TECHNICAL REPORT
9-72
業 績 報 告 書

LONGEVITY IN RADIATED HUMAN POPULATIONS, WITH PARTICULAR REFERENCE TO THE ATOMIC BOMB SURVIVORS

放射線被曝人口集団，特に原爆被爆者における寿命

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ATOMIC BOMB CASUALTY COMMISSION

国立予防衛生研究所－原爆傷害調査委員会

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

TECHNICAL REPORT SERIES

業 績 報 告 書 集

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A Cooperative Research Agency of
U.S.A. NATIONAL ACADEMY OF SCIENCES - NATIONAL RESEARCH COUNCIL
and
JAPANESE NATIONAL INSTITUTE OF HEALTH OF THE MINISTRY OF HEALTH AND WELFARE
with funds provided by
U.S.A. ATOMIC ENERGY COMMISSION
JAPANESE NATIONAL INSTITUTE OF HEALTH
U.S.A. PUBLIC HEALTH SERVICE

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との日米共同調査研究機関

米国原子力委員会，厚生省国立予防衛生研究所および米国公衆衛生局の研究費による

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Approved 承認 *13 April 1972*

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SUMMARY

Life shortening is one of the late consequences of exposure of a variety of laboratory animals to biologically significant amounts of ionizing radiation. Evaluation of several human populations accidentally and/or therapeutically exposed to radiation suggests a similar phenomenon among the radium dial painters and pioneer American radiologists which persists even when appropriate corrections are made for the known tumorigenic effects of such exposure. A similar relationship is at most equivocally reflected in the experience to date pertinent to the survivors of the atomic bombs of Hiroshima and Nagasaki. Reviewed here are the available data in this regard, with particular reference to the information relevant to the atomic bomb survivors.

INTRODUCTION

In the experimental situation, life shortening is one of the delayed effects of exposure to sublethal amounts of ionizing radiation.[1] The reduction of life span is proportional to dose, in either a curvilinear or linear fashion depending on species and strain,[2-5] and is closely related to age at the time of exposure.[6] With single exposures, the radiobiologic effectiveness (RBE) of the various

要　約

各種の実験動物では，生物学的に有意な線量の電離放射線照射を受けた時，晩発性影響の一つとして寿命短縮が起こる．ヒトの場合でも，放射線事故や放射線療法のために被曝したいくつかの人口集団の調査によれば，すでによく知られている放射線の腫瘍誘発効果に対して適当な補正を行っても，ラジウム蛍光塗料工や初期の米国放射線科医に前者と同様の現象のみられることを示唆する所見が認められている．広島・長崎の原爆被爆者にあっては，今日までの経験において，この種の関係を示す所見はせいぜい不確実にみられるにすぎない．本報告では，この問題について入手し得た資料，特に原爆被爆者に関する情報について再検討を行った．

緒　言

実験的状況下では，致死量以下の電離放射線照射の晩発性影響の一つとして寿命短縮が認められている．[1] この寿命短縮の程度は，動物の種類や系統によって線量と曲線的または直線的な比例関係を示し，[2-5] 被曝時の年齢と密接な関係がある．[6] 1回照射の場合，寿命短縮を起こすための各電離粒子の生物学的効果比（RBE）は，急

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ionizing particles with respect to abbreviated longevity is approximately the same as for acute effects, i.e., neutrons are more effective than gamma rays by a factor of two-three.[7] By pooling the data obtained in a number of studies utilizing gamma or X-rays and several mouse strains, it would appear that roughly 5 % of murine life span is lost per 100 rad of exposure.[8] The available experimental evidence neither supports nor refutes the existence of a threshold effect, a dose below which no life shortening is apparent.

The life shortening response cannot be attributed to a specific cause and persists even when appropriate corrections are made for the increased prevalence of tumors after exposure to radiation.[9] In general, the exposed animals die at an earlier age from the same general disease entities that affect their nonirradiated contemporaries.[1,10-12] This increase in the age-specific death rate has been variously termed as accelerated, premature or precocious aging, or as a nonspecific effect of radiation, depending upon the individual observer's interpretation of the data.

Several human populations have similarly been exposed to biologically significant amounts of ionizing radiation. Perhaps the most extensively evaluated group in this regard is the atomic bomb survivors of Hiroshima and Nagasaki. Twenty-seven years have elapsed since the exposure of these persons, and considerable data are now available for review. A portion of the relevant information is in the form of unpublished data or is contained in Atomic Bomb Casualty Commission (ABCC) Technical Reports, and therefore not available to much of the scientific community. My purpose here is threefold: (1) to summarize the ABCC experience to date; (2) to re-examine the concept of accelerated aging with respect to exposed human beings; and (3) as a part of the latter objective, to review briefly related experience with other irradiated human populations.

RADIATED POPULATIONS

A significant number of human beings have been accidentally or therapeutically exposed to radiation. However, evaluation of the majority of these, in the context of this report, is not feasible because of incomplete follow-up or insufficient demographic data. The study of additional populations exposed to radiation is precluded by the absence of an epidemiologically comparable "control" group.

性影響のためのそれとほぼ同じであり，中性子はガンマ線より2ないし3倍も効果的である.[7] 数種類のマウスについてガンマ線あるいはX線を用いて実施されたいくつかの研究の成績をまとめてみると，マウスでは被曝線量100 rad当たり約5％の寿命短縮が起こるようである.[8] 入手された実験結果によると，閾効果，すなわち，これ以下では寿命短縮が現われない線量の存在を肯定も否定もできない.

この寿命短縮反応は，特定の原因に帰することのできないものであり，放射線被曝後の腫瘍有病率増加に対して適当な補正を行っても依然として認められる.[9] 一般に被曝動物は，非被曝動物と同じ一般的疾病をより早期に発症して死亡する.[1,10-12] この年齢特殊死亡率の増加というものに対しては，資料についての各研究者の解釈に従って，加齢促進，早期加齢，早発性加齢あるいは非特異的放射線影響といったような種々の名称が与えられている.

