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BONE MATURATION IN CHILDREN EXPOSED IN UTERO TO THE ATOMIC BOMB

原爆胎内被爆児における骨格熟成

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ATOMIC BOMB CASUALTY COMMISSION

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ATOMIC BOMB CASUALTY COMMISSION HIROSHIMA AND NAGASAKI, JAPAN

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SONE MATURATION IN CHILDREN EXPOSED IN UTERO TO THE ATOMIC BOMB

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BONE MATURATION IN CHILDREN EXPOSED IN UTERO TO THE ATOMIC BOMB 原爆胎内被爆児における骨格熟成

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SUMMARY

Five hundred and fifty-six subjects exposed while in utero to the Hiroshima and Nagasaki A-bombs, and comparison subjects were observed by postero-anterior hand and wrist roentgenograms for epiphyseal closure. There were delays in closure of 6-7 and 8-9 months for males and females respectively, as compared with published results for Japanese and American children. These findings did not correlate with the A-bomb exposure doses of the mothers of these children. Brachymesophalangia occurred in 11% of males and 19% of females in Hiroshima. Possible contributory factors to the relative delay in maturation are discussed.

BACKGROUND

During the course of investigations by ABCC for late radiation effects among survivors of the Hiroshima and Nagasaki A-bombs, several studies have elucidated growth and development. Three of these have included roentgenographic assessments of bone maturation and two of these reflected delayed skeletal maturation among Japanese in comparison to American children. The third, a study of Nagasaki children exposed in utero, attributed an apparent delay in epiphyseal center closure to fetal exposure to the ionizing radiation from the A-bombs. That report was based on a cross-sectional analysis with fewer observation points in fewer subjects during only three examination.

The present study established the time of closure of the epiphyseal centers in the left hands and wrists of in utero survivors who were in various stages of

要約

広島および長崎における原爆胎内被爆者 556人およびその対照群について、手および手首の背腹方向 X 線検査によって骨端核閉鎖の調査を行なった。その結果、骨端核の閉鎖が日米両国の子供について報告されている資料に比べて、男・女それぞれ6-7か月および8-9か月遅滞していることが認められた。これらの所見と対象者の母親の原爆放射線被曝線量との間には相関はなかった。広島では、男子の11%、女子の19%に短中指節症が認められた。成熟の相対的遅滞の原因と考えられる要因について考察を行なった。

背景

ABCCが実施している広島・長崎の原爆被爆者の放射線による後影響についての調査によって、成長および発育に関する調査研究が数件報告されている. 1-6 これらの調査のうちの三つでは、1-3 X線撮影による骨格熟成の評価が行なわれており、そのうちの二つでは、日米両国の子供の骨格熟成が比較され、その結果日本人において遅滞が認められた. 1-2 残りの一つの調査は、長崎の胎内被爆児に関するもので、骨端核閉鎖の遅滞は胎児の原爆電離放射線への被曝に原因があるとしている. 3 この報告は対象者数も観察箇所の数も少ない3回だけの検査に関する断面的解析をもとにまとめたものである.

本調査では,原爆時に種々の妊娠期にあった胎内被爆者 の左手および左手首の骨端核閉鎖の時期を,母親の被爆 gestation at the time of the bombs (ATB), taking into consideration the location and A-bomb dose of their mothers. The data were analyzed to detect any delay of maturation attributable to exposure to ionizing radiation from the A-bombs, and to establish norms for comparison with results of other investigators.

場所と線量とを考慮して確かめた. 原爆の電離放射線被 曝に起因する熟成遅滞の有無を検知し, また, 他の研究 者らの調査結果との比較のための基準を設定するため, 調査資料の解析を行なった.

MATERIALS AND METHODS

Selection of Sample. The ABCC in utero exposed sample (PE86) consists of 1613 Hiroshima and Nagasaki subjects in three major comparison groups by the mother's distance from the hypocenter (0-1999 m, 3000-4999 m, and not in the city). The children were born between August 1945 and May 1946. Radiation dose estimates based on shielding information were available for the exposed mothers. 8

The subjects in the present study were selected from those undergoing examination in the PE86 Included in these examinations were posteroanterior (PA) roentgenograms of the teft hand and wrist within 1 month of their birthdays. Selection of index subjects was restricted to those within 2000 m from the hypocenter ATB and already having on file a minimum of five routine hand-wrist roentgenograms. Control subjects, matching on sex and trimester of gestation ATB and with a minimum of four roentgenograms were from the 3000-4999 m group (too distant to have experienced significant radiation but within the region of blast effect), and the not-in-city group who experienced neither radiation nor blast. At the time of selection, there was a potential of nine films per control subject. In the event that two or more subjects met the criteria for selection, the ones with the maximum number of X-ray films on file were selected.

Based on medical chart reviews, four cases of mental deficiency, and one each with metabolic or endocrine imbalance, congenital syphilis, infantile cerebral palsy, renal rickets with delay of skeletal maturation, and epilepsy were excluded from the study. Replacements were selected for 3000-4999 m and not-in-city subjects, but not for the "index" (under 2000 m) subjects. The sample as ultimately defined is shown in Table 1.

The study subjects with greater number of examinations prior to age 17 years might conceivably have differed from those with fewer examinations, result-

資料および方法

対象者の選択、 ABCC の胎内被爆者集団 (PE 86)は、1613名の広島・長崎対象者から成り、被爆した母親の爆心地からの距離、すなわち、0-1999 m、3000-4999 m、および市内にいなかった者によって大きく三つの比較群に分類されている。この胎内被爆児は、1945年8月から1946年5月の間に生まれた者である。7 被爆した母親については遮蔽資料に基づいた被曝線量の推定値が入手されている。8

本調査の対象者は、PE 86胎内被爆児調査プログラムの 被検者から選択した、これらの対象者の受けた検査には、 その誕生日を中心とする1か月以内における左手および 左手首の背腹方向 X 線撮影が含まれている. 指標対象者 は原爆時に爆心地から2000 m未満の距離にいた者で、手 および手首の通常 X 線写真が最低 5 枚撮影されている者 に限定した. 対照者となる子供は, 3000-4999 m の距離 で被爆した者, すなわち距離が遠いため有意な放射線は 受けなかったが爆風の影響は受ける圏内にいた者と,放 射線も爆風も受けなかった市内不在者とであって, 性お よび原爆時の妊娠期が対象者と対応し、かつ、最低4枚 の X 線写真が撮影されていた者から選んだ. 選択の時点 では、各対照者には9枚のX線写真が撮影されていたこ とが十分考えられる. 2名以上の対照者が選択基準に合 致していたような場合には、撮影枚数の多い者のほうを 選んだ.

診療録の検討で、精神薄弱児4例ならびに代謝または内分泌の失調、先天性梅毒、小児脳性麻痺、骨格熟成遅滞を伴う腎性くる病および癲癇各1例を認めたので、これらは本調査から除外した。これらの各例の対照である3000-4999mで被爆した者と市内不在の者の代わりの者は選んだが、「指標例」(2000m未満の被爆者)のそれは選び替えなかった。最終的な調査集団は表1に示す。

17歳以前に受けた X 線検査回数の多い対象者と検査回数の少ない者との間に何らかの差異があり、その結果偏り

TABLE 1 NUMBER OF IN UTERO CHILDREN IN BONE MATURATION STUDY, BY SEX, TRIMESTER OF GESTATION ATB. AND DISTANCE FROM HYPOCENTER, HIROSHIMA AND NAGASAKI

表1 骨格熟成調査における原爆時胎内児数:性・原爆時妊娠期・爆心地からの距離別,広島・長崎

	Trimester of	Total	Hiro	shima		Naga	saki	
Sex	Gestation ATB	Total -	0-2000 m	3000-4999 m	Not in City	0-2000 m	3000-4999 m	Not in City
Total	2. 発数まる音集区	556	147	75	150	73	36 10 1 - 11	75
Male		331	87	45	90	43	21	45
	1st Trimester	109	27	15	30	15	7	15
	2nd	112	30	15	30	15	7	15
	3rd	110	30	15	30 30	13	and ye 7 a banky	15
Female		225	60	30	60	30	15	30
	1st Trimester	75	20	10	20	10	5	10
	2nd	75	20	10	20	10	5	10
	3rd	75	20	10	20	10	5	10

There were too few eligible children in the 3000-4999 m group to match on a one to one basis. This group was limited to halfsize to retain proportionate balance.

 $3000-4999\,\mathrm{m}$ 群では、 $1\,\mathrm{M}\,1$ の基準で対応させるには、該当する子供の数があまりに少なすぎた。つりあいのとれた均衡を保つため、本群は 5000 がんききに制限された。

ing in bias. It would be difficult to disprove this by comparing closure rates because roentgenograms are necessary to determine such rates. However, comparison of head circumferences at various ages for subjects who were examined at 17 years of age and for those not clinically examined at 17⁶ did not indicate that the availability of an examination was related to the past or future physical development or maturation of the subject. Further analysis for possible bias is presented in the Appendix 1.

Roentgenography and Interpretation. An epiphysis is an osseous body which in early life is separated from a large body of bone by cartilage. Growth of the length of the bone occurs at the location of this cartilage, and the epiphysis later unites with and becomes a part of the larger body of bone. Throughout the body, epiphyses form, develop, and eventually unite with other bodies of bone from birth to about 30 years of age. The time of appearance of epiphyseal centers and the time at which they unite with the main portion of a bone can be readily determined roentgenographically. The time of appearance and closure can be altered by factors such as disease, malnutrition, and in relatively heavy exposure to ionizing radiation. 9,10

Ideally, roentgenographic assessment of epiphyseal centers should be made semiannually or quarterly, especially to observe the rapidly occurring developments when centers appear (from birth to 6 years),

の生じた可能性があった.しかし、骨端核閉鎖率を求めるにはX線写真が必要であるので、閉鎖率の比較によって、これが誤りであることを証明することは困難であるようであった.しかしながら、17歳時に臨床検査を受けた対象者と17歳時に臨床検査を受けなかった対象者 6 についての各年齢ごとの頭囲の比較では、検査結果の有無とその対象者の過去または将来の発育ないし成熟との間に関係のあることは認められなかった.偏りについてさらに実施した解析の結果は、補遺1に示してある.

X線撮影および読影. 骨端は骨質体であって, 若い年齢では骨本体から軟骨によって隔離されている. 骨の長軸方向への成長はこの軟骨の個所で起こり,後に骨端が結合して大きい骨の一部となる. 出生時からほぼ30歳ごろまで,全身のいたる所において骨端が形成され,発育し,そして他の骨と結合する. 骨端核の出現時期および骨と結合する時期は, X線撮影により容易に確認できる. 骨端核の出現と閉鎖の時期は,疾病,栄養不良および比較的強度の電離放射線被曝などの要因によって変化する. 9,10

理想的には年2回ないし4回骨端核をX線撮影によって調べることが望ましく,特に急速に変化の起こる出生時から6歳までの骨端核が出現する時期と,13歳から21歳

and close (from 13 to 21 years). However, the design of the investigation of the in utero exposed sample did not permit more frequent than annual examinations.

The left hand and wrist was selected for observing skeletal maturation because of its accessibility and ease of examination. It is the generally accepted body site used for this purpose. There is no significant difference in the rate or pattern of bone maturation between the left and the right hands and wrists. Those of the left hand reportedly mature somewhat faster than those of the right, the difference being more prevalent among boys, but it is not statistically significant, and any such differences are too small to limit the usefulness of assessments based on one hand and wrist area. It

More consideration has reportedly been given the ages at which centers ossify than those when fusion of epiphyses and diaphyses occur. 12 There are 19 short, 8 round, and 2 long bones for observation in the hand and wrist, 13 and these three types of bones can vary widely in their development patterns. There are greater variations in time of appearance of carpal bones than in the long bones of the hand. 14 In 1954 Dreizen reported that the middle and distal phalanges were more often retarded in chronic nutritive failure. 15 In 1958 he reported that acrpal bones not only are more variable in time of appearance, but more vulnerable to retarding influences of protracted undernutrition.16 We restricted our observations to the epiphyses of the long bones of the left hand and wrist.

Roentgenologic methods of observing developing skeletal structures have included planimetry for area measurement, ¹⁷ the measurement of bone diameters, ¹⁸ and the overall appearance of carpals, metacarpals and phalanges. ¹⁹ The latter has proved satisfactory for most investigators. ²⁰ Some have also documented the times of appearance of the sesamoid bones. We did not do so; epiphyseal fusion can be more clearly and objectively assessed.

