of the effects of low doses of irradiation on the membranal properties of either neurons or the radial glial cells which serve as their guidance mechanism, there is a growing body of data that very low doses of irradiation, 0.01 Gy or so, can and do produce changes in cellular thymidine kinase and in the plasma membrane of hematopoietic stem cells.[26,27] Though these effects are transitory, lasting 10-14 hours, in a process timed as neuronal migration appears to be, any delay seems destined to culminate in dysfunctional cells through their failure to achieve their normal functional sites.

各皮質ニューロンには特定の生年月日があるだけでなく，一定の機能的部位が付与されていることは明瞭である．ニューロンの増殖はすべて特定の脳室周囲の領域で起こるので，各細胞が適切に機能するためには移動する必要がある．この移動は数週間にわたって行われるが，個々の細胞は長くとも数日間で移動し目的部位へ達する．未分化のニューロン細胞が増殖領域から最終的な正常な機能的部位へ移動する過程は，細胞表面間の相互作用に大きく依存する活発な時限が定められた現象である．細胞の表面へのいかなる障害も，それがたとえ一過性であっても，移動の時期を狂わせ得る．ニューロン又はその案内役のグリア細胞の表面の特性に及ぼす低線量被曝の影響を示す直接的な証拠はないが，0.01 Gy ほどの極めて低い被曝線量が細胞のチミジンキナーゼ及び造血幹細胞の原形質膜に変化をもたらすことを示すデータが増加している．[26,27] このような影響は一過性で10～14時間しか継続しないが，ニューロンの移動のように時期が決定されている過程では，いかなる遅れが生じても，正常な機能的部位へ到達できないことによる細胞の機能障害が起こる．

Other less inferential lines of evidence also suggest an important role for migration. First, four of those survivors exposed in utero have come to autopsy; brain weights of the two mentally retarded were 840 g (at age 16) and 1,000 g (at age 20); whereas the brain weights of the two not retarded were normal, 1,440 g (at age 9) and 1,450 g (at age 29). One of the retarded individuals, a male (MF [redacted], was exposed in Nagasaki in the 12th week of gestation and the other, a female (MF [redacted]), in Hiroshima at 31 weeks after conception. The retarded male, exposed to an estimated DS86 dose of 1.18 Gy, exhibited massive ectopic gray areas[28]; in the other, the female, exposed to less than 0.01 Gy, the brain though small was histologically normal. Second, very recent, still quite limited and as yet unpublished magnetic resonance images of the brain of

より具体的な証拠によっても，移動の役割が重要であることが示唆されている．第一に，これらの胎内被爆者のうち4例の剖検が行われたが，精神遅滞者2例の脳の重量が840g（16歳）と1,000g（20歳）であったのに対し，精神遅滞者でない2例の脳の重量は1,440g（9歳），1,450g（29歳）と正常であった．精神遅滞者のうち1例は，妊娠第12週に長崎で被爆した男性（MF [redacted] であり，ほかの1例は，受胎後第31週に広島で被爆した女性（MF [redacted]）であった．男性の方はDS86線量1.18 Gyに被曝しており，異所性の大きな灰白質を示していた．[28] 女性の方は，被曝線量0.01 Gy未満で，脳は小さかったが組織学的には正常であった．第2に，ごく最近に，8～15週に胎内被爆したが社会的適応状況の良い精神遅滞者

the first in a series to be examined of the sociologically better adapted mentally retarded individuals exposed at 8-15 weeks disclose substantial, abnormal circumventricular areas of gray matter suggesting an impairment of migration.[29] Other investigators have shown that nonradiation-related mental retardation is frequently associated with areas of ectopic gray matter.[30-33] Third, experimental observations on the effects of low doses of ionizing radiation (0.05 to 0.10 Gy) on the developing brain of rats exposed prenatally further support the belief that abnormal migration may be an important mechanism through which damage occurs. These studies reveal marked dysplasia of the cingulum, the band of association fibers in the medial portion of the centrum ovale of each hemisphere at doses as low as 0.05 Gy.[34]

Patently, the evidence is still too sparse to be reassuring; however, newer noninvasive techniques for the study of the living brain, such as magnetic resonance imaging, offer immense potential and may, in time, provide the means to understand the biological events that subtend the occurrence of radiation-related mental retardation.