ヒトでも，同じように生物学的に有意な量の電離放射線照射を受けた集団がいくつかある．その中で最も広範囲にわたって調査が行われたものは，おそらく広島・長崎の原爆被爆者であろう．被爆後27年が経過しており，現在では相当の資料が検討に利用できる．関係資料の一部は未発表であったり，ABCC業績報告書に掲載されたりしているために，学界で広く利用されるわけには行かない．そこで，今回の報告には次の三つの目的をもたせてある：(1) 現在までのABCCの経験をまとめること；(2) 放射線被曝を受けたヒトについての加齢促進の概念を再検討すること；および(3) 後者の目的の一部として，放射線に被曝したその他の人口集団との関連経験の簡単な検討を行うことである.

放射線被曝人口集団

放射線事故または放射線療法のために被曝した人々は有意な数に上る．しかし，その大部分は追跡調査が不完全であったり，人口統計学的資料が不十分であったりするために，今回の報告の観点からは評価ができない．そのほかの放射線被曝人口集団は，疫学的に対応する「対照」群がないために検討が不可能である．このように，ヒト

Thus, much of our knowledge of the delayed effects of ionizing radiation with respect to life span in man has been obtained from an evaluation of seven populations (Table 1), and even in these select groups an interpretation of aging phenomena is not without severe limitations which may be summarized as follows.

The British adults with spondylitis constitute a group with preexisting disease of significant magnitude who were exposed in a regional manner. Experimentally, the effect of partial-body exposure on shortening the life span is considerably less than an identical dose administered in whole-body fashion.[13-17] Similarly, infants treated with X-rays for "status thymolymphaticus" were exposed in a regional manner. The radium dial workers were exposed in protracted fashion to particles with a defined propensity for localization in specific sites. Some of the early American radiologists were apparently exposed to considerable radiation attendant to poor shielding, but the dosimetry is unknown. Although congenital malformations have been documented after in utero radiation, the consequences of such exposure with respect to life span are not known. On the basis of the foregoing discussion, it would appear that the majority of information with respect to the relationships between radiation and aging in man will be derived from the exposed and nonexposed populations of Hiroshima, Nagasaki and Rongelap Atoll.

Eighty-two inhabitants of Rongelap in the Marshall Islands were accidentally exposed in 1954 to varying amounts of fallout released during a series of tests on Bikini Island. A significant proportion of the radiation absorbed by these Islanders was occasioned by deposition of radionuclides. The maximum estimated exposure was 175 r. Subsequent follow-up has been extremely careful, and the population under evaluation now also includes a control group and totals 334 persons.[18] Unfortunately, post-mortem examinations are virtually precluded by logistic, climatic and cultural circumstances, and therefore evaluation is fundamentally related to vital statistics, clinical and laboratory observations admixed with morphologic interpretation of a number of thyroid glands, or portions thereof, removed at surgery.

The estimated civilian populations of Hiroshima and Nagasaki in August 1945 were 255,000 and 174,000, respectively. Of these persons, approximately 106,200 died within the initial several weeks after the bombings.[19] Excellent dosimetry is now available for the majority of the survivors.[20-22]

における電離放射線の晩発性影響と寿命との関係についての知識の大部分は，七つの人口集団の評価から得られたものであり（表１），これらの特定の集団においてさえも，以下に要約するように，加齢現象の解釈には非常な制約がないというわけには行かない．

英国の成人の脊椎炎患者には，予め有意な程度の疾患があって局所的照射を受けた１群がある．実験によれば，身体の部分的照射では，同一線量の全身照射に比べて寿命短縮効果がかなり弱い．[13-17] 「胸腺リンパ体質」のためにＸ線療法を受けた幼児の場合も局所照射であった．ラジウム蛍光塗料工では，特定の部位に限局して沈着する傾向のあることの確認されている粒子に長期間被曝していた．初期の米国放射線科医の一部は，遮蔽が不良であったことのためにかなりの放射線に被曝したと思われるが，その線量は不明である．放射線胎内被曝後に先天性奇形の発生が報告されているが，この種の被曝の寿命に及ぼす影響は不明である．以上の記述からも明らかであるが，ヒトにおける放射線と加齢との関係についての情報の大部分は，広島・長崎およびRongelap環礁での被曝および非被曝人口集団から得られることになるであろう．

Marshall群島におけるRongelap住民82人が，1954年Bikini島で行われた一連の核実験の際に偶然に種々の程度の放射性降下物に被曝した．これらの島民では，放射性核種の蓄積による線量が吸収線量の有意な割合を占めていた．その最大推定被曝線量は175 rである．その後，きわめて注意深い経過観察が実施され，調査対象集団は現在では対照群を含んでおって，合計334人である．[18] 残念ながら，施設，気候および文化的状況のために剖検の実施はほとんど不可能である．したがって，根本的には人口動態統計，臨床診察所見および検査所見を中心として評価が行われ，若干例では，外科手術で切除した甲状腺またはその一部についての形態学的解釈がこれに加わっている．

1945年８月現在の広島および長崎における民間人口はそれぞれ255,000人および174,000人であった．このうち約106,200人が原爆後数週間以内に死亡した．[19] 原爆被爆生存者の大部分について現在は優秀な線量推定値が計算されている．[20-22] 無遮蔽の者が受ける可能性のある線量

TABLE 1 SUMMARY: AGING PARAMETERS IN IRRADIATED HUMAN POPULATIONS

Population under Evaluation	Type of Radiation	Region Irradiated	Sample Size	Life Span	Prevalence of Malignant Neoplasms
Japanese atomic bomb survivors	Gamma plus neutrons	Whole body	120,000*	Reduced	Increased (leukemia and related disorders; thyroid; major salivary glands; ?lung; ?breast; variety of tumors in exposed children)
Rongelapese	Gamma plus internally deposited radionuclides	Whole body but with disproportional irradiation of thyroid	334*	No information as yet available	Probably increased (thyroid)
Children irradiated for enlarged thymus and other benign lesions of neck and chest	X-rays	Mediastinum	24,604*†	Reduction attributed primarily to leukemia	Increased (thyroid, leukemia, salivary glands)
British adults irradiated for ankylosing spondylitis	X-rays	Spine	13,352	No information	Increased (leukemia, lymphoma)
American radiologists	X-rays, radium	Partial to whole body	425-82, 441*	Reduced	Increased (leukemia, lymphoma, skin)
Radium dial painters and related workers; adults treated with radium	Gamma, alpha and beta particles (^{226}Ra, ^{228}Ra)	Skeleton	760†	Reduced	Increased (osteogenic sarcoma and other tumors of bone and periosteum; epithelial tumors of nose and paranasal sinuses; probably leukemia)
Children irradiated in utero during diagnostic pelvimetry	X-ray	Whole body	7,346	No information	Possibly increased (leukemia)