The children in this study routinely received PA roentgenograms of the left hand and wrist within 1 month of their birthdays, between the ages of 9 and 21 years. The maturity indicators of Greulich and Pyle¹⁴ were used as criteria for closure. Complete closure consisted of fusion of the epiphysis with the main body of bone, with or without a residual epiphyseal line. The stages of closure in a phalanx are illustrated in Figure 1. The epiphyses so observed are indicated by numbers in Figure 2.

までの閉鎖の起こる時期に観察を行なうべきである. しかし、胎内被爆者の調査計画のもとでは、検査を年1回よりも多く行なうことはできなかった.

骨格熟成の観察において、検査を実施するうえで部位的に容易であることから、左手と左手首とを選択した。この部位はこの種の検査において通常使用されている場所である。左右の手および手首の骨格熟成度合いまたはその像の間には、有意の差はない。"左手は右手に比べて、特に男子において骨格熟成が多少早いといわれているが、その差は統計的には有意ではなく、片方の手および手首だけについて調査を行なうことの有用性を制限するには、その差はあまりに小さすぎる。"

骨端と骨幹の融合が起こる年齢よりも骨端核が骨化する年齢に考慮が払われているとの報告がある.12 手と手首には観察の対象となる短骨19,円骨8および長骨2があり,13 これら3種の骨の発育像には広範にわたる変動がある.出現時期においては長骨よりも手根骨のほうにより大きな変動がある.14 1954年 Dreizen は、慢性栄養不良者においては、中節骨および末節骨にしばしば発育遅滞が認められると報告した.15 1958年にかれは長期にわたる栄養不良では手根骨の出現時期に変動が起こりやすいばかりでなく遅発性影響も受けやすいと報告した.16 著者らは、左手および左手首の長骨の骨端に観察を限定した.

発育中の骨格構造の放射線学的観察では,面積測定法,¹⁷ 骨径測定法¹⁸ ならびに手根骨,中手骨および節骨の全体的概貌観察法が用いられた.¹⁹ 後者の方法が大多数の研究者の必要を十分に満たすものであった.²⁰ 種子骨の出現時期を記録にとった者もいたが,骨端の融合のほうが,より明確かつ客観的に評価することができるので,著者らはこれを実施しなかった.

本調査の対象者は通常年齢9-21歳の間に毎年誕生日から1か月以内に左手および左手首の背腹方向のX線検査を受けた。Greulich および Pyle¹⁴の熟成指標を閉鎖の基準として使用した。完全な閉鎖とは、骨端と骨本体との融合のことであって、骨端残留線のあるものとないものとがある。節骨における閉鎖の各段階は図1に示す。このような観察を行なった骨端は、図2に番号によって示す。

FIGURE 1 MATURITY INDICATOR

DATE OF THE STATE OF THE STATE

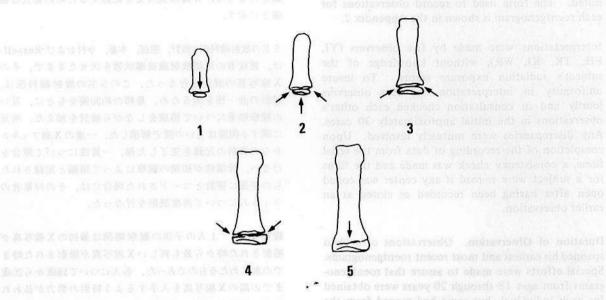
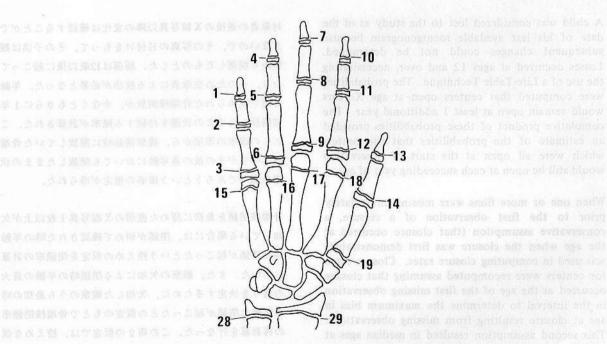


FIGURE 2 EPIPHYSES OBSERVED



Pseudoepiphyses have been reported indicative of ossification disturbances.²¹ Their presence was therefore recorded. Anticipating that brachymesophalangia might interfere with the closure of respective centers, the presence of this anomaly was noted. The form used to record observations for each roentgenogram is shown in the Appendix 2.

Interpretations were made by five observers (YI, FH, TK, KI, WR), without knowledge of the subject's radiation exposure status. To insure uniformity in interpretation the five observers jointly and in consultation checked each other's observations in the initial approximately 30 cases. Any discrepancies were mutually resolved. Upon completion of the recording of data from the serial films, a consistency check was made and the films for a subject were re-read if any center was coded open after having been recorded as closed at an earlier observation.

Duration of Observation. Observations of a child spanned his earliest and most recent roentgenograms. Special efforts were made to assure that roentgenograms from ages 18 through 20 years were obtained for each individual, but some had moved from the contacting area and others refused the examinations.

The number of persons observed at each year of age and the number lost from observation by age is shown in Table 2.

A child was considered lost to the study as of the date of his last available roentgenogram because subsequent changes could not be determined. Losses occurred at ages 12 and over, necessitating the use of a Life-Table Technique. The probabilities were computed that centers open at age X years would remain open at least 1 additional year. The cumulative product of these probabilities provided an estimate of the probabilities that the centers which were all open at the start of observation would still be open at each succeeding year of age.

When one or more films were missing immediately prior to the first observation of a closure, a conservative assumption (that closure occurred at the age when the closure was first demonstrated) was used in computing closure rates. Closure rates for centers were recomputed assuming that closure occurred at the age of the first missing observation in the interval to determine the maximum bias in age at closure resulting from missing observations. This second assumption resulted in median ages at closure ¼ to ½ year earlier than when the conserva-

偽骨端は化骨作用の障害を示すものであると報告されている. 21 したがって,偽骨端の有無についても記録を行なった.短中指節症がそれぞれの骨端核の閉鎖を阻害することも考えられるので,この異常の有無についても記録を行なった.X線検査所見を記録するための書式は補遺2に示す.

5名の放射線科医(飯野,服部,木暮,今村および Russell)は,被検者の原爆放射線被曝状態を伏せたままで,その X 線写真の読影を行なった.この5名の放射線科医は,読影の画一性を図るため,最初の約30例をもとに,互いの観察結果について協議をしながら検討を加えた.所見に関する相違は互いの間で解消した.一連の X 線フィルムからの資料の記録を完了した後,一貫性について照合を行ない,骨端核が初期の観察によって閉鎖と記録されたものが後に開放とコードされた場合には,その対象者のフィルムについて再度読影を行なった.

観察期間. 1人の子供の観察期間は最初の X 線写真が撮影された時から最も新しい X 線写真が撮影された時までの間にわたるものであった。各人について18歳から20歳までの間の X 線写真を入手するよう特別の努力が払われたが、連絡地域外に移転したり、検査を拒否した者もあった。

各年齢ごとの受診者数および年齢別脱落者数は,表2に示す.

対象者の最後の X 線写真以降の変化は確認することができないので、その写真の日付けをもって、その子供は観察から脱落したものとした。脱落は12歳以後に起こっており、そのため生命表による技法が必要となった。年齢 X 歳で認められた骨端核開放が、少なくともさらに 1 年間開放したままの状態を持続する確率が計算された。これらの確率の累積から、観察開始時に開放していた骨端核すべてがその後の各年齢においても開放したままの状態を保つであろうという確率の推定が得られた。

骨端核閉鎖を最初に認めた直前のX線写真1枚以上が欠如している場合には、閉鎖が初めて確認された時の年齢時に閉鎖が起こったという控えめの仮定を閉鎖率の計算に用いた。また、観察の欠如による閉鎖時の年齢の最大の偏りを決定するために、欠如した観察のうち最初の時の年齢に閉鎖が起こったとの仮定のもとで骨端核閉鎖率の再計算を行なった。この第2の仮定では、控えめな仮定が用いられた場合よりも閉鎖時の中間年齢の¼-½年

TABLE 2 NUMBER OF IN UTERO CHILDREN UNDER OBSERVATION* AND NUMBER WITHDRAWN FROM OBSERVATIONS BY AGE, SEX, AND DISTANCE FROM HYPOCENTER, HIROSHIMA AND NAGASAKI

表2 観察中の原爆時胎内被爆児数および観察調査からの脱落者数:

年齢・性・爆心地からの距離別、広島および長崎

or o	Total S	ubjects	0-20	000 m	3000-4	999 m	Not-i	n-City
City, Sex, Age	Observed at age X	Withdrawn between X and X+1	Observed at age X	Withdrawn between X and X+1	Observed at age X	Withdrawn between X and X+1	Observed at age X	Withdrawn between X and X+1
Hiroshima Male	TOTAL CONTRACT	当日至6万年	· 斯内部 . 中	- agobil	nating fata	ties of bores	ilb gmod v	Unistrus in
9-13 yrs.	222		87		45		90	
14	222	2	87	1 had-	alor 45		90	0 201501
15	220	6	86	3 300	45		89	17 30 30
16	214	15	83	9.000	45	1001 2	86	1 4 E
17	199	85	74	33	43	16	82	36
18	114	45	41	19	27	10	46	16
19	69	59	22	16	17		30	27
20	10	10	6	6	0.01 1 ₀₀	1	3	3
Hiroshima Female								
9-13	150		60		30		60	
1.4	150	3	60	11000	30	atositta 1 sob l	60	neo sidifac
15	147		59		29	northwest of	59	
16	147	29	59	9	29	7	59	13
17	118	73	50	28	22	13	46	32
18	45	20	22	10	9	4	14	6
19	25	24	12	12	5	4	8	8
20	ber 1 1 M	14 cm 1 m 2	r to as of all spring	755.1 m	1	1	on to both	-unio luani.
Nagasaki Male								
9-11	109		43		21		45	
12	109	secol plan	43		21		45	1
a = 13 n a 5 1	108	1 1 1	43		21		44	î
14	107	3	43	1	21	1	43	1
15	104	8 7 8	42	6	20		42	2
16	96	4	36	1	20	1	40	2
17	92	41	35	14	19	10	38	17
18	51	39	21	13	9	7	21	19
19	12	11	8		2	1	2	2
20	1	î		adi o	i mushi i	î .		lean age at
Nagasaki Female								
9-13	775		30		15		30	
14	75	3	30	1	15	2 00	30	
581 00 15 A 58 H	72	5 9	29		13		30	divine 15 c
16	67	15	27		11	2	29	5
17	52	24	19	11	9	5	24	8
18		18	8	6	4		16	8
19	10	7	2	1	agric Boange	legiteLi4	8	6
20	14013	# 2 + 3 33	sometime	101		redmind line	2	2

^{*}Examined at age X, or before and after age X. 年齢 X 歳で、または年齢 X 歳前後で検査を受けたもの

資料出所源 Tab. 1633-1 & 2-C, Center 20 骨端核 tive assumption was used. Bias from the true median age at closure with the conservative assumption would be one-half the above differences or a 1/8 to 1/4 year delay. Similar bias estimates were obtained for ages at which 10% and 90% of centers were closed. Bias was similar for each of the four distance comparison groups.

Radiation Exposure. Revised individual whole-body radiation dose estimates (T65D)8 are the most accurate measure of degree of exposure to radiation from the Hiroshima and Nagasaki bombs. Efforts are currently being directed to estimating fetal dose for in utero exposed subjects, but such dose estimates are not yet available. The whole-body doses of the mothers are available and have been used in the search for the effect of fetal exposure upon subsequent skeletal maturation. The analysis for an exposure effect was limited to the 331 children who were within 5000 m from the hypocenter ATB. While subjects beyond 10,000 m received no radiation from the bombs,8 these subjects were excluded from the analysis to avoid possible confounding of dose effects with differences in maturation related to migration and the consequent nutritional differences. T65 dose information used in the analysis is summarized in Table 3.

About one-third of the sample in each city is in the less than 1 rad group, while 8% and 13% respectively of Hiroshima and Nagasaki children were born to mothers whose whole-body exposure exceeded 100 rad. Exposure to neutrons was largely confined to Hiroshima, radiation in Nagasaki having been primarily gamma rays.

RESULTS

Mean age at closure, by center, for children in the less than 1 rad group, one-third of those used in the dose analysis, were compared with the mean age at closure for subjects exposed to 100 or more rad and with those exposed to 40 rad or more. While the contrast involving the 100 or more rad group provided a more satisfactory dose differential, the ability to establish statistical significance was impaired due to the small number of children (32) or 10% for the combined cities) with this high level of exposure. The 40 rad or more group provided a smaller difference in doses, but the group included 78 children, nearly 25% of those exposed within 5000 m of hypocenter. differences between means were tested using Student's "t" test, Table 4.