を磁気共鳴法により，初めて検査した．その結果は極めて限定されたものでまだ発表していないが，移動障害を示唆する脳室周囲の異常な灰白質の領域が明らかに存在することを示している．[29] ほかの研究者により，放射線に関連しない精神遅滞が異所性灰白質の領域と関連をもつことが多いと報告されている．[30-33] 第3に，胎内ラットの脳の発達への低線量電離放射線（0.05～0.10 Gy）の影響に関する実験の観察結果は，異常な移動が障害を起こす重要な機序であることを裏付けている．これらの調査は，わずか0.05 Gyの低線量で，帯状束，すなわち各大脳半球の半卵円中心の中央部分における連合線維束に著しい形成異常が起きることを明らかにしている．[34]

明らかに，これまでに得られた証拠は不十分であるが，磁気共鳴撮影法などの，生体の脳を検査するための新しい非侵襲性の技法がもつ将来の可能性は大きく，それによりやがて放射線に関連する精神遅滞を発生させる生物学的事象を理解できるようになるかもしれない．

APPENDIX 1 SEVERELY MENTALLY RETARDED SUBJECTS EXPOSED IN UTERO TO THE ATOMIC BOMB BY CITY

付録 1　都市別原爆胎内被爆者の重度精神遅滞

Continue続く→

MF No.	Sex	Date of birth from chart review	Gestational weeks after fertilization	Kerma dose (T65DR)			Fetal absorbed dose (T65DR)			Uterus dose (DS86)			Koga IQ 1955-56
				D_T	D_γ	D_ν	D_T	D_γ	D_ν	D_T	D_γ	D_ν	
				(Unit = Gy)									
Hiroshima													
[redacted]	M	12 Dec 45	20	0	0	0	0	0	0	0	0	0	
	F	11 Jan 46	15	0.05	0.04	0.01	0.02	0.02	0	0.06	0.06	0	
	M	15 Jan 46	15	0.87	0.72	0.15	0.33	0.31	0.02	0.61	0.61	0	
	F	5 Mar 46	8	1.76	1.12	0.64	0.61	0.52	0.09	1.40	1.39	0.01	
	M	28 Feb 46	8	1.94	1.25	0.69	0.68	0.58	0.10	0.87	0.87	0.00	64
	F	5 Jan 46	16				Not in city						
	F	22 Sep 45	31	0	0	0	0	0	0	0	0	0	
	F	15 Feb 46	11	5.23	4.00	1.23	1.94	1.77	0.17	2.22	2.21	0.01	
	M	25 Feb 46	9	2.93	2.42	0.51	1.13	1.06	0.07	1.36	1.35	0.01	
	M	12 Dec 45	19	2.57	1.92	0.65	0.95	0.86	0.09	1.23	1.22	0.01	64
	F	6 Feb 46	12	0.96	0.79	0.17	0.36	0.34	0.02	0.56	0.56	0	
	F	27 Jan 46	13	2.36	1.49	0.87	0.81	0.69	0.12	1.64	1.63	0.01	56
	M	12 Feb 45	10	1.98	1.58	0.40	0.75	0.69	0.06	1.02	1.02	0.00	
	M	18 Aug 45	36				Not in city						
	F	23 Jan 46	13	0.28	0.24	0.04	0.11	0.10	0.01	0.29	0.29	0	
	M	1 Mar 46	8	0.17	0.12	0.05	0.06	0.05	0.01	0.14	0.14	0	
	F	8 Dec 45	20	0.05	0.04	0.01	0.02	0.02	0	0.03	0.03	0	
	M	29 Oct 45	26				Not in city						60
	M	22 Nov 45	22	1.88	1.50	0.38	0.71	0.66	0.05	1.00	1.00	0.00	59
	F	4 Feb 46	12	3.82	3.08	0.74	1.45	1.35	0.10	1.39	1.38	0.01	
	M	24 Feb 46	9	0.81	0.67	0.14	0.31	0.29	0.02	0.69	0.69	0	
	M	11 Feb 46	11	0.05	0.04	0.01	0.02	0.02	0	0.05	0.05	0	
Nagasaki													
[redacted]	F	22 Apr 46	1	0	0	0	0	0	0	0	0	0	
	F	25 Sep 45	31	0	0	0	0	0	0	0	0	0	
	F	2 Nov 45	25	4.85	4.77	0.08	2.02	2.01	0.01	1.79	1.79	0	60
	M	27 Feb 46	9	3.12	3.08	0.04	1.31	1.30	0.01	1.16	1.16	0	62
	M	6 Feb 46	12	3.75	3.70	0.05	1.57	1.56	0.01	1.18	1.18	0	
	M	15 Jan 46	15	5.50	5.42	0.08	2.29	2.28	0.01	1.46	1.46	0	
	F	15 Jan 46	15				Not in city						56
	M	26 Jan 46	13				Not in city						