表 1　総括：放射線被曝集団の加齢に関するパラメーター

調査対象集団	放射線の種類	照射部位	調査対象者数	寿　命	悪性新生物の有病率
日本人原爆被爆者	ガンマ線と中性子	全身	120,000人*	短縮あり	増加あり（白血病および関連疾患；甲状腺；主要唾液腺；肺？；乳房？；小児期被爆者の各種腫瘍）
Rongelap 住民	ガンマ線と放射能性核種体内蓄積	全身，ただし，甲状腺の被曝が特に著しい	334人*	資料はまだない	おそらく増加あり（甲状腺）
胸腺肥大，その他の頸部および胸部の良性病変のために放射線療法を受けた小児	X線	縦隔洞	24,604人*†	主として白血病のために短縮あり	増加あり（甲状腺，白血病，唾液腺）
強直性脊椎炎のために放射線療法を受けた英国の成人	X線	脊椎	13,352人	資料なし	増加あり（白血病，リンパ腫）
米国の放射線科医	X線，ラジウム	部分的ないし全身	425—82,441人*	短縮あり	増加あり（白血病，リンパ腫，皮膚）
ラジウム蛍光塗料工および関連作業従事者；ラジウム療法を受けた成人	ガンマ線とアルファおよびベーター粒子（^{226}Ra, ^{228}Ra）	骨格	760人†	短縮あり	増加あり（骨肉腫や骨および骨膜のその他の腫瘍，鼻および副鼻腔の上皮性腫瘍，おそらく白血病）
診断用骨盤計測中に放射線胎内照射を受けた小児	X線	全身	7,346人	資料なし	増加の疑いあり（白血病）

**Includes comparable group of nonexposed ("control") individuals.*
対応する非被曝（「対照」）群を含む．

†May be some overlap in reported persons.
報告例の重複が若干あるかもしれない．

Mortality apart from Neoplasms	Disease Entities Other than Malignant Tumors	Physiologic Functions	Biochemical & Related Parameters
Not uniformly reduced to date (see text)	Increased (microcephaly and mental retardation of persons exposed in utero; retarded skeletal development; degenerative changes involving skin, testes, and occular lens; benign skin tumors)	Probably altered (see text)	Probably no change from control values (see text)
No information	Increased (thyroid nodules with hypothyroidism; retardation of growth and development; increased incidence of miscarriages and stillbirths)	No significant differences between exposed and non-exposed groups	No significant differences between exposed and non-exposed groups
No information	Increased (thyroid adenomas, benign breast tumors; osteochondromas; neurilemmomas)	No information	No information
No information	No information	No information	No information
Reduced	No information	No information	No information
Reduced	Increased (osteomyelitis; dental abnormalities; ?aplastic anemia, ?osteosclerosis)	No information	No information
No information	No information	No information	No information

新生物以外の死因による死亡率	悪性腫瘍以外の疾病	生理学的機能	生化学的および関連パラメーター
現在までは一貫した低下なし（本文参照）	増加あり（胎内被爆者の小頭症および知能遅滞；骨格発育遅滞；皮膚，睾丸および水晶体の退行性変化；良性皮膚腫瘍）	おそらく変化あり（本文参照）	おそらく対照値と差なし（本文参照）
資料なし	増加あり（甲状腺結節および甲状腺機能減退；成長発育の遅滞；流産および死産の頻度増加）	被曝群と非被曝群との間に有意差なし	被曝群と非被曝群との間に有意差なし
資料なし	増加あり（甲状腺腺腫，良性乳房腫瘍；骨軟骨腫；神経鞘腫）	資料なし	資料なし
資料なし	資料なし	資料なし	資料なし
低下あり	資料なし	資料なし	資料なし
低下あり	増加あり（骨髄炎；歯牙異常；再生不良性貧血？；骨硬化症？）	資料なし	資料なし
資料なし	資料なし	資料なし	資料なし

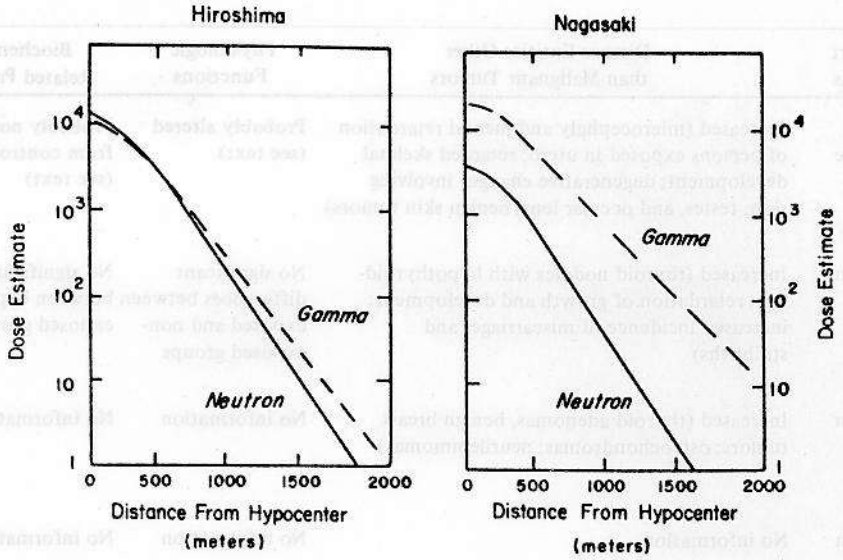

FIGURE 1. Tentative 1965 air dose (T65D) estimates, Hiroshima versus Nagasaki, gamma rays versus neutrons.