ほど早くなった。控えめの仮定では閉鎖時の真の中間年齢からの偏りは、上述の差の光すなわち%-光年の遅滞となる。骨端核の10%および90%に閉鎖が認められた年齢についても同様の偏差推定値が入手された。四つの比較群についても偏差は類似したものであった。

両市における対象者の約%は、1 rad 未満の被曝群に属しており、他方、広島と長崎の対象者のそれぞれ8%と13%が100 rad 以上の全身被曝の母親から生まれた。広島における被曝放射線は主として中性子であり、長崎における放射線は主としてガンマ線であった。

結 果

線量解析に用いられた子供の%に相当する1 rad 未満群の骨端核別平均閉鎖時年齢を100 rad 以上および40 rad 以上の被曝対象者の閉鎖時平均年齢と比較した。100 rad 以上の被曝群における差異は線量による差をよりよく示したが、この高線量被曝群の人数が少なく、広島・長崎両市合計で32名、すなわち全数のわずか10%であったため統計的有意性を確立することはできなかった。爆心地から5000 m未満の距離で被爆した者のほぼ25%に当たる78名の子供からなる40 rad 以上の被曝群では、線量による差は小さかった。平均値間の差は表4に示すようにStudentの"Y"検定を用いて検討した。

TABLE 3 WHOLE-BODY GAMMA AND NEUTRON RAD DOSE (T65D) TO MOTHERS OF IN UTERO CHILDREN WITHIN 5000 m FROM HYPOCENTER IN BONE MATURATION STUDY, HIROSHIMA AND NAGASAKI

表3 骨格熟成調査における爆心地から5000 m未満の原爆時胎内被爆児の母親への 全身ガンマおよび中性子放射線量(T65D), 広島・長崎

Mother's Whole-b	ody	Hiro	shima	Na	gasaki
T65 Dose		No.	%	No.	%
Number of Subjects	but +84-	222	100.0	109	100.0
Total dose	<1 rad	76	34.2	41	37.6
	1-19	76	34.2	13	11.9
	20-39	24	10.8	21	19.3
	40-59	11	5.0	10	9.2
	60-79	9	4.1	5	4.6
	80-99	6	2.7	5	4.6
	100 +	18	8.1	14	12.8
	Unknown	2	0.9	0	0.0
Gamma radiation	<1 rad	76	34.2	41	37.6
4.0	1-19	86	38.7	13	11.9
	20-39	17	7.7	22	20.2
	40-59	13	5.9	9	8.3
	60-79	9	4.1	5	4.6
	80-99	11	5.0	5	4.6
	100 +	8	3.6	14	12.8
	Unknown	2	0.9	0	0.0
Neutrons	<1 rad	79	35.6	94	86.2
	1-19	126	56.8	14	12.8
	20-39	9	4.1	1	0.9
	40-59		1.4	0	0.0
	60-79	2	0.9	0	0.0
	80-99	0	0.0	. 0	0.0
	2.0 100 +	1	0.5	0	0.0
To be	Unknown	2	0.9	0	0.0

2296 Test Tables 1 A, B, C

The observed differences in mean ages at which the various epiphyseal centers closed revealed no consistent evidence of a radiation effect. The most heavily exposed males (the 100 rad or more group) tended toward earlier closure (19 of a total of 21 centers), compared with the less than 1 rad group. In females, 20 of the 21 centers analyzed by dose closed at an older age in the most heavily exposed group. The observed differences were 6.8 months earlier to 1.5 months later in males in the 100 rad and over group compared with 0.4 months earlier to 10.4 months later for females. Two of the 42 differences (female, centers 10 and 13) were significant in the direction of delayed development with Considering the number of tests of significance performed and the similarity of results expected when each of 21 observations on the same children are analyzed, the observed differences are attributable to chance.

3252 L8

各骨端核の閉鎖する平均年齢における観察差では、一貫した放射線影響の形跡は認められなかった。最強度被曝の男子(100 rad 以上の被曝群)は、1 rad 未満群と比較して、閉鎖が早期に起こる傾向があった(骨端核21のうち19).女子では、線量別に調べた骨端核21のうち20は最強度被曝群において遅く閉鎖した。観察された閉鎖時期の差は、線量100 rad 以上を受けた男子群では、6.8か月早くから1.5か月遅くまでであったのに対して、女子では0.4か月早くから10.4か月遅くまでであった。差を示した42のうち二つ、すなわち、女子における骨端核10および13には、被曝によって有意の発育遅滞が認められた。実施した有意性検定の数および同じ子供についての21の観察を個々に解析した場合に期待される結果の類似性を考慮に入れると、認められた差異は偶然に起因しているものとすることができる。

TABLE 4 DIFFERENCE IN MEAN AGES (MONTHS) AT CLOSURE OF EPIPHYSEAL CENTERS OF IN UTERO CHILDREN, HIGH DOSE GROUPS (40+ RAD AND 100+ RAD TO MOTHER) COMPARED WITH LOWER DOSE GROUP (<1 RAD), BY SEX — CITIES COMBINED

表 4 原爆時胎内被爆児群 (母親の被曝線量40 rad 以上および 100 rad 以上の者) と低線量群 (1 rad 以下の者) の 骨端核閉鎖時における平均年齢 (月)差:男女別,広島・長崎両市合計

	Diezeu)		Artifes	reld		100000	IngW.z'gertol		
	an and an	Male	18	cV		Female	IDAT COT		
Center	40+ rac	l .	100+	rad	40+ rad		100+ rad		
Contor		sed	07/0	osed	Close		Closed		
	Earlier than	Later than <1 rad	Earlier than <1 rad	Later than	Earlier than L	ater than <1 rad	Earlier than	Later than <1 rad	
1	1.4 mont	h gr	3.8			1.1		2.9	
2	3.4.1.1		6.0			< 0.05		0.7	
3		0.1	4.5			1.6		3.7	
4	0.7		2.6			1./		3.3	
5	1.8		4.1		2.3		0.4		
6	0.8		4.8			0.5		2.7	
7	2.4		4.2			2.4		6.4	
8	2.5		4.8			0.3		2.1	
9	0.8		3.1			0.3		1.6	
10	3.4.2.4		6.6 Sugg			1.0		10.4*	
11	8.5 1.8		2.6	8	1.1 + 001			0.1	
12	0.6		5.2		0.3			1.2	
13	1.7		2.8			3.4		7.5*	
14		0.7	1.0		1.3			0.2	
15	2.7		6.8 Sugg		29-39	3.4		4.1	
16	1.1		3.4			3.8		6.3	
17	0.01.4		3.7			2.3		4.2	
18	0.0 2.7		4.6			0.5		1.6	
19	6.0 1.1		3.9			4.7		4.7	
28		1.3		1.5		7.1 Sugg		8.7 Sug	
29		3.6		1.1	0.3			0.6	

Sugg = $.1 \ge P > .05$ (Statistically suggestive); * = $.05 \ge P > .01$ (Statistically significant)

2296 Tables 1A-20A

A more detailed analysis of centers 10 and 13 (those for which the observed differences were significant) and for centers 16 and 28 (generally the first and last centers to close) directed to quantifying the effect of dose upon age at closure supports this conclusion. No expousre effect appeared when trimester of gestation ATB and gamma and neutron doses were considered in the analysis.

The ages at which each epiphyseal center was closed for 50% of the children are shown by sex for each city in Table 5. Six to 7 years elapsed from the earliest age at which closure was observed and the age when the last clousre occurred for a given center. This range was considerably greater than the difference between centers and sexes. In general, the maturation of centers in the female

閉鎖時の年齢に対する線量の影響を量的に調べるために 行なわれた観察差が有意であったところの骨端核10およ び13,ならびに通常には最初と最後に閉鎖する核である ところの16および28についてのより詳細な解析は、この 結論を支持するものである。解析において、原爆時の妊 娠3か月期およびガンマ線と中性子線の量について考察 してみたが、被曝の影響は認められなかった。

表5では、各骨端核において50%の対象者に閉鎖の認められた時の年齢を都市別および男女別に示す。特定の骨端核について、閉鎖が最初に観察された者の年齢と最後に観察された者の年齢との間に6-7年の差があった。この差の範囲は、骨端核相互間および男女間における差よりもはるかに大であった。一般に、女子の骨端核の成熟度は、男子のそれよりも約1½年早かった。最初に閉鎖

TABLE 5 MEDIAN AGE AT CLOSURE OF EPIPHYSEAL CENTERS OF HAND AND WRIST BY SEX, HIROSHIMA AND NAGASAKI

表5 手および手首の骨端核閉鎖時の中央値年齢: 男女別, 広島・長崎

99.00	al5 &			Male	•				Fe	male			
Fun	enter		Hiroshima		Nag	Nagasaki		Hir	oshim	a	Nagasaki		
Normal	1	monE	16	1/4	16	1/2	luniso	14	1/2	WE.	14	1/2	
	2		16	3/4	17			15			15		
	3		16	1/2	16	3/4		15			15		
	4		16	1/4	16	1/2		14	3/4		14	3/4	
	2		17		17	1/4		15	1/2		15	1/2	
	6		16	3/4	17			15	1/4		15		
	1		16	1/4	16	1/2		14	1/2		14	3/4	
	8		17		17	1/4		15	1/2		15	1/2	
	9		16	3/4	16	3/4		15	1/4		15		
	10		16	1/4	16	1/4		14	1/2		14	1/2	
	11		16	3/4	17			15	1/2		15		
	12		16	3/4	16	3/4		15	1/4		15		
	13		16		16	1/4		14	1/4		14	1/2	
	14		16	3/4	16	3/4		15	1/4		15		
	15		17		17	1/4		15	3/4		15	1/2	
	16		16	3/4	17			15	1/2		15	1/4	
	17		16	3/4	17	1.81		15	1/2		15	1/4	
	18		16	3/4	17			15	1/2		15	1/2	
	19		16	1/2	16	1/4		14	3/4		14	3/4	
	28		18	1/4	18	1/2		17	1/2		17	1/2	
	29		18	3/4	18	1/2		17	3/4		18		

Tab 1633-1 & 2-C

50th percentile age — earliest age to nearest 1/4 year interval at which at least 50% closure is reached. Age within year intervals interpolated graphically using normal probability paper.

第50百分位数年齢―少なくとも骨端核閉鎖率50%の認められた最も早い年齢でその最も近い 四半期. 正規確率紙を用いて年齢を1年以下の間隔に区切ってダラフにより補間した.

was about 1½ years in advance of that in males. The first center to close (13) preceded the last closing center (29) by 2½ years for males and 3½ years for females. No difference in ages at closure in the two cities was seen.