$D_T = D_\gamma + D_\nu$, D_γ = gamma-ray dose and D_ν = neutron dose.

$D_T = D_\gamma + D_\nu$,　D_γ = ガンマ線量，D_ν = 中性子線量．

†MF# [redacted] was listed as MF# [redacted] with a misprint in Wood et al.[2]

Wood ら[2] の報告では誤まって MF# [redacted] を MF# [redacted] と記している．

††This classification of small head size was determined roughly by sex with a criterion with at least two standard deviations below mean between 16 and 19 years of age. x denotes a small head size, and o not so. Note that the death information is of 1 April 1987.

小頭症の分類は，16歳から19歳までの平均を少なくとも2標準偏差下回る判定基準によって，性別に概算的に決定した．xは小頭症を示し，0は小頭症でないことを示す．死亡情報は1987年4月1日付であることに注意．

*Principal cause of death and others.　主要死亡その他

a　Heart failure (ICD = 428), Epilepsy (345)
心不全（ICD＝428），てんかん（345）

b　Tuberculosis of intestines, peritoneum and mesenteric glands (014), pulmonary tuberculosis (011), Tuberculosis of bones and joints (015).
腸，腹膜及び腸間膜リンパ節の結核（014），肺結核（011），骨及び関節の結核（015）

c　Malignant neoplasm of liver and intrahepatic bile ducts (155)
肝臓及び肝臓内胆管の悪性新生物（155）

d　Heart failure (428), Epilepsy (345)
心不全（428），てんかん（345）

e　Other ill-defined and unknown causes of morbidity and mortality (799)
疾病及び死亡の原因が不明（799）

APPENDIX 1 付録 1 (Continued 続き)