図1　1965年暫定的空気線量（T65D）推定値，広島・長崎，ガンマ線および中性子別

The magnitude of possible exposure by an unshielded person as a function of the distance from the hypocenter is shown in Figure 1.[22] The intercity discrepancies are primarily due to differences between the involved bombs. The fissionable material in the Hiroshima bomb was ^{235}uranium, and the resultant radiation spectrum contained a mixture of gamma rays and neutrons; the Nagasaki bomb contained ^{235}plutonium and released primarily gamma rays admixed with relatively few neutrons. In this connection, it should be emphasized that the life-shortening effects of gamma rays and neutrons are probably not equivalent in man; fast neutrons are apparently more effective than gamma rays in producing most of the delayed effects thus far studied at ABCC.[23]

Prior to the recent availability of accurate dosimetry data, many calculations were, of necessity, based on an individual's distance from the hypocenter at the time of the explosion. Such a maneuver, although ignoring critical shielding factors, allowed comparisons between groups of people who, in general, received different magnitudes of radiation. Thus, the Life Span Study Sample, which represents the primary population under evaluation at the ABCC, was originally defined by distance gradients.

の程度を爆心地からの距離の関数として図1に示した.[22] 両市の間にみられる差は主としてそれぞれの原爆の相違のためである．広島における原爆の核分裂材料はウラニウム235で，それによって生じた放射線スペクトルはガンマ線と中性子との混合であった．一方，長崎の原爆はプルトニウム235からなっていて，主としてガンマ線を放出し，中性子は比較的少なかった．この点に関連して，ガンマ線および中性子のヒトの寿命に対する短縮効果はおそらく等しくないであろうということを指摘しておきたい．ABCCで今日までに調査した晩発性影響の大部分では，速中性子がガンマ線よりも効果的であるように思われる.[23]

正確な線量資料の最近の入手以前には，必然的に各被爆者の爆心地からの距離に基づく計算が多かった．この方法では重要な遮蔽因子が無視されているとはいえ，概ね異なる程度の放射線を受けた各群の間の比較は可能であった．したがって，ABCCの主要調査対象である寿命調査集団は，元来，被爆距離区分群別に決定されたものである．

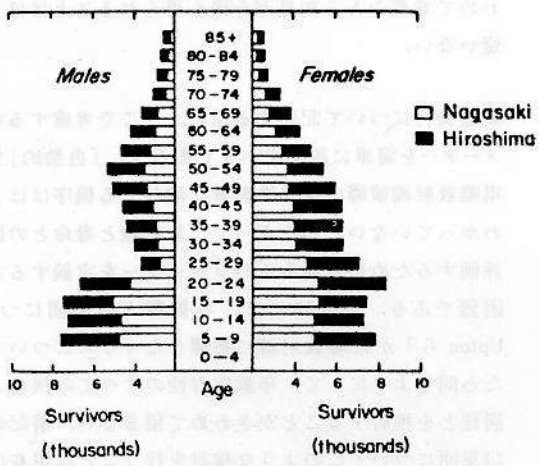

FIGURE 2. Atomic bomb survivors by age at time of exposure, males versus females, 1950 census.

図2　原爆被爆者：原爆時年齢および男女別，1950年国勢調査

This approach implies that the demographic composition of the surviving populations of Hiroshima and Nagasaki is not comparable with the population which occupies the remainder of Japan. This is true and several attendant points deserve emphasis.

(1) As shown in Figure 2, the Study Population is fixed and, therefore, progressively ages; on this basis, whereas Figure 2 shows no one less than 5 years of age available to be recorded in the 1950 census, today the youngest survivor is 27 years of age.

(2) Also as shown in Figure 2, there is a pronounced paucity of exposed young and middle aged men. The majority of such persons were presumably in the Armed Forces and, therefore, away from Hiroshima and Nagasaki at the time of the explosions. In addition, it is possible that the residual men, now included in the Life Span Study Sample, represent a biased group by reason of their exclusion from the military.

(3) In construction of the Life Span Study Sample, survivors were not randomly assigned to dose categories so that putative later consequences of their pre-1945 demographic, social and economic characteristics may be confounded with dose in some comparisons.

(4) Exposure to radiation represents only one of several possible effects of the atomic bombs and these other effects are confounded with dose.

Despite these problems, there is little doubt that the survivors of Hiroshima and Nagasaki will con-

広島・長崎でこのようにして編成された被爆者調査集団の人口統計学的構成は，その他の日本各地における人口と異なるであろうと推測される．事実はそのとおりであり，このことに付随するいくつかの点を指摘したい．

(1) 図2に示したように，この調査対象集団は固定されているので，しだいに加齢する；こんなわけだから，図2に示したように，1950年の国勢調査時に5歳未満であった該当者はいなかったので記録されていないのだが，現在では，その最も若年であった被爆者は27歳になっている．

(2) その上，図2にみられるように，被爆者に青壮年層の男性が著しく少ない．この年齢層の男性は，兵役に服していた者が多いために原爆時に広島・長崎にいなかったと想像される．しかも，当時両市に残っていて，現在の寿命調査集団に属している男性は，兵役免除ということのために偏りのある群を代表している可能性がある．

(3) 寿命調査集団を編成するにあたり，被爆者は各線量区分に無作為的に割当てられたのではないので，ある種の比較においては，1945年以前の人口統計学的，社会的ならびに経済的特性に起因し，その後に現われたと推測される影響が放射線量と混同されるかもしれない．

(4) 放射線被曝は，原爆によるいくつかの効果の中の一つにすぎず，これらの他の効果は線量と混同される．

以上の種々の問題があるにもかかわらず，広島・長崎における被爆者からは，寿命と放射線との関係についてき

tinue to provide exceedingly meaningful information with respect to the relationship between longevity and radiation.