A short middle phalanx for the fifth digit was seen in Hiroshima in 24 males (11%) and 29 females (19%), but occurred rarely in Nagasaki. Suspecting that this abnormality might be accompanied by earlier maturation, average ages at closure were recalculated for normal and short phalanx subjects as shown in Table 6. Although variation in age at closure was seen, there is no strong evidence that the true ages at closure differ by sex. In males, closure in subjects with short phalanx occurred 3 months earlier to 3 months later, depending upon the center. In females, the range was 17 months

する骨端核13は、最後に閉鎖する骨端核29よりも、男子については2 ½年、女子については3 ½年それぞれ早く起こった。広島・長崎両市における骨端核閉鎖時の年齢に差は認められなかった。

広島においては、第5指の中節骨の短縮が男子24人(11%)、女子29人(19%)に認められたが、これは長崎ではほとんど認められなかった。この異常が早期熟成に伴って起こるかもしれないとの疑いのもとに、表6に示すように、正常節骨および短節骨を有する対象者について閉鎖時の平均年齢の再計算を行なった。閉鎖時の年齢には差異が認められたが、閉鎖時の真の年齢に男女差があるという確固とした証拠はない。男子では、短節骨を有する対象者における閉鎖は、骨端核によって3か月早くから3か月遅く起こった。女子では、この範囲は17か月早く、ない

TABLE 6 AGE IN YEARS OF IN UTERO CHILDREN AT WHICH 10% AND 50% CLOSURE OF EACH EPIPHYSEAL IS ATTAINED, NORMAL AND SHORT PHALANX, HIROSHIMA

表6 正常および短節骨における各骨端の10%および50%が閉鎖した時の原爆時胎内被爆児の年齢,広島

		10%	Closure			50% (Closure	
Center	Male	amisteo	Female	e want	Male	EL .	Femal	e
	Normal	Short	Normal	Short	Normal	Short	Normal	Short
1	15 21	14 3/4	12 3/4	12 1/4	16 1/4	16 1/4	14 1/2	14 1/4
2	15 1/2	15 1/4	13 1/2	12 1/4	16 3/4	16 1/2	15 1/4	14
3	15 1/4	15 1/4	13 1/2	13	16 1/2	16 1/2	15 1/4	14 3/4
4	15	15	12 3/4	12 1/2	16 1/4	16 1/4	14 3/4	14 1/4
5	15 1/2	15 1/2	14 1/4	13	16 3/4	16 3/4	15 1/2	15
6	15 1/4	15 1/4	13 1/2	13	16 1/2	16 1/2	15 1/4	14 1/2
7	15	15 2\1	12 3/4	12 1/2	16 1/4	16	14 1/2	14 1/4
8	15 1/2	16 1/2	14 1/4	13	15 3/4	16 3/4	15 3/4	15 1/4
9	15 1/4	15 1/4	13 3/4	13	16 1/2	16 1/2	15 1/4	14 3/4
10	15	15	12 3/4	12 3/4	16 1/4	16 1/4	14 1/2	14 1/4
11	15 1/2	15 1/2	14 1/4	13	16 3/4	16 3/4	15 1/2	15 1/4
12	15 1/2	15 1/4	13 3/4	13	16 3/4	16 1/2	15 1/4	14 3/4
13	14 1/2	14 1/2	12 1/2	12 1/4	16	16	14 1/2	13 3/4
14	15 1/2	15 1/4	13 3/4	13	16 3/4	16 3/4	15 1/4	15
15	15 3/4	15 3/4	14 1/4 ~	14	17	16 3/4	15 3/4	15 3/4
16	15 1/2	15 1/2	14 1/4	13 1/2	16 3/4	16 3/4	15 1/2	15 1/2
17	15 1/2	15 1/2	14 1/4	13	16 3/4	16 3/4	15 1/2	15
18	15 1/2	15 1/2	14 1/4	13 1/2	16 3/4	16 3/4	15 1/2	15 1/4
19	15	15 1/4	13 1/4	12 1/2	16 1/2	16 1/2	14 3/4	14 1/2
28	17 1/4	17 1/4	16 1/4	15 3/4	18 1/4	18 1/2	17 1/2	17 1/4
29	17 1/4	17 1/2	16 1/4	15 3/4	18 3/4	18 3/4	17 3/4	17 1/2

Tab 1633-1. 3-C

Percentile age determined graphically by interpolation to nearest 1/4 years using normal probability paper. 百分位数年齢は、正規確率紙を用いて、最も近い四半期を補間法によりグラフで求めた。

early to 0.2 month late, but the difference was significant for only one of the 21 centers studied. The consistency with which earlier maturation occurred is a reflection of the correlation expected between the occurrence of related events in the same individual.

The closure data are reported in two ways besides mean age at closure:

- 1. The percentage of centers closed at successive years of age (birth anniversaries), and
- 2. the estimated ages in ¼ year intervals at which 10%, 50%, and 90% closure occurred for each center.

The percentages of centers closed at successive birth anniversaries were recorded directly from the computation worksheets, and are shown in Table 7. し0.2か月遅く起こったが、その差は調査した骨端核21 のうち一つのみに有意であった。早期熟成の一貫性は、 同一個人における関連事象の発現との間に期待された相 関関係を反映するものである。

閉鎖に関する資料は閉鎖時の平均年齢の他に,次の二つ の方法で報告されている:

- 1. 毎年の誕生日における骨端核閉鎖の百分率(%).
 - 2. 各骨端核別に10%, 50%および90%に閉鎖の認められた, ¼年間隔による推定年齢.

毎年の誕生日における骨端核閉鎖の百分率は計算用紙から直接記録した、それを表7に示す。

TABLE 7 PERCENTAGE OF EPIPHYSEAL CENTERS CLOSED AT STATED AGES BY SEX, HIROSHIMA AND NAGASAKI

表7 各年齢時における骨端核閉鎖の百分率: 男女別, 広島および長崎

Con	Contor				Yeges	Age in	Years							
Sex	Center	10 % 11	12	13	14	15	16	17.1	18	19	20	21		
						Hirosh	nima							
Male	0.101			0.0	1.8	10.8	39.8	81.2	97.0	98.8	100.0			
	2			0.0	0.9	3.6	22.7	67.0	92.1	97.8	98.9	100.0		
	3			0.0	1.4	4.5	27.2	73.1	95.1	98.6	100.0			
	4			0.0	1.8	9.5	39.8	81.6	96.9	98.8	100.0			
	5			0.0	0.9	2.7	17.7	58.6	89.3	97.0	98.8	100.0		
	6			0.0	1.4	4.5	25.9	72.2	95.5	98.9	100.0			
	7			0.0	2.2	10.8	43.2	84.5	97.0	98.8	100.0			
	8			0.0	0.9	2.7	17.7	58.6	89.8	96.6	98.9	100.0		
	9			0.0	1.4	5.0	25.4	71.2	95.5	98.9	100.0			
	10			0.0	1.8	11.7	40.7	84.5	97.0	98.8	100.0			
	110			0.0	0.9	3.6	21.8	64.2	91.7	97.2	98.9	100.0		
	12			0.0	0.9	3.6	24.5	70.8	94.6	98.4	100.0			
	13			0.0	2.2	18.5	52.3	87.4	97.0	98.8	100.0			
	14			0.0	0.9	4.0	26.8	70.7	94.5	97.8	100.0			
	15			0.0	0.9	2.7	16.3	54.9	88.2	96.3	98.8	100.0		
	16			0.0	0.9	3.6	21.8	61.4	93.2	98.4	99.5	100.0		
	17			0.0	0.9	3.2	24.5	61.8	93.1	98.4	99.5	100.0		
	18			0.0	0.9	4.5	24.1	61.3	92.2	97.8	99.4	100.0		
	19		0.0	0.4	1.8	9.5	36.8	79.6	96.5	98.3	100.0	100.0		
	28		0.0	0.4	1.0		2.3	9.3	46.8	69.8	91.0	100.0		
	29						0.4	6.0	32.3	58.8	89.0	100.0		
Female	1 2	$0.0 0.7 \\ 0.0 0.7$	2.0	17.3	32.7 20.0	72.7 50.0	92.0 79.4	98.7 94.5	100.0 100.0					
		0.0	0.7	6.7	18.0	48.7	81.5	95.2	100.0					
	0.301			12.7	29.3	67.3	90.5	98.6	100.0					
	4	0.0 0.7	2.0	4.0	10.7	34.7	66.7	92.5	100.0					
*	5		0.0	7.3	18.7	47.3	83.6	95.9	100.0					
	6	0.0	0.7	14.7	30.7	73.3	92.0	98.7	100.0					
	7	0.0 0.7	0.0	2.7	8.7	34.7	69.4	92.5	100.0					
	8	0.0	0.7	5.3	15.3	44.7	82.9	96.6	100.0					
		0.0 0.7	2.0	14.0	32.7	76.0	94.7	98.7	100.0					
	10		0.7	4.0	10.0	38.7	74.8	93.9	100.0					
	11		0.7	6.0	16.7	48.0	82.2	96.6	100.0					
	12 13	0.0	2.0	23.3	40.7	81.3	95.3	98.7	100.0					
					15.3	44.0	80.9	96.6	100.0					
	14	0.000.0	0.7	2.0	6.7	24.7	60.6	83.7	96.5	100.0				
	15		0.0		8.0	35.3	69.4	90.5	100.0	100.0				
	16		0.0	2.0	11.3	42.0	72.0	90.5	100.0					
	17		0.0	3.3 2.7	10.0	36.7	71.4	91.2	100.0					
	18		0.0		27.3		88.5	97.3	99.3	100.0				
	19		0.0	12.0		0.0	10.9	38.8	72.3	86.2	99.2	100.0		
	28								66.0	81.7	97.3	100.0		
	29					0.0	10.2	32.0	0.00	01./	91.3	100.0		

Tab 1633-1-C

TABLE 7 Continued 続き

Sex	Center				10.09	Age	in Yea	ırs				
SCA	Center	10 1	1 12	13	14	15	16	17	18	11 19 01	20	21
III.					10.0	Nagas	aki					H.F.
Male	1			0.0	0.9	15.0	40.1	67.9	93.4	98.7	100.0	
	2			0.0	0.9	9.3	29.6	55.9	88.2	97.6	100.0	
	3			0.0	0.9	9.3	32.5	57.8	90.3	98.8	100.0	
	4			0.0	0.9	16.8	41.0	67.8	94.4	98.9	100.0	
	5				0.0	5.6	26.8	48.0	87.0	97.6	100.0	
	6				0.0	11.2	31.5	54.7	91.4	98.8	100.0	
	7			0.0	0.9	19.6	42.9	69.8	94.4	98.9	100.0	
	8				0.0	4.7	26.8	44.8	88.1	97.6	100.0	
	9				0.0	11.2	33.4	57.7	92.4	98.7	100.0	
	10			0.0	0.9	16.8	43.9	71.4	95.6	100.0		
	11				0.0	4.7	26.8	53.0	88.2	97.6	100.0	
	12			0.0	0.9	9.3	35.4	58.7	89.1	98.6	100.0	
	13			0.0	0.9	19.6	49.6	75.9	95.4	100.0		
	14			0.0	0.9	6.5	31.6	57.9	92.4	98.7	100.0	
	15				0.0	3.7	20.1	41.4	82.6	96.0	100.0	
	16					5.6	25.8	51.3	84.8	96.2	100.0	
	17					4.7	28.7	53.2	86.9	96.1	100.0	
	18					4.7	26.8	52.3	88.1	96.0	100.0	
	19			0.0	0.9	14.0	45.9	71.9	94.4	98.9	100.0	
	28			5.074			0.0	5.2	32.6	78.5	100.0	
	29							4.2	28.7	74.2	97.7	100.0
Female	1		0.0	12.0	24.0	77.3	97.0	98.5	100.0			
	2		0.0	8.0	13.3	53.3	84.0	94.2	98.5	100.0		
	3		0.0	5.3	10.7	57.3	80.1	95.7	97.2	98.6	100.0	
	4		0.0	9.3	18.7	72.0	97.0	98.5	100.0			
	5		0.0	1.3	5.3	36.0	71.6	87.2	94.3	97.2	100.0	
	6		0.0	5.3	10.7	54.7	85.8	97.2	98.6	100.0		
	7		0.0	9.3	22.7	76.0	98.4	100.0				
	8			0.0	4.0	37.3	71.5	88.6	95.7	98.6	100.0	
	9		0.0	5.3	9.3	60.0	88.2	97.0	98.5	100.0		
	10	0.0 1	.3 2.7	16.0	29.3	81.3	96.9	98.4	98.4	100.0		
	11		0.0	4.0	6.7	50.7	79.7	92.8	97.1	98.6	100.0	
	12		0.0	6.7	10.7	58.7	86.7	97.0	98.5	100.0		
	13		0.0	14.7	26.7	84.0		100.0				
	14		0.0	6.7	10.7	52.0	84.0		98.6	100.0		
	15			0.0	2.7	37.3	67.2		91.5	- 94.9	100.0	
	16			0.0	4.0	42.7	72.8		92.8	96.4	100.0	
	17			0.0	4.0	45.3	74.1	87.1	97.1	98.6	100.0	
	18			0.0	2.7	40.0	70.0		95.7	97.1	100.0	
	19	0.000	.0 1.3	13.3	24.0	73.3		100.0	0.6	100000000	(E)	
	28				0.0	9.3	17.7		69.9	84.0	93.2	100.0
	29				0.0	2.7		25.8	53.1	80.9	93.6	100.0