Principal cause of Death(ICD)*	Date of death	Age at the time of examination of head circumference (cm)											Small head size††	Significant clinical findings**	MF No.
		9	10	11	12	13	14	15	16	17	18	19			
															Hiroshima
(428)[a]	19 Sept. 56	49.8	-	-	-	-	-	-	-	-	-	-	o	1	[redacted]
		-	-	-	-	-	-	-	51.2	51.3	51.3	51.4	x		
(014)[b]	30 Aug. 58	46.6	46.5	48.8	-	-	-	-	-	-	-	-	x		
(155)[c]	14 Jan. 53	Chart record: 43.3 (Oct 50)											x	2	
		46.5	46.5	47.0	47.5	-	-	-	49.0	49.8	50.7	-	x		
		Chart record: 46.2 (Jan 52)											x		
(428)[d]	26 Mar. 66	46.6	47.3	48.0	38.4	-	-	-	50.0	-	52.0	52.3	o		
(799)[e]	21 Jan. 52	Chart record: 38.9 (Aug 49): 38.4 (Aug 50): 39.8 (Feb 51)											x		
		42.1	42.8	42.3	-	-	-	-	-		-	-	x		
(586)[f]	18 Feb. 70	48.8	49.5	49.5	49.5	51.0	52.7	53.8	53.5	53.6	53.8	53.8	o		
(E910)[g]	28 Jun. 52	Chart record: 45.1 (Feb 50) and 47.4 (Aug 55)											x	3	
		45.5	46.3	47.0	47.0	47.0	-	51.0	49.6	49.6	49.6	49.6	x		
		-	47.4	-	-	-	-	-	-	-	-	-	x		
		46.1	45.9	46.2	-	-	47.5	47.5	47.1	47.6	49.2	49.5	x	3	
		44.8	45.8	-	-	-	47.2	-	46.9	46.9	47.5	47.0	x	3	
		47.5	-	-	-	-	-	51.4	-	-	-	-	x		
		49.6	50.1	50.3	49.8	-	-	-	53.7	53.5	-	-	o	4	
		50.0	53.3	-	-	-	-	-	54.5	54.6	54.6	55.4	o		
		48.4	48.3	48.4	48.3	-	-	-	50.7	50.8	51.0	51.0	x		
		-	-	45.8	-	-	-	47.5	47.2	47.4	47.4	47.5	x		
		-	44.0	-	44.9	-	-	47.0	47.0	-	-	-	x		
		-	-	-	-	-	51.8	-	53.3	-	-	-	o		
															Nagasaki
		50.0	50.3	51.7	50.4	51.8	51.9	52.5	-	-	-	-	o	5	[redacted]
		52.4	52.3	53.4	54.4	54.7	55.0	55.9	56.6	56.9	56.5	56.5	o	6	
		47.5	48.4	49.0	49.8	51.1	51.7	52.2	52.7	52.7	-	-	o		
		47.9	48.2	48.9	49.1	49.1	50.3	51.8	52.3	53.0	53.2	53.5	o	7	
(799)[h]	14 Mar. 62	42.9	43.0	43.3	43.9	44.4	45.1	45.2	45.2	-	-	-	x		
		47.4	47.7	48.3	48.7	49.2	49.8	50.3	50.5	51.2	50.9	50.9	x		
		-	52.9	53.2	51.6	55.2	56.2	56.5	56.4	56.6	56.6	-	o		
		-	50.8	51.2	51.6	52.0	52.6	-	-	-	-	-	o		

f Renal failure, unspecified (586), Nephrotic syndrome (581)
腎不全，詳細不明(586)，ネフローゼ症候群(581)

g Accidental drowning and submersion (E910)
事故による溺死(E910)

h (ICD 799) = e, General symptoms (780), Meningitis of unspecified cause (322)
(ICD 799) = e，一般的症状(780)，原因不明の髄膜炎(322)

**Significant clinical findings 有意な臨床所見

1 Retarded sibling 精神遅滞の同胞
2 Neonatal jaundice 新生児黄疸
3 Down's syndrome Down 症候群
4 Japanese B encephalitis at age 4 4歳で日本脳炎
5 Possible birth trauma 不確実な分娩時外傷
6 Congenital lues 先天性梅毒
7 Neurofibromatosis 神経線維腫症

APPENDIX 2 THE DISTRIBUTION OF DS86 "FETAL" DOSE ESTIMATED BY DOSE GROUPS AND THE METHOD OF DOSE ESTIMATION

付録2　DS86 "胎児" 吸収線量推定値の分布，線量群別及び線量推定法別

Method of estimation	DS86 Dose Category (Gy)				
	<0.01	0.01-0.09	0.10-0.49	0.50-0.99	1.00+
Direct		187	199	39	25
Indirect	559	14	8	3	1
Total	559	201	207	42	26

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