Prior to addressing the relevant data, perhaps a word of explanation should be included about the parameters to be considered. Relatively little is known with respect to the mechanisms involved in "spontaneous" aging or the late consequences of exposure to ionizing radiation; therefore, it is difficult to define meaningful parameters for an evaluation of radiation-related longevity. Theoretically, it would be highly desirable to examine all age-dependent diseases and degenerative processes in each irradiated population in the same way Upton et al[2] did in mice exposed to atomic bomb radiations. Such an approach with the human populations listed is not presently feasible, and therefore I will pay primary attention here to the following parameters:

(1) Life span. Mortality data provide the simplest and most accessible quantitative criterion for aging in man. In adult life, the age-specific death rate increases by a constant factor as a function of time.

(2) Prevalence and appearance time of tumors. In man, malignant neoplasms appear also to follow a Gompertz pattern and such information in irradiated populations is generally readily available.

(3) Mortality apart from malignant neoplasms. Radiation in sufficient amounts is tumorigenic. Therefore, in the absence of counterbalancing beneficial effects, a decrease in over-all life span could be expected in most, if not all, of the populations reviewed herein. However, the concept of accelerated and/or precocious aging implies a nonspecific effect which persists after appropriate corrections are made for an increased prevalence of neoplasms.

(4) Specific disease entities other than malignant tumors.

(5) Physiologic tests and observations. These parameters are relatively easy to apply to large populations but occasionally are difficult to quantitate and often are not age-dependent until middle age.[24]

(6) Biochemical and related parameters. A limited number of determinations of this type have been shown to be age-related in experimental animals and a few have been successfully applied to human populations.

わめて意義のある知見が今後も得られることはほとんど疑いない.

関連資料について記述する前に，ここで考慮する各パラメーターを簡単に説明すべきであろう.「自動的」加齢や電離放射線被曝の晩発性影響に関与する機序はほとんどわかっていない. したがって，放射線と寿命との関係を評価するために意義あるパラメーターを定義することは困難である. 理論的には，各被曝人口集団について，Upton ら[2]が原爆放射線に被曝したマウスについて行ったと同じようにして，年齢依存性のすべての疾患と変性過程とを検討することがきわめて望ましい. 前記の各人口集団についてこのような検討を行うことは現在は不可能であるので，ここでは主として次のパラメーターに対して注意を払いたい:

(1) 寿命. 死亡率に関する資料は，ヒトの加齢について最も簡単で，かつ，最も入手し易い定量的基準である. 成人期においては，年齢特異死亡率は，時間の関数として一定の係数に従って増加する.

(2) 腫瘍の有病率と発生時期. ヒトの悪性新生物も Gompertz のパターンに従うようであり，このような資料は，一般に各被曝人口集団について容易に入手できる.

(3) 悪性新生物による以外の死亡率. 適当量の放射線は造腫瘍性である. これを相殺する好効果は存在しないので，ここで検討する人口集団のすべてとはいかないまでもその大部分では寿命全長の短縮が予期されるであろう. しかし，加齢促進または早期加齢の概念は，新生物有病率の増加に対して適当な補正を行った後にもみられる非特異的な影響の存在を意味する.

(4) 悪性腫瘍以外の特殊疾病項目.

(5) 生理学的の検査および観察. この種のパラメーターは，大規模な人口集団への適用が比較的容易であるが，その定量化が困難であることがあり，また，中年期に至るまで年齢依存性を示さないことが多い.[24]

(6) 生化学的パラメーターおよびそれに関連するパラメーター. この種の測定項目では，実験動物で年齢との関係を示すものと認められたものはごく限られており，人口集団への適用が成功したものは少ない.

LIFE SPAN

Probably the most satisfactory information in this regard will eminate from ABCC where the involved population is large and the Japanese family registration system virtually ensures adequate follow-up information for each survivor. For every citizen, a registrar (Koseki) is maintained at a specific location (Honseki) which generally coincides with the place of birth. If the person moves to a new residence, this information is recorded at the Honseki. Vital events are entered in the Koseki with an effectiveness rate of 99%.[25]

In a study which covered the period 1950-60, Jablon et al.[26] noted that mortality ratios were higher for survivors located within 1400 m of the hypocenter than in those who were more distally located. Such ratios were particularly high in 1950-52 (almost 25% above expectation for males and 50% for females), and an incremental difference was noted for all causes of death; all natural causes; leukemia; all malignancies, excluding leukemia; and tuberculosis; the latter found only in reference to Hiroshima males. Although the total number of deaths was small, the greatest relative increase in mortality appeared to occur among young people. Finally, the average dose estimates were significantly larger for those persons who died of natural causes during 1950-60 than for those who survived this period. A subsequent evaluation[27] failed to shed light on the factors operative during the 1950-54 interval except to cast serious doubt on the hypothesis that the excess mortality observed during this period represented a "late" acute effect, a phenomenon initially very large after August 1945 which slowly diminished to background levels in the mid 1950's.

In 1965, Ciocco[28] extended the foregoing studies, placing particular emphasis on persons who were age 45 or older at the time of the explosions as they represented the fraction of the Life Span Study Sample subject to the highest disability and mortality risks, and were at that time rapidly approaching the modal age of death. The results of this study are summarized in Figure 3. A discrepancy between the proximal and distal groups is again evident, and is greater in Hiroshima than in Nagasaki, and is particularly pronounced in the female portion of the Life Span Study Sample in which it is significant at the 2% level.