Tab 1633-2-C

TABLE 7 Continued 続く

Corr	Contor						Age in	Years					
Sex	Center	10	11	12	13	14	15	16	17	18	19	20	21
	Brex	1 mile		-na -15 5 7	Hiro	shima	and Na	gasaki	gue	is and			
Male	BH 1					1.5	12.2	39.9	77.1	95.8	98.8	100.0	
	2					0.9	5.5	24.9	63.6	90.9	97.7	99.1	100.0
	3					1.2	6.1	28.9	68.4	93.6	98.7	100.0	
	4					1.5	11.8	40.2	77.5	96.2	98.8	100.0	
	11815					0.6	3.7	20.6	55.4	88.6	97.3	99.1	100.0
	6					0.9	6.7	27.7	66.8	94.2	98.8	100.0	100.0
	7				100000000000000000000000000000000000000	1.8	13.7	43.2	80.1	96.2	98.9	100.0	
	1 8 1 8					0.6	3.3	20.6	54.5	89.3	96.9	99.1	100.0
				. 81		0.9	7.0	28.0	67.1	94.6	98.8	100.0	100.0
				511.11	3655330	1.5	13.4	41.7	80.5	96.6	99.1	100.0	
	10				200		4.0	23.4	60.7	90.6	97.4	99.1	100.0
	11					0.6	5.5	28.0	67.1	92.9	98.4	100.0	100.0
	12					1.8	18.8	51.4	83.9	96.5	99.4	100.0	
	13					0.9	4.9	28.3	66.8	93.9	99.2	100.0	
	14											98.9	100.0
	15					0.6	3.1	17.6	50.8	86.5	96.2	99.4	100.0
	16					0.6	4.3	23.1	58.3	90.6	97.7	99.4	100.0
	17					0.6	3.6	25.9	59.2	91.2	97.7		
	18			0.0		0.6		25.0	58.6	90.9	97.2	99.5	100.0
	19			0.0		1.5	10.9	39.7	77.3	95.9	98.5	100.0	100.0
	28						0.0	1.5	8.0	277	72.2	93.1	100.0
	29						0.0	0.3	5.5	31.2	63.2	91.2	100.0
Female	e 681 1	0.0			15.6	29.8	74.2	93.6	98.6	100.0			
	2	0.0	0.4	0.9	9.8	17.8	51.1	80.9	94.4	99.5	100.0		
	8 16 3		0.0	0.4	6.2	15.5	51.6	81.1	95.4	99.1	99.5	100.0	
	A E E B A	0.0	0.4	1.3		25.8	69.7	92.8	98.6	100.0			
	1115			0.0	3.1	8.9	35.1	68.2	90.8	98.2	99.1	100.0	
	6 16 16			0.4	6.7	16.0	49.8	84.3	96.3	99.5	100.0		
	AEEE 7	0.0	0.4	1.3	12.9	28.0	74.2	93.9	99.1	100.0			
	AE 11 8			0.0	1.8	7.1	35.6	70.1	91.3	98.6	99.5	100.0	
	9			0.4		13.3	49.8	84.7	96.7	99.5	100.0		
	10	0.0	0.9	2.2		31.6	77.8	95.4	98.6	99.5	100.0		
	11163/		0.0	0.4	4.0	8.9	42.7	76.4	93.5	99.1	99.5	100.0	
	11 0 12		0.0	0.4	6.2	14.7	51.6	83.7	96.7	99.5	100.0		
	11 2 13	0.0	0.4	1.3	20.4	36.0	82.2	96.3	99.1	100.0			
	14			0.4	5.8	13.8	46.7	81.9	96.3	99.5	100.0		
	15			0.0		5.3	28.9	62.8		94.8	98.4	100.0	
	16			0.0	1.3	6.7	37.8	70.5	89.4	97.6	98.8	100.0	
	17			0.0		8.9	43.1	72.7		99.1	99.5	100.0	
	18			0.0	1.8	7.6	37.8	71.0		98.6	99.0	100.0	
	19			0.4	12.4	26.2		89.8			100.0		
	28			2		0.0		13.2			85.5	97.6	100.0
	29					0.0		10.5		61.9		96.2	100.0

Tab 1633-1 & 2-C

TABLE 8 AGE IN YEARS OF IN UTERO CHILDREN AT WHICH 10%, 50% AND 90% CLOSURE OF EACH EPIPHYSEAL CENTER IS ATTAINED BY SEX, HIROSHIMA AND NAGASAKI

表8 骨端核閉鎖10%, 50%および90%に達した際の原爆時胎内被爆児の年齢:

性別,広島および長崎

Sex	Center 01	H	roshima	0.0	Na	gasaki	103311.3
	Conto	10th P	50th P	90th P	10th P	50th P	90th P
Male	0.001 1 8 8	15 9.20	16 1/4	17 1/2	14 3/4	16 1/2	18
	1.00 2 7.70	15 1/4	16 3/4		0.0 15	16 3/4	18 1/4
	0.000 3 TA	15 1/4	16 1/2		0.0 15	16 3/4	18
	0.001 4 8.8	15	16 1/4		14 1/2	16 1/4	17 3/4
	1.00 5 1.41	15 1/2	16 3/4		15 1/4	17	18 1/4
	6 8 8	15 1/4	16 1/2	17 3/4	0.0 15	16 3/4	18
	0.001 7 9.8	15	16 1/4		14 1/2	16 1/4	17 3/4
	1.00 8 0.00	15 1/2	16 3/4		15 1/4	17 1/4	18 1/4
	0.001 9 8.8	100000000000000000000000000000000000000	16 1/2		15	16 3/4	18
	0.001 10 1.00	14 3/4	16 1/4		14 1/2	16 1/4	17 3/4
	1.00 11 4.50	15 1/2	16 3/4		15 1/4	17	18 1/4
	12	15 1/4	16 1/2		0.0 15	16 3/4	181/4
	0.001 13 1.0		16		14 1/2	16	17 3/4
	0.691 14 1.8		16 1/2		15 1/4	16 3/4	18
	0.89 15 0.34		8 17 a.T.		15 1/2	17 1/4	18 1/2
	A 69 16 T.T		16 3/4		15 1/4	17	18 1/2
	1.00 17 0.00	G0 62 0 G 0 2 0 0	16.3 / 4		15 1/4	17	18 1/2
	2.00 18 2.50		16 3/4		15 1/4	17	18 1/4
	0.001 19 2.80		16 1/4		14 3/4	16 1/4	17 3/4
	28		18	20	17 1/4	18 1/2	19 1/2
	29 5.6		18 3/4	20	17 1/4	18 1/2	19 3/4
Female	1	12 1/2	14 1/2	16 8.85	12 3/4	14 1/2	15 3/4
	2 0.0	13	0.15 0.08	16 3/4	13 1/2	15	16 1/2
	0.001 3 2.0	13 1/4	4 15 F.18	16 3/4	14	14 3/4	16 3/4
	4	12 3/4	14 1/2	16	13	14 1/2	15 3/4
	0.001 5 1.0	14	15 180	1.17	14 1/4	15 1/2	17 1/2
	6 9.0	13 1/4	£ 15 € 18	16 1/2	7.8 14 .0	1.0 15	16 1/2
	7	123/4	14 1/2	28.0 61.2	13	14 1/2	15 3/4
	0.001 8 7.0	14 0.88	15 1/2	17 TA	14 1/4	15 1/2	17 3/4
	9	13 1/2	15 1/4	16 1/2	8.8 14 0	14 3/4	16 1/4
	10	12 3/4	15 1/2	15 3/4	12 1/2	14 1/2	15 1/2
	0.661 11 2.89	The State of the S	15 1/4	16 3/4	0.4 14 0	1.0 15	16 3/4
	12	13 1/2	15	16 1/2	5.8 14 .0	14 3/4	16 1/2
	13	12 1/2	14 1/4	15 3/4	12 3/4	14 1/2	15 1/3
	14 0 0		15 1/4	16 1/2		15	16 1/2
	6.601 15 2.80	14 1/4	15 1/2	17 1/2	14 1/4	15 1/2	18
	0.001 16 8.81	14 a 19	15 1/2	8.17 1.5	14 1/4	15 1/4	17 1/3
	0.001 17 2.00	13 3/4	15 1/4	1.17 0.8	14 1/4	15 1/4	17 1/4
	0.001 18 0.00	14 3.89	15 1/2	8.17 a.V	14 1/4	15 1/4	17 1/4
	19 0.00	12 3/4	14 3/4	16 1/4	12 3/4	14 1/2	16
	28 28	16 8.15	17 1/2	19 1/4	15	17 1/2	19 3/4
	29	16	17 1/2	19 1/2	16	18	19 3/4

Percentile age determined graphically by interpolation to nearest 1/4 years using normal probability paper.

Tab 1633-1 & 2-C

百分位数年齢は、正規確率紙を用いて、最も近い四半期を補間法によりグラフで求めた。

TABLE 9 AGE IN YEARS OF IN UTERO CHILDREN AT WHICH 10%, 50% AND 90% CLOSURE OF EACH EPIPHYSEAL CENTER IS ATTAINED BY SEX, CITIES COMBINED

表 9 各骨端核の10%, 50% および90% が閉鎖した時の原爆時胎内被爆児の年齢: 性別, 広島・長崎両市合計

\$2200000000	10% Closure			50% Closure			90% Closure	
Center	Male	Female	1	Male	Female	Male	Female	
1	15	A3 13 T		16 1/2	14 1/2	17 3/4	15 3/4	
2	15 1/2	13 1/4		16 3/4	15	18	16 3/4	
3	15 1/2	13 1/2		16 3/4	15	18	16 3/4	
4	15	13		16 1/2	14 3/4	17 3/4	16	
5	15 1/2	14 1/4		17	15 1/2	18 1/4	17	
6	15 1/4	13 1/2		16 3/4	15 1/4	17 3/4	16 1/2	
7	15	13		16 1/4	14 1/2	17 1/2	15 3/4	
8	15 3/4	14 1/4		17	15 1/2	18 1/4	17	
9	15 1/4	13 3/4		16 3/4	15	17 3/4	16 1/2	
10	15	12 3/4		16 1/4	14 1/2	17 1/2	15 3/4	
11	15 1/2	14 1/4	030	16 3/4	15 1/4	18	16 3/4	
12	15 1/2	13 3/4		16 3/4	15	18	16 1/2	
13	14 3/4	12 3/4		16	14 1/2	17 1/2	15 1/2	
14	15 1/2	13 3/4		16 3/4	15 1/4	18	16 1/2	
15	15 3/4	14 1/2		17	15 3/4	18 1/4	17 1/2	
16	15 1/2	14 1/4		17	15 1/2	18	17 1/4	
17	15 1/2	14 1/4		16 3/4	15 1/4	18	17	
18	15 1/2	14 1/4		16 3/4	15 1/2	18	17 1/4	
19	15	13		16 1/4	14 3/4	17 3/4	16 1/4	
28	17 1/4	15 3/4		18 1/4	17 1/2	20	19 1/4	
29	17 1/2	16		18 3/4	17 3/4	20	19 1/2	

Tab 1633-1 & 2-C

Percentile age determined graphically by interpolation to nearest 1/4 years using normal probability paper. 百分位数年齢は、正規確率紙を用いて、最も近い四半期を補間法によりグラフで求めた.

The interpolation of percentile ages was facilitated by the fact that age at closure appears to be normally distributed and a straight line results when the percentages of centers closed are plotted by age on normal probability paper (Figure 3).

When the data were plotted, the successive points were connected with straight lines and the nearest completed ¼ year of age with at least 10%, 50%, and 90% of centers closed was read by inspection. The results are shown by city in Table 8, and for both cities combined in Table 9 and Figure 4.

正規確率紙に骨端核閉鎖の百分率をプロットした場合, 閉鎖時の年齢が正常に分布しており,直線を示すようで あるので,百分位年齢の補間は容易にできた(図3).

資料をプロットしたあと、各点と点を直線で結び、少なくとも骨端核閉鎖が10%、50%および90%に認められた年齢に最も近い対歳の時点を読み取った。核閉鎖が10%、50%および90%に認められた時の結果は、表8に都市別に示し、両市合計の結果は、表9および図4に示す。

FIGURE 3 EXAMPLE OF INTERPOLATION TO ESTIMATE PERCENTILE AGES HIROSHIMA MALE, CENTER NO. 1

図3 百分位年齢推定のための補間法適用例,広島男子, 骨端核1

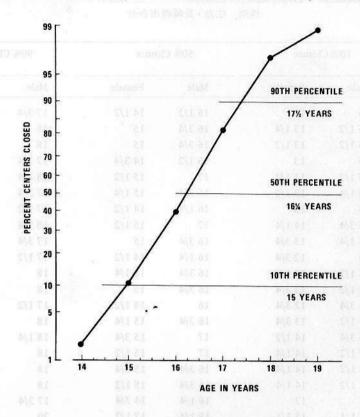
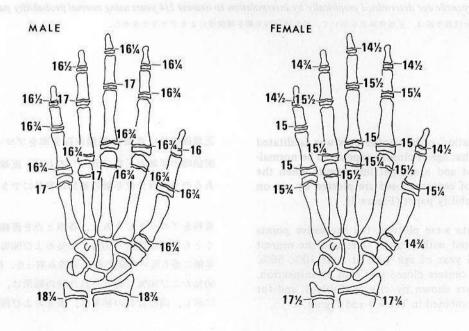


FIGURE 4 MEDIAN AGES OF CHILDREN AT CLOSURE OF EPIPHYSEAL CENTERS OF HAND AND WRIST, HIROSHIMA AND NAGASAKI

図4 手および手首骨端核閉鎖時の中央値年齢,広島および長崎



DISCUSSION

Hand and Wrist Roentgenograms in Assessing Bone Maturation. Hand and wrist roentgenograms are easily obtained, incur small radiation doses, and are most widely used for assessing bone maturation. Variations occur in the beginning and final phases of maturation according to whether the long, short, or round carpal bones of the hand and wrist are observed. The long and short bones vary less in development than the carpal bones.