In the most recent study,[29] which includes the period 1950-70 and 21,447 deaths, mortality was higher among those whose average dose estimates

寿　命

この点については，おそらくABCCから最も満足すべき資料が得られるであろう．それは，その調査対象集団が大規模であり，日本の戸籍制度を通じて各被爆生存者についての十分な追跡調査資料がほぼ確実に入手されるからである．日本人には，一般に出生地と一致する本籍地に戸籍がある．移住者については，新住所が本籍で記録される．戸籍における人口動態統計事項の記載は99%完全である．[25]

Jablonら[26]は，1950－60年の期間について調査を行い，爆心地から1400m未満の被爆者の死亡比が遠距離被爆者よりも高いことを認め，これは1950－52年の期間において特に著しかった（男性では期待数よりほとんど25%多く，女性では50%も多かった）．増加していると認められたのは全死因，全病死，白血病，白血病を除くすべての悪性新生物，ならびに結核による死亡であり，この最後の結核の増加は広島の男性のみにみられた．死亡総数が少ないとはいえ，死亡率の増加が相対的に最も著しかったのは若年齢群であるようであった．最後に，1950－60年に病死した者の平均推定線量は，同期間の生存者よりも有意に高かった．その後に行われた評価[27]では，1950－54年に作用していた諸要素を解明できなかったが，この期間にみられた死亡率の増加は「後発」急性効果のためであろうという仮説に対しては重大な疑問が持たれた．なお，この現象は1945年8月以後において当初は非常に大きかったがその後徐々に減弱して1950年代の半ばには背景水準に達したのであった．

1965年にCiocco[28]は，前述の調査の延長として，寿命調査対象集団中，疾病による障害と死亡の危険率が最も高く，しかも，死亡が最も起こる年齢に急速に近づいていた原爆時年齢45歳以上の群について特に重点的に検討した．その調査の結果の要約を図3に示した．ここでも近距離被爆群と遠距離被爆群との間に差が認められ，その差は長崎よりも広島で著しい．これは寿命調査対象集団中の女性において特に顕著であり，2%の水準で有意であった．

最近の調査[29]では，1950－70年の死亡者21,447人の検討が行われ，平均推定線量の高い群における死亡率が低線

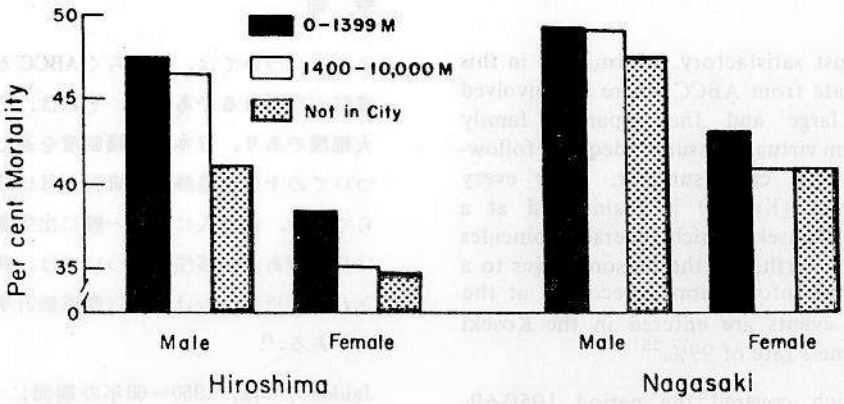

FIGURE 3. Percent mortality among atomic bomb survivors 45 years of age or older in 1945 as a function of exposure status, male versus female, Hiroshima versus Nagasaki (after Ciocco[28]).

図3　1945年に年齢45歳以上であった原爆被爆者の被爆状態の関数としての死亡百分比，男女別，広島・長崎（Ciocco[28]による）

were large than among those whose dose estimates were small or among those who were away from the cities at the time of the bombings. The excess mortality was particularly prominent with respect to (1) leukemia, where it extended to the group with a dose estimate of 10 to 49 rad (Figure 4); (2) malignancies other than leukemia, where, however, an effect could be documented with reliability only in the group with a dose estimate ⩾ 200 rad (Figure 5); and (3) children who were less than 10 years of age at the time of exposure. In the latter connection (Figure 6), mortality ratios (observed:expected) from all causes of death in those with a dose estimate of ⩾ 200 rad decreased with increasing age at exposure, with an especially sharp drop between the ages of 0 to 9 and 10 to 19 years.

Life shortening has also been documented among the early American radiologists on the basis of at least three semi-independent evaluations of overlapping data (Table 2).[30-33] Perhaps the most comprehensive of these evaluations is the study of Seltser and Sartwell,[33] and a portion of their data is summarized in Figure 7. The unfavorable position of the radiologists is particularly apparent during the early time intervals and involves each of the disease groupings evaluated. In a recent review, Warren and Lombard[34] noted that the life-shortening effect had decreased remarkably by 1945 and had vanished by 1960, these changes presumably occasioned by improvements in safety practices.

量群や原爆時に市内にいなかった群よりも高いと認められた．死亡率の増加が特に顕著であったのは次の項目である：(1) 白血病—推定線量が10—49 rad の群にも増加が及んでいた（図4）；(2) 白血病以外の悪性新生物—この場合の影響は推定線量 200 rad 以上の群のみに確実に認められた（図5）；(3) 原爆時年齢10歳未満の者—この最後の項目（図6）に関しては，推定線量 200 rad 以上の群における全死因による死亡比（観察数対期待数）は原爆時年齢の増加とともに下降し，特に0—9歳群から10—19歳群の間で著しい低下がみられた．

初期の米国放射線科医にも寿命短縮が記録されておるが，これは重複資料について半独立的に行われた少なくとも三つの評価に基づいたものである（表2）.[30-33] その中で最も総括的なものは，おそらく Seltser および Sartwell[33] の調査であろう．その資料の一部を図7に要約したが，放射線科医の不利な状況は，初期の頃に特に顕著にみられ，かつ評価の対象となった各疾病分類群にわたっていた．Warren および Lombard[34] の最近の検討によれば，この寿命短縮効果は1945年までに著しく減少し，1960年にはもはや認められなかった．この変化は，安全防御対

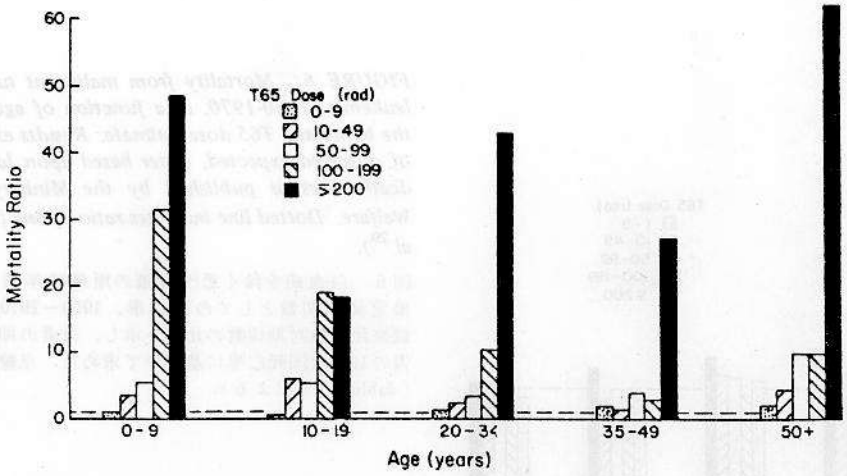

FIGURE 4. Mortality from all causes, 1950-1970, as a function of age at the time of the bomb and T65 dose estimate. Results expressed as ratio of observed:expected, latter based upon Japanese national death rates as published by the Ministry of Health & Welfare. Dotted line indicates ratio of one (after Jablon et al.[29]).

図4　全死因の原爆時年齢およびT65線量推定値の関数としての死亡率，1950－1970年．この結果は観察死亡数対期待数の比率を示し，後者の期待数は厚生省報告の日本全国死亡率に基づいて求めた．点線は比率1を示す（Jablon ら[29]による）．

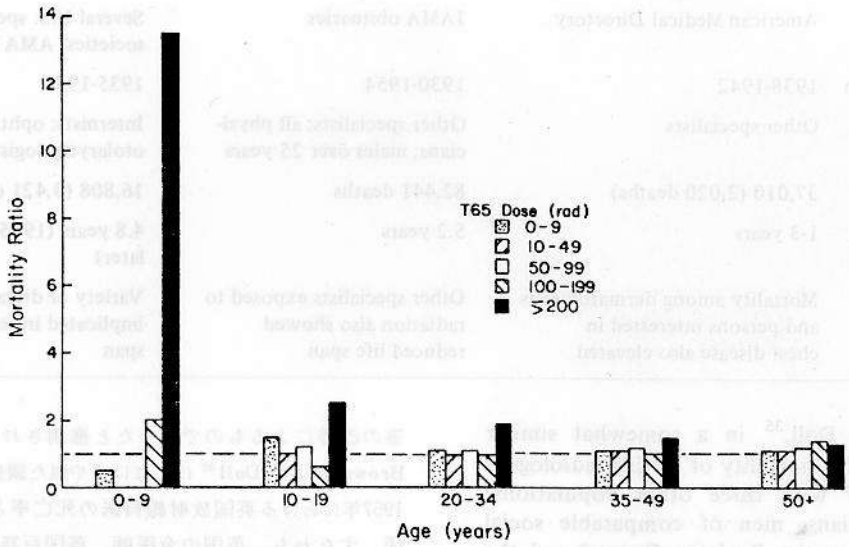

FIGURE 5. Mortality from leukemia, 1950-1970, as a function of age at the time of the bomb and T65 dose estimate. Results expressed as ratio of observed:expected, latter based upon Japanese national death rates as published by the Ministry of Health & Welfare. Dotted line indicates ratio of one (after Jablon et al.[29]).

図5　白血病の原爆時年齢およびT65線量推定値の関数としての死亡率，1950－1970年．この結果は観察死亡数対期待数の比率を示し，後者の期待数は厚生省報告の日本全国死亡率に基づいて求めた．点線は比率1を示す（Jablon ら[29]による）．

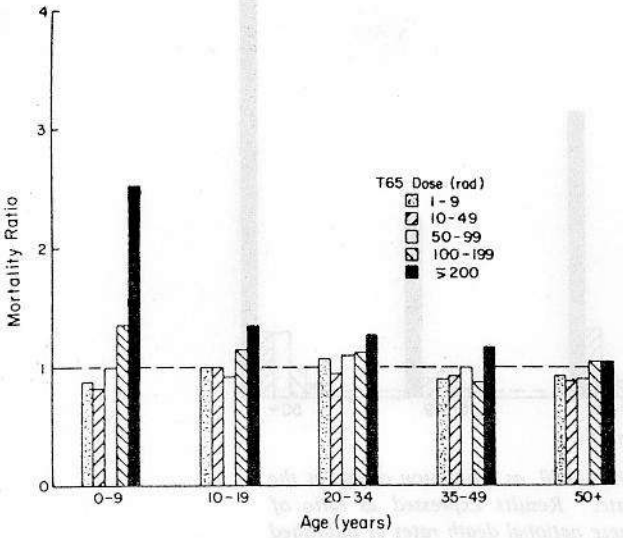

FIGURE 6. Mortality from malignant tumors excluding leukemia, 1950-1970, as a function of age at the time of the bomb and T65 dose estimate. Results expressed as ratio of observed:expected, latter based upon Japanese national death rates as published by the Ministry of Health & Welfare. Dotted line indicates ratio of one (after Jablon et al [29]).

図6　白血病を除く悪性腫瘍の原爆時年齢およびT65線量推定値の関数としての死亡率，1950－1970年．この結果は観察死亡数対期待数の比率を示し，後者の期待数は厚生省報告の日本全国死亡率に基づいて求めた．点線は比率1を示す（Jablon ら[29]による）．

TABLE 2 LIFE SHORTENING AMONG AMERICAN RADIOLOGISTS: SUMMARY OF THREE PERTINENT STUDIES

表2　米国放射線科医の寿命短縮：関係ある三つの調査の要約

	Dublin and Spiegelman[30,31]	Warren[34]	Seltser and Sartwell[33]
Source of data	American Medical Directory	JAMA obituaries	Several U.S. specialty societies, AMA records
Period of observation	1938-1942	1930-1954	1935-1958
Comparison groups	Other specialists	Other specialists; all physicians; males over 25 years	Internists; ophthalmologists-otolaryngologists
Sample size	37,010 (2,020 deaths)	82,441 deaths	16,808 (3,421 deaths)
Estimated reduction of life span	1-3 years	5.2 years	4.8 years (1935-1944, less later)
Remarks	Mortality among dermatologists and persons interested in chest disease also elevated	Other specialists exposed to radiation also showed reduced life span	Variety of disease processes implicated in reduced life span