Skeletal age is best assessed by roentgenograms throughout their development period. The beginning and terminal events occur in relatively rapid sequence — from birth to 6, and from 13 to 20 years. Only the terminal stages of skeletal maturation could be observed in the study subjects. The serial roentgenograms of the hand and wrist commenced at the age of 9 years.

Epiphyseal ossification is a delicate objective indicator of the health of the subject, more so than his height or weight.²² Infants with gastrointestinal upsets, though not retarded in body length, exhibit delays in epiphyseal ossification, the earliest and often the only indicators of a metabolic or constitutional disturbance.²³

The final shapes and dimensions of bones, as well as epiphyseal closure, are reportedly under separate endocrine control,²⁴ and genetic factors are also involved.²⁵ Even in the absence of major growth-retarding conditions, atypical ossification patterns can occur.²⁶

Comparison by Norms and Atlases. Takamori²⁷ reported earlier bone maturation among his Japanese subjects in 1955 than in U.S. children studied through 1942.¹⁴ In 1966, Suzuki²⁸ reported maturation of carpal bones among Japanese to be slower than that in U.S. children, by Greulich and Pyle standards. Eto²⁹ found hand centers of Tokyo students to close earlier than those of U.S. children by the Greulich and Pyle atlas.

Though all subjects in a study may not have "balanced" hands with proportional development of the three types of bones, use of atlases of the Greulich and Pyle type for comparisons of series is a justifiable procedure. Sugiura and Nakazawa assessed closure of hand epiphyseal centers for the Japanese subjects according to the method of Greulich and Pyle. The 50th percentile values for ages at which each of the 21 hand and wrist centers were found to close in the Greulich and Pyle, the

手および手首の X線撮影による骨格熟成の評価. 手および手首の X線写真は容易に撮影でき、必要とする放射線量は少なく、骨格熟成を評価するのに最も広く使用されている。手および手首の長骨、短骨または円形の手根骨のうち、いずれについて観察したかによって、骨格熟成の開始時期および最終時期に差異が起こる. 13 発育においては、手根骨よりも長骨や短骨の変化は少ない.

骨格年齢は、その全発育期を通じて、X線写真により最もよく評価できる。その開始期および終末期は、出生時から6歳までと13歳から20歳までであって、比較的急速に起こる。本調査対象者では、骨格熟成の終末期段階のみを観察することができた。手および手首についての一連のX線写真撮影は、年齢9歳から始められた。

骨端の化骨は、身長や体重よりも対象者の健康状態を示す微妙かつ客観的な指針である.22 胃腸傷害を有する乳幼児では、体長の発育には遅滞を示さないが、骨端の化骨に遅滞がみられる.これは代謝性または体質上の障害を最も早く示す所見であり、また多くの場合唯一の所見である.23

骨格の最終的な形状および寸法ならびに骨端核の閉鎖は、それぞれ別の内分泌制御機構のもとにおかれており、²⁴ 遺伝的因子も関与していると報告されている。²⁵ 大きな成長が認められない場合、すなわち、遅滞のある時においても、非定型的な化骨像は得られる。²⁶

基準および図譜による比較. 高森は、 27 1942年に骨格熟成について調査を受けた米国の子供よりも、 14 1955年にかれが調査した日本の対象者の熟成度のほうが早いと報告した. 1966年、鈴木が Greulich および・Pyle の基準をもとに調べたところでは、米国の子供よりも日本人の手根骨の熟成が遅れていると報じた. 28 江藤は Greulich と Pyle の X 線像図譜に示された米国の子供の手の骨端核閉鎖よりも東京の学童のほうが早く閉鎖することを認めた. 29

特定の調査の対象者全員が 3 種の骨の発育程度につりあいのとれた、いわゆる「均衡のとれた」手をしていなくても、一連のX線写真の比較を行なうには Greulich と Pyle のまとめたような図譜を使用することが妥当な方法である. 18 杉浦および中沢 30 は、Greulich と Pyle の方法によって日本人対象者の手における骨端核の閉鎖を調べた.手および手首の 21 の骨端核のそれぞれが閉鎖する年齢の第50百分位数値について Greulich と Pyle、杉浦および

Sugiura and Nakazawa, and the present study are shown in Table 10. While the Greulich and Pyle data were collected in 1942, and while some alterations in rate of development may have resulted from dietary changes, the Greulich and Pyle atlas, nevertheless, remains the authoritative reference. Without access to the original statistical data of the other studies, such as standard deviations, it was impossible to compare more accurately their results with ours.

The average of median ages at closure of a uniform set of 18 hand centers for males was 1 month later in the Sugiura and Nakazawa than the Greulich and Pyle study. Sugiura and Nakazawa's female subjects showed closure 2 months later than those of Greulich and Pyle. Epiphyseal closure in the present study occurred later than in the Greulich and Pyle study by 7 and 9 months for males and females, and later than in the Sugiura and Nakazawa study by 6 and 8 months for males and females, respectively.

Earlier Bone Maturation Studies in Hiroshima and Nagasaki. Greulich1 studied hand and wrist roentgenograms and body measurements of Hiroshima and Nagasaki school children and Kure and Sasebo comparisons in 1946 and 1947, including some follow-up cases. Some of the index subjects were in the cities ATB. The skeletal maturation of the Japanese was delayed compared to U.S. children according to Greulich and Pyle standards. The Hiroshima boys were skeletally retarded compared to those of Kure, and were more retarded than Hiroshima girls. The Hiroshima and Nagasaki children in the cities ATB were reported to have been adversely affected in growth and development and skeletal maturation. By 1946 and 1947, their heights and weights were still below National standards. As in other studies,31 the boys did not withstand the adverse environment as well as the girls, but it was impossible to attribute the results clearly to ionizing radiation though the degree to which it may have influenced this cannot be Physical and psychic trauma, and determined. malnutrition were very likely poverty and responsible.

In 1951 and 1952, Sutow² studied left hand and wrist roentgenograms made within 1 month of the birthdays of 2370 nonexposed Hiroshima boys and girls 6-19 years of age, according to Greulich and Pyle ratings, and found the Japanese to be consistently slower in skeletal maturation than American children. Postwar poverty, malnutrition, and racial

中沢ならびに本調査の結果をそれぞれ表10に示す。Greulich と Pyle の資料は、1942年に収集されたものであり、その後今日まで食生活の変化により、発育の割合にある程度の変化が生じたかもしれないが、Greulich と Pyle の 図譜は、依然として権威ある参照資料である。他の調査で用いられた標準偏差などのような統計資料が入手できなかったので、それらの調査結果と本調査のそれとをより厳密に比較することはできなかった。

男子において同じ18個の骨端核閉鎖時の正中年齢の平均は、Greulich と Pyle の調査の結果よりも杉浦および中沢のほうが1 か月遅かった。杉浦および中沢の女子対象者では、Greulich と Pyle の調査のそれよりも2 か月遅かった。本調査では骨端核閉鎖は、Greulich と Pyle 調査におけるよりも、男子と女子でそれぞれ7 か月と9 か月遅く、また、杉浦および中沢の調査におけるよりも、それぞれ6 か月と8 か月遅く起こった。

広島・長崎における初期の骨格熟成調査。 Greulich は、 1946年および1947年に広島・長崎の子供ならびに比較対 照者として呉, 佐世保の子供について手および手首のX線 写真および身体計測を実施し、その一部について経過観 察も行なった.1 指標対象者若干名は,原爆時市内にい た者である. Greulich と Pyle の基準によれば、日本人 の骨格熟成は、米国の子供のそれと比べ遅滞していた. 広島の男子は呉の男子に比べ骨格に遅滞がみられ、また 広島の女子よりも遅滞していた。 原爆時に市内にいた 広島・長崎の子供は、そのため発育および成長ならびに 骨格熟成に悪影響を受けたと報ぜられている。1946-47年 の時点では、その身長および体重は依然として全国基準 以下であった.他の調査31における検診結果と同様に、 男子は女子ほど逆境には耐えられなかったが、これを明 確に電離放射線の影響に起因するものとすることはでき なかった. また、それがどの程度影響したかも確認でき なかった. 肉体的および精神的障害, 貧困および栄養不 良がその原因であった可能性は強い.

1951年および1952年に、Sutow は Greulich と Pyle の測定基準によって、年齢6-19歳の広島の非被爆男女2370名の左手および左手首の X 線撮影を誕生日から1 か月 以内に実施したが、その結果、日本の子供は米国の子供よりも骨格熟成が一様に遅滞していることがわかった.2 戦後の貧困状態、栄養不良および人種による差が原因では

TABLE 10 MEDIAN AGE (YEARS) AT CLOSURE OF EPIPHYSEAL CENTERS BY SEX, GREULICH-PYLE (AMERICAN), SUGIURA AND NAKAZAWA (JAPANESE), AND PRESENT STUDY (HIROSHIMA AND NAGASAKI, JAPAN)

表10 骨端核閉鎖時の中央値年齢(歳): 性別, Greulich-Pyle (米)調査, 杉浦および中沢(日)調査, 現調査 (広島および長崎)

Sex	Center	Greulich-Pyle	Sugiura & Nakazawa	Present Study	
Male	to the second second	15 1/2	15 1/2	16 1/2	
	2	16	16 1/2	16 3/4	
	3	16	16 1/2	16 3/4	
	4	15 1/2	15 1/2	16 1/2	
	5	17	16 1/2	yem st 17noBmutter	
	6	16	16 1/2 vis bins	16 3/4	
	7803	15 1/2	15 1/2	16 1/4	
	8	国权专用7 四限率	16 1/2	17	
	9	16	16 1/2	16 3/4	
	10	15 1/2	15 1/2	16 1/4	
	11	16	16 1/2	16 3/4	
	12	16	16 1/2	16 3/4	
	13	15	15 1/2	besons 16 maye to	
	JQ A 014 000;	16 16 4 8 8	bresse 16 1/2 hvogs // h	16 3/4	
	15	17 (17)	. • 000,000; = 19vo driw	este ligazioni im	
	16	17	16 1/2	1900 917 Ingim no	
	17	17	16 1/2	16 3/4	
	18	17	16 1/2	16 3/4	
	19	15 1/2	15 1/2	16 1/4	
	28	18		18 1/4	
	29	19	-	18 3/4	
Female	na# 1555	13 1/2	13 1/2	14 1/2	
	2	15	15 1/2	15	
	3	14	14 1/2	15	
	4	13 1/2	13 1/2	14 3/4	
	5	15	15 1/2	15 1/2	
	6	14	bras 5 14 1/2 asiam	15 1/4	
	MARTINE	13 1/2	finishing 13 1/2 () and 1/2	14 1/2	
	8	15 4 4	15 1/2	15 1/2	
	9	15	14 1/2	enti not 15 offat of	
	10	13 1/2	13 1/2	14 1/2	
	11	14	14 1/2	15 1/4	
	12	14	14 1/2	15	
	13	13 1/2	13 1/2	14 1/2	
	14		11110		
	1.5	15			
	16	15	15 1/2		
		15	13 1/2		
	18	15	15 1/2		
	3262	14	13 1/2		
	28	17	18 1/2	17 1/2	
	29	18	18 1/2 s system	17 3/4	

differences were considered possible causes. That study's children were from the general school population, in all parts of Hiroshima, and all socioeconomic levels. No other Japanese data were available for comparison, and subsequent studies were considered important to determine whether recovery might occur.

Sutow and West³² found no difference in frequency of skeletal anomalies among 160 Nagasaki males and females proximally and distally exposed in utero.

Because of improved diets of the Japanese, their skeletal maturation rate may now be approximating that for children in the U.S. and elsewhere. The degree to which the second World War and its aftermath contributed to Japanese dietary deficiencies is not precisely known; the caloric intake of the Japanese has always been less than that of Westerners. There may have been a greater disaster impact in the A-bombed cities than others. However, the area burned out from fire bombing in Nagoya, for example, exceeded that of Hiroshima by a factor of almost three, and Nagova's widespread surrounding industrial area with over 1,000,000 population might have coped less well with food problems than the rural areas surrounding Hiroshima and Nagasaki. 33 Nonetheless, nutritional deficiencies were probably responsible, at least in part, for maturation delays.

Short Middle Phalanges. In this study, short middle phalanges of the fifth digits did not influence closure of the corresponding epiphyseal centers. Data for these cases were therefore included in the analyses. Sugiura et al³⁴ reported frequency of brachymesophalangia of the fifth digit as 14.7% and 23.4% for females and males. In Pryde and Kitabatake's³⁵ Hiroshima study, the corresponding figures were 14.1% and 21.3%. Its prevalence according to Caffey³⁶ for the sexes combined in the United States is 1%. In the present study, it was found in 11% and 19% of Hiroshima male and female subjects, respectively, but infrequently observed in Nagasaki.

The films for both cities were reexamined by one of the authors (W.R.) and the earlier diagnosis of a short middle phalanx was largely confirmed. In Hiroshima, the diagnosis was confirmed for 40 subjects while 13 subjects were considered essentially normal on reevaluation and five subjects changed from normal to abnormal. The net result was that 45 subjects were considered to have a short middle phalanx in Hiroshima, (12.1% of study subjects).

ないかと考えられた。Sutowの調査の対象となった子供は、広島市全域の一般学校児童で、あらゆる社会経済水準から選ばれたものであった。比較のための日本の資料が他になく、後日調査を行なうことによって回復するかどうかを調べることが重要であると考えられた。

Sutow および West³²は、長崎の近距離および遠距離胎 内被爆男女160名について調査したが、骨格異常の頻度 に差異を認めなかった。

日本人の食生活改善によって、子供の骨格熟成率は現在 米国その他におけるものに近づきつつあると思われる。 第2次世界大戦とその余波がどの程度まで日本人の栄養 不足に影響を及ぼしたかは正確にはわかっていないが、 日本人のカロリー撮取量は西洋諸国のそれよりも常に低 かった。被爆した両市は、他の諸都市よりも戦災の打撃 が大きかったのかもしれない。しかしながら、たとえば、 名古屋の焼夷弾攻撃による焼失地域は、広島のほとんど 3倍に及び、人口1,000,000人以上を有した名古屋市周 辺は広範囲におよぶ工業地帯であり、市周辺部が田園地 域であった広島・長崎よりも食糧問題が困難であったと 思われる。33 いずれにしても、骨格熟成遅滞の原因の 少なくとも一部が栄養不足によるものであったと考えられる。

短中節骨. 本調査では、第5指の中節骨が短いことは関係の骨端核閉鎖に影響を及ぼさなかった. したがって、これらの調査例に関する資料はこの解析の中に含めた. 杉浦らは、第5指の短中節骨症の発現率は男子14.7%、女子23.4%と報告した.34 Pryde および北畠の広島における調査では、この数値は男子14.1%、女子21.3%であった.35 Caffey によれば、米国における男女合計の有病率は1%である.36 本調査では、有病率は広島の男女対象者のそれぞれ11%および19%であったが、長崎ではまれにしか観察されなかった.

広島・長崎両市におけるこれらの例の X 線写真を著者の一人 (Russell) が再検討したが、大部分の場合において前の診断である短中節骨が確認された。広島では、40名の診断が確認され、13名は本質的には正常と判断され、5名が正常から異常に変わった。結局は、広島では45名、すなわち、調査対象者の12.1%に短中節骨があると考えられた。長崎では、最初の所見が短中節骨であった者

In Nagasaki the initial finding of short middle phalanx was confirmed in six subjects, not confirmed for only one subject, and four subjects were reclassified from normal to abnormal. The net result was that 10 Nagasaki subjects (5.4%) are considered to have a short middle phalanx. The difference between cities, while smaller, is still significant at the 5% level.

Neither methodology nor radiation was found responsible for city differences, and there appeared to be a true difference in prevalence of this anomaly by city. This is but one of several unexplained manifestations of differences between the populations of the two cities.

Nutrition. Bones of laboratory animals are deprived of nutrients during severe nutritional disturbances, in favor of other more "critical" organs. The bones recover completely on restoring normal nutrition, with residual scars (growth lines).³⁸ Patients with nutritive failure have a significantly higher rate of these scars.³⁹

Protracted undernutrition in infancy, childhood and adolescence causes asymmetry in maturation of the hand skeleton, with increased frequency of bone anomalies, transverse lines in the radius distally, and delayed fusion of the epiphyses of the hand, wrist, and ulna. Correction of the malnutrition restores a normal maturation rate and form in development, and the bone scars resolve.

Minor illnesses and decreased calcium intake in Australian children 2 to 7 years of age showed no influence on skeletal maturity. Skeletal maturation progressed regularly in that study, even among subjects who missed some examinations because of illness.

Optimum quantities of vitamin D and available minerals prevent delays in skeletal maturation. On the other hand, vitamin A intoxication also causes growth retardation²³ and early epiphyseal closure.⁴¹ Withdrawal of the vitamin can result in some recovery, but in some cases, permanent bone changes remain due to irreparable damage to cartilage cells. Disrupted dietary patterns in postwar Hiroshima and Nagasaki undoubtedly resulted in dietary deficiencies.

Ionizing Radiation and Bone Maturation. Nearly all available reports of effects of ionizing radiation on bone development deal with large doses, 9,10 as in radiotherapy patients and in animal studies. Sutow et al⁴² observed retarded skeletal maturation and

6名にそれが確認され、確認できなかったのは1名のみで、4名が正常から異常へと再分類された、結局、長崎では10名(5.4%)に短中節骨があったと考えられる。両市間の差は、小さいけれども、依然として5%水準において有意である。

調査の方法も,放射線も,両市間の差の原因ではなく, この異常性の有病率には市別に真に差があるようであっ た.これは両市の人口集団の間に認められる説明のでき ない多くの差異の中の一つである.

栄養. 実験動物に重篤な栄養障害がある場合には骨の 養分は他のより「重要な」臓器に奪われる. 栄養が正常に 得られるようになると骨格は完全に回復するが、瘢痕 (発育線)が残る.³⁸ 栄養不足の患者に,これらの瘢痕が 有意に高い頻度で認められる.³⁹

・ 乳児期,小児期および思春期における長期の栄養欠乏は、 骨格異常,携骨遠位部における横線の出現頻度の増加お よび手,手首ならびに尺骨の骨端融合遅滞などを伴う手 の非対称性熟成の原因となる.16 栄養失調状態を治せば、 発育の熟成度と形態が回復して正常となり、16 骨の瘢痕 は消滅する.

軽い疾病を有するものやカルシウム摂取量が減少していた2-7歳までの豪州の子供には骨格の熟成に影響はみられなかった.40 この調査の対象者では病気のため一部の検査を受けなかった者を含めて、骨格熟成は順調であった.

ビタミンDとミネラルの適量摂取によって骨格熟成の遅滞を防止できる。他方、ビタミンA中毒は成長の遅滞²³ および早期骨端閉鎖⁴¹ の原因となる。ビタミンの投与中止によって、ある程度の回復は得られるが、一部のものでは、軟骨細胞に回復不能の損傷のため永久的な骨変化が残る。広島および長崎の戦後における食生活の崩壊のため、栄養不足が起こったものと考えられる。

電離放射線と骨格熟成. 骨格の発育に対する電離放射線の影響に関するほとんどすべての報告は,放射線治療を受けた患者および動物についての調査のように,大線量と関係がある. 9,10 Sutow らは,マーシャル群島で放射性降下物に被曝した子供38名の骨格熟成遅滞と発育に

growth in 38 children, 4 of whom were in utero when exposed to fallout radiation in the Marshall Islands. His subjects received relatively higher doses than the mothers of the subjects in the present study.

It was observed that closure of an individual center in a given sex spanned a period of some 6 years, from the earliest to last observed closures. This amount of variation between subjects has an effect upon the magnitude of the expousre effect that we can expect to detect. Our sample provided 90% assurance of detecting a delay in closure at the 5% level provided the true exposure effect was a delay of 9 months. Our experience indicated that an effect, if present was considerably smaller. Unfortunately, the size of our experience was somewhat limited by the availability of serial X-rays.

Burrow et al3 considered delayed epiphyseal closure among Nagasaki females proximally exposed in utero to the A-bomb a radiation effect, having observed 137 girls an average of 2.6 times each at 13, 14 and 15 years of age (closure in males was delayed, preventing meaningful exposure comparisons). In the present study, 556 boys and girls from both cities selected according to the number of roentgenograms they had on file, were observed an average of 8.4 years each from age 9, and the ages at closure of each of 21 epiphyseal centers were observed; not just the total number of centers closed at each examination as in the Burrow et al study. We could not demonstrate a difference in epiphyseal closure rates either by distance from hypocenter or dose to the mothers.

Pryor²⁵ originally suggested a genetic role as a cause for differences in rates of skeletal maturation. Dreizen et al43 postulated that protracted undernutrition might adversely influence genetic determinents for the postnatal sequence in ossification. The generally reported differences in skeletal maturation rates between Japanese and American children are difficult to explain, but may have been contributed to by nutritional and genetic factors. The impact of the war, malnutrition, and other adverse conditions no doubt had a prominent but transient role in the skeletal maturation delay in Hiroshima and Nagasaki, and the impact might have been more severe in these cities than in Japan in general. There was slower maturation by 6 and 8 months for Nagasaki males and females in the present study as compared to American children. 14 We could demonstrate no radiation effect as responsible. Slower maturation is attributable to nutritional, and possibly genetic factors. The delay

ついて観察したが、そのうち4名は当時母親の胎内にあった.42 これらの対象者は本調査における対象者の母親よりも比較的高い線量を受けた.

著者らの調査では男女いずれにおいても特定の骨端核の閉鎖は、最初に閉鎖が観察されてから最後の閉鎖が認められるまで約6か年の期間にわたった。対象者間におけるこの差異は、探知できると考えられる被曝影響の大きさに影響を及ぼす。著者らの対象集団では、真の被曝影響による遅滞が9か月であった場合、5%水準において閉鎖遅滞は90%の確実度で探知できるはずである。本調査の結果、被曝影響がたとえあったとしてもかなり小さいものであったことがわかった。遺憾ながら本調査においては撮影された連続X線写真の枚数が限られていたため多少制約された。

Burrow らは、13、14および15歳の長崎の女子137名を平均2.6回観察した結果、近距離で胎内被爆した者における骨端閉鎖の遅滞は放射線による影響であると考えた³(男子では、閉鎖が遅滞し、被爆影響について有意な比較ができなかった). 本調査では、X線写真の枚数をもとに広島・長崎両市の男女556名を選択し、9歳から平均8.4年間観察した。また、Burrowらの調査におけるように、各検査時ごとに核閉鎖総数のみを観察したのではなく、21個の骨端核それぞれにおける閉鎖時年齢を観察した。著者らは、爆心地からの距離別、または母親の被曝線量別によって、骨端閉鎖率における差異を証明することはできなかった。

Pryor は、最初骨格熟成度における差の原因は遺伝学的なものであると示唆した。25 Dreizen らは、長期に及ぶ栄養不良が生後の骨化の順位を決定する遺伝要因に悪影響を及ぼすかもしれないと述べた。43 一般に報告されている日米両国の子供間の骨格熟成度の差について説明することは困難であるが、栄養および遺伝要因がこれに寄与したかもしれない。戦争の打撃、栄養失調、およびその他の悪条件が、広島・長崎における骨格熟成遅滞に顕著ではあるが一時的な影響を与えたことは明らかであり、戦争の打撃は、総体的に日本の他の地域よりもこの両市におけるほうが一段とひどいものであったかもしれない。本調査では、米国の子供に比べて長崎の男女にそれぞれ6か月および8か月の熟成遅滞が認められた。14 栄養およびおそらく遺伝的要因も骨格熟成遅滞の原因であるが、著者らは、放射線影響が遅滞の原因であることを立証す

detected in the present study was considerably less than that Greulich detected among Hiroshima and Nagasaki children immediately after World War II. It is our impression that subjects in the present study have for the most part recovered from any transient retarded maturation originally based on nutritional deficit.

Review of the literature revealed no strong evidence of delay in skeletal maturation attributable to the ionizing radiation of the A-bombs. The present investigation likewise failed to disclose such a cause-effect relationship for in utero exposed survivors.

ることはできなかった. 本調査で認められた熟成遅滞は, Greulich が第2次世界大戦直後の広島および長崎の子供 に認めた遅滞よりもかなり少ない. 本調査の対象者は, 本来, 栄養不足に起因した一過性の熟成遅滞からすでに ほとんど回復したものと考えられる.

文献調査からは、骨格熟成遅滞が原爆の電離放射線に起 因するという有力な証拠は認められなかった。本調査に おいても胎内被爆者にこのような因果関係を認めること はできなかった。

APPENDIX 1: ANALYSIS FOR BIAS

The object of the study was to use serial X-rays of the hand and wrist to establish the ages at which the 21 epiphyseal centers close. However, children were selected for study in 1963 when the youngest child in the in utero sample was 17 years old and the majority of centers would already have closed. Therefore, the selection of children for study was accomplished to maximize the number of available examinations between 9 and 17 years of age, raising the possibility that the study sample did not represent a cross-section of the skeletal maturation experience. An attempt was made to measure this bias in the sample, based on indirect evidence since the absence of hand and wrist films for unselected subjects prevented a direct comparison of maturation with the study sample.

The entire in utero sample (revised 1959-60) was tabulated according to whether the children had had five or more examinations for ages 9-17 years. The results showed no bias for Nagasaki since 332 subjects (95.4%) of the in utero sample were eligible for inclusion in the bone maturation study (Table A). The reduction to the 184 children studied was accomplished by controlled selection procedures, producing a study group of predetermined composition as to sex and trimester ATB for each exposure group.

調査の目的は、手および手首の一連のX線写真を使用して21の骨端核が閉鎖する年齢を確定するにあった.しかし、最若年の子供が17歳であった1963年にこの対象者が選択されたので、骨端核の大部分はすでに閉鎖していたはずである.したがって、9-17歳の間の検査数をできるだけ多くするような方法で子供の選択が実施されたが、これにより骨格熟成調査のための調査対象集団の横断面を代表しない可能性が生じた.選択されなかった者は手および手首のX線写真が欠如しているため骨格熟成について調査対象者との直接比較ができなかったので、間接的な所見をもとに調査集団における偏りを測定しょうとした.

胎内被爆の全臨床集団 (1959-60年修正) は9-17歳の子供で5回以上検査を受けたかどうかによって集計を行なった. 長崎では対象者 332名 (95.4%) は,この骨格熟成調査に含めるのに適当であったので,調査結果に偏りはなかった (表A).一定の選択要領によって被検者数を184名に削減し,各被爆群別に性と原爆時の妊娠期とをもとに調査群を構成した.

TABLE A. EXAMINATION HISTORY OF THE IN UTERO EXPOSED CLINICAL SAMPLE (PE86) BY AGE AT EXAMINATION, SEX, AND DISTANCE FROM HYPOCENTER, HIROSHIMA AND NAGASAKI

表A 胎内被爆臨床集団(PE86)の検査歴:検査時の年齢・性・爆心地からの距離別,広島および長崎

City, Sex, Exam. History	0-2000 m		2000-4999 m		Not in City	
City, Sex, Exam. Instity	No.	%	No.	%	No.	%
Hiroshima male, total	226	100.0	221	100.0	201	100.0
<5 exams, age 9-17 yrs.	95	42.0	147	66.5	45	22.4
≥5 exams, age 9-17 yrs.	3 3 1 131	58.0	74	33.5	156	77.6
Hiroshima female, total	209	100.0	211	100.0	197	100.0
<5 exams, age 9-17 yrs.	99	47.4	146	69.2	66	33.5
≥5 exams, age 9-17 yrs.	110	52.6	65	30.8	131	66.5
Nagasaki male, total	54	100.0	71		60	100.0
<5 exams, age 9-17 yrs.	_	-	2	2.8	5	8.3
≥5 exams, age 9-17 yrs.	54	100.0	69	97.2	55	91.7
Nagasaki female, total	48	100.0	61	100.0	54	100.0
<5 exams, age 9-17 yrs.	3	6.2	1	1.6	5	9.3
≥5 exams, age 9-17 yrs.	45	93.8	60	98.4	49	90.7

APPENDIX 1: ANALYSIS POR BIAS

Tab. 1462

In Hiroshima, only 667 children (52.7%) of the in utero sample (revised 1959) had five or more examinations by 17 years of age. When one examines the number of subjects with fewer than five examinations seen at each year of age (Table B), it is apparent that few of these children were being examined before age 14.

A review of the development of the in utero sample for Hiroshima indicated that the composition of the Hiroshima in utero population was fluid prior to 1959. Furthermore, efforts to recall in utero subjects for annual examinations varied somewhat according to whether or not a research project involving this group was active at the time. In 1959, when the in utero sample was revised and fixed to its present composition, 380 subjects were added as a result of an extensive search for in utero ATB children.

The fact that the number of available examinations on a given child is related to the manner in which the in utero sample was constructed reduces concern for possible developmental differences between frequently examined and infrequently examined subjects. However, since virtually all of the Nagasaki in utero sample was eligible for the bone maturation study on the basis of the number of available examinations, and the reduction to 184 study subjects was accomplished on an essentially random basis, the Nagasaki experience can be used as a

広島では、胎内被爆児集団 (1959年修正) 中 667名 (52.7%) のみが17歳までに5回以上の検査を受けていた。各年齢時で受けた検査回数が5回以下であった対象者数について検討したところ(表B),14歳以前に検査を受けた子供はほとんどなかったことがわかる。

広島の胎内被爆児集団の成長についての検討の結果, 1959年以前にはその構成は流動的であった。さらに, この群についての調査が活動的に行なわれていたか否かによって対象者に年次検診のための来所を求める努力に多少の差異があった。1959年に胎内被爆児集団に修正が加えられ, 現在の構成に固定されるにあたり, 胎内被爆児についての広範にわたる探索調査の結果, 380名が新たに加えられた。

特定の子供の受けた検査回数と、胎内被爆児集団の構成との間には関係があるので、頻繁に受診した対象者とあまり頻繁に受診しなかった対象者との間に発育の差があるかもしれないという懸念は減少する。しかし、長崎の対象集団のほとんど全員は、受けた検査回数から骨格熟成調査の対象者として適格であったので、184名への人数の削減は本質的には無作為に行なわれたものであり、長崎での調査結果は基準線として用いることができる。

TABLE B. EXAMINED IN UTERO CLINICAL SAMPLE (PE86) BY AGE AT EXAMINATION AND NUMBER OF EXAMINATIONS AT AGES 9-17 YEARS INCLUSIVE, HIROSHIMA

表B 胎内被爆臨床集団(PE86)の受診者数: 検査時の年齢 および9-17歳時までの検査回数別, 広島および長崎

	Number	Number of Exams at Ages 9-17 yrs.					
Age at Examination		<5 M	≥5				
io. Standing Height	No.	1121-11 %	No.	%			
9 yrs.	33	5.5 138	232	34.8			
10	99	16.6	581	87.1			
11 51 55	64	10.7	543	81.4			
12	54	9.0	572	85.8			
13	67	11.2	616	92.4			
14	328	54.8	605	90.7			
15	302	50.5	574	86.1			
16	277	46.3	545	81.7			
17	371	62.0	612	91.8			
18	309	51.7	557	83.5			
19	221	37.0	423	63.4			
Total Subjects	598	100.0	667	100.0			

baseline. The median age af closure for Hiroshima males is generally less than that for Nagasaki subjects, but not more than ¼ year for any of the 21 centers. The median ages of closure were nearly identical for Hiroshima and Nagasaki females. For three centers the Hiroshima age was less than that for Nagasaki, while in eight centers the median age at closure for Hiroshima females was higher than that for Nagasaki; only one difference exceeded ¼ year.

To determine whether rate of maturation was related to frequency of examination in Hiroshima, it was assumed that attained height is related to bone maturity. The mean standing height was computed at each age for (a) subjects with five or more examinations by age 17, (b) subjects with fewer than five examinations who were examined at 18 or 19 years of age, and (c) subjects with fewer than five examinations who were not examined at 18 or 19 years of age. Virtually all group "b" subjects were examined at 18 years of age and a comparison of mean standing height with group "a" revealed differences which are well within the limits of chance.

広島の男子の閉鎖時の中央値年齢は、全般的に長崎の対象者のそれよりも低いが、21の骨端核のいずれの場合でもその差は¼年以上ではない。広島および長崎の女子では、閉鎖時の中央値年齢はほとんど同じであった。三つの骨端核では、広島群の年齢は長崎のそれよりも低く、他方、八つの骨端核では、広島の女子の閉鎖時の中央値年齢は長崎のそれよりも高く、差が¼年を超過したのは一つだけであった。

広島において、熟成率が検査回数と関係があるかどうかを明確にするために、身長は骨格熟成に関係があるとの仮定のもとに以下の三つの対象者群の各年齢における平均身長が測定された: (a)17歳までに5回以上受診した対象者; (b)18歳または19歳で受診し、その総受診回数が5回以下の対象者; (c)18歳または19歳時で受診しておらず、しかも受診回数が5回以下のもの。事実、"b"の対象者のほとんど全員は18歳時に検診を受けており、"a"群との平均身長の比較に差が認められたが、これは十分偶然の範囲内にあった。

Group	Male	Female	
a	165.4 cm	153.5 cm	
b	166.3 cm	154.0 cm	

TABLE C MEAN STANDING HEIGHT BY EXAMINATION HISTORY, AGE, AND SEX, HIROSHIMA

表C 平均身長:検査歴,年齢および性別,広島

Sex	Age at Exam.	≥5 Exams by age 17			< 5 Exams by age 17, and not Examined at 18 or 19		
Jex 8	Age at Exam.	No.	Mean Standing Height	.014	No.	Mean Standing Height	
Male	Total	361	8	.66	138	and B	
	9 yrs.	125	123.0 cm		13	119.5 cm	
	10	315	127.5		32	125.8	
	11	292	132.3		24	129.7	
	12	313	137.5		16	138.2	
	13	337	142.8		21	144.0	
	14	333	150.6		43	148.4	
	15	320	157.3		31	154.1	
	16	310	162.9		22	163.4	
	17	332	164.9		38	166.8	
Female	Total	306			136		
	9	107	121.2		12	120.6	
	10	266	128.9		41	128.6	
	11	251	133.2		23	134.3	
	12	259	140.2		27	140.0	
	13	279	145.1		25	144.2	
	14	272	148.4		39	149.4	
I was to see	15	254	149.8		21	149.9	
	16	235	152.9		21	154.9	
	0 17 L 13 1	280	153.3		30	155.1	

Groups "a" and "c" are compared according to mean standing height in Table C.

Few of the group "c" subjects were examined in any given year. Furthermore, this group of subjects appears to have contributed nearly as many examinations annually prior to as after age 14, indicating that this group was not a result of the in utero sample revision. It is more likely that group "c" persons were merely less inclined to accept the annual examinations offered by ABCC. Of the 274 in utero children in group "c", 72 had not been examined at 9 years of age or since. Ten of the 72 cases were deceased at age 18 years. However, insofar as the available standing height information is representative of group "c" subjects, there is no reason to suspect that group "c" subjects were maturing at a different rate than their more frequently examined counterparts. None of the differences are statistically significant and the direction of the differences varies from one age to another.

表Cでは"a"群と"c"群の平均身長の比較がなされている。

どの年度においても"c"群対象者で検診を受けた者はほとんどなかった。さらに、この群の対象者は14歳以前と14歳以後においてほとんど同回数検査を受けていることから、この群は、対象集団の修正の結果、構成されたものではないことを示している。"c"群の対象者は単にABCCの年次検診を受けたがらない傾向があったにすぎないようである。"c"群における対象者 274 名中、72 名は9歳時またはそれ以降に検査を受けていなかった。この72 名中、10名は18歳時で死亡していた。しかし、身長に関する資料は"c"群の対象者を代表するものであるので"c"群対象者が頻繁に検査を受けた群と異なる速度で成熟していたことを疑う理由はない。その差異は統計学的に有意なものではなく、しかも差異の方向は年齢によって異なる。

During the selection of the bone maturation study sample, it was correctly decided that it was important to select the cases who had the more complete series of roentgenograms. The alternative would have resulted in large gaps between observations, and would have strained methodology.

骨格熟成の調査集団を選択する段階で、一連の X 線写真がより完全にそろっている者を選択することが重要であると判断したことは正しかった。他の方法では、観察と観察との間に大きな間隙が生じ、無理が生じたであろう。

APPENDIX 2

RENAMEDS ELECTION throad development of Election with midnen exposed to the atomic bomb. Three-year study.

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