Court-Brown and Doll,[35] in a somewhat similar study, compared the mortality of British radiologists during 1897-1957 with three other populations: all British physicians, men of comparable social class as defined by the Registrar-General and the general population of Great Britain. In this study, the number of deaths observed in the radiology group was less than the number expected in all the comparisons employed, despite an excess number of deaths due to tumors of the skin, pancreas and (possibly) leukemia among the radiologists. This unexpected finding may be related to epidemiologic discrepancies between the populations under com-

策の改善によるものであったと推測されている．Court-Brown および Doll[35] はこれにやや似た調査を行い，1897－1957年における英国放射線科医の死亡率とその他三つの集団，すなわち，英国の全医師，英国戸籍本署による分類で医師と同等の社会的階級に属している男性，ならびに英国の一般人口の死亡率とを比較した．その調査において行われたすべての比較では，放射線科医に皮膚や膵臓の腫瘍あるいは白血病（と思われる）による死亡が多いにもかかわらず，観察死亡者数は期待数よりも少なかった．この予想外の結果は，比較の対象となった各集団の間に疫学的な差異があることと関係があるかもしれない．そ

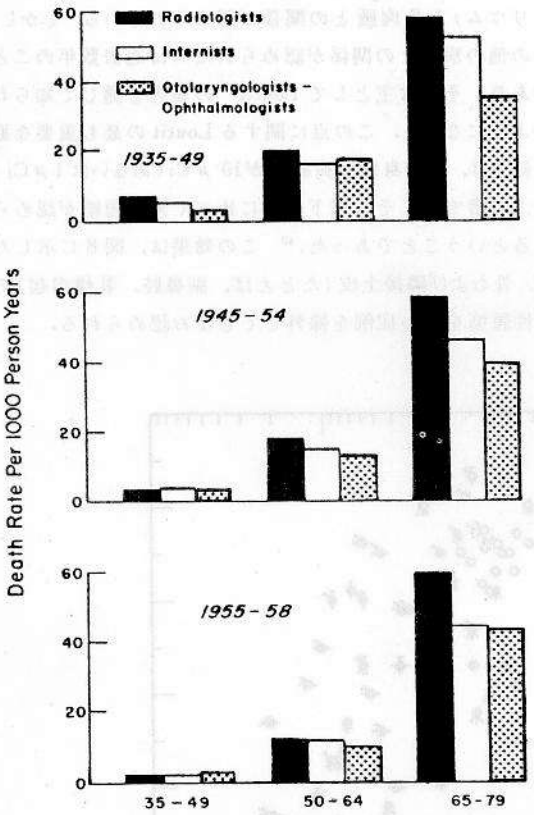

FIGURE 7. Age-adjusted death rate as a function of medical specialty and calendar period (after Seltser and Sartwell[33]).

図7　医学専門分野別および期間の関数としての年齢補正死亡率（Seltser および Sartwell[33] による）.

parison. Whatever the etiology, the failure to document life shortening among radiologists in Great Britain does not necessarily weaken the case for such an effect among their American counterparts since rather marked differences existed in the practice of this specialty in the two countries during much of the period in question.

No mortality data are as yet available with respect to persons exposed in utero during maternal pelvimetry. The number of deaths in children radiated for an "enlarged" thymus is excessive after the first year of life and is attributable to the defined leukemogenic effect.[36] As already noted, comparable information with respect to the British adults with spondylitis would be extremely difficult to interpret. The small size of the Marshall study population in conjunction with the relatively short time interval between exposure and the most recent evaluation makes it too early to detect putative life shortening effects.

The relationship between radium (and mesothorium) and osteogenic sarcoma of bone among the radium

れがいかなる原因のためであったにしても，英国の放射線科医に寿命短縮が認められなかったことは，米国放射線科医に対して影響があるという所見を必ずしも弱めるものではない．すなわち，問題となった期間の大部分において両国の放射線学的活動にかなり著しい差異があったからである．

母体の骨盤計測の際に胎内被曝した者の死亡率に関する資料はまだ報告されていない．胸腺「肥大」のために放射線照射を受けた子供では，生後1年以降に死亡者数の過多があって，これはすでに立証されている白血病誘発効果に起因するものである．[36] 前述のように，英国の成人における脊椎炎患者の資料については解釈が困難である．Marshall 群島の住民の調査では，対象群が小規模であることに加えて被曝時から最近の評価までの期間が比較的短いことのために，起こりうると思われる寿命短縮効果が発見されるまでに至っていない．

New Jersey 州におけるラジウム蛍光塗料工では，

dial painters in New Jersey has been recognized since the early reports of Martland.[37,38] Only in the past several years, however, and primarily via the reports of Loutit,[39] has the association of other disease entities been appreciated. Of primary importance in this regard is the observation of Loutit that life shortening is apparent in persons with estimated body burdens in excess of 10 μCi (and possibly 1 μCi) in comparison to persons subjected to smaller doses.[40] This effect, summarized in Figure 8, persisfs even when cases with malignant tumors of the bone and adjacent epithelium (e.g., nasal sinuses, mastoid) are excluded.

Martland[37,38] の初期の報告以来，ラジウム（およびメソトリウム）と骨肉腫との関係が認められている．しかし，その他の疾患との関係が認められたのは過去数年のことであり，それは主として Loutit[39] の報告を通じて知られるようになった．この点に関する Loutit の最も重要な観察結果は，推定身体負荷線量が10 μCi（あるいは1 μCi）以上の者では，それ以下の者に比べて寿命短縮が認められるということであった．[40] この効果は，図8に示したが，骨および隣接上皮（たとえば，副鼻腔，乳様突起）の悪性腫瘍をもつ症例を除外してもなお認められる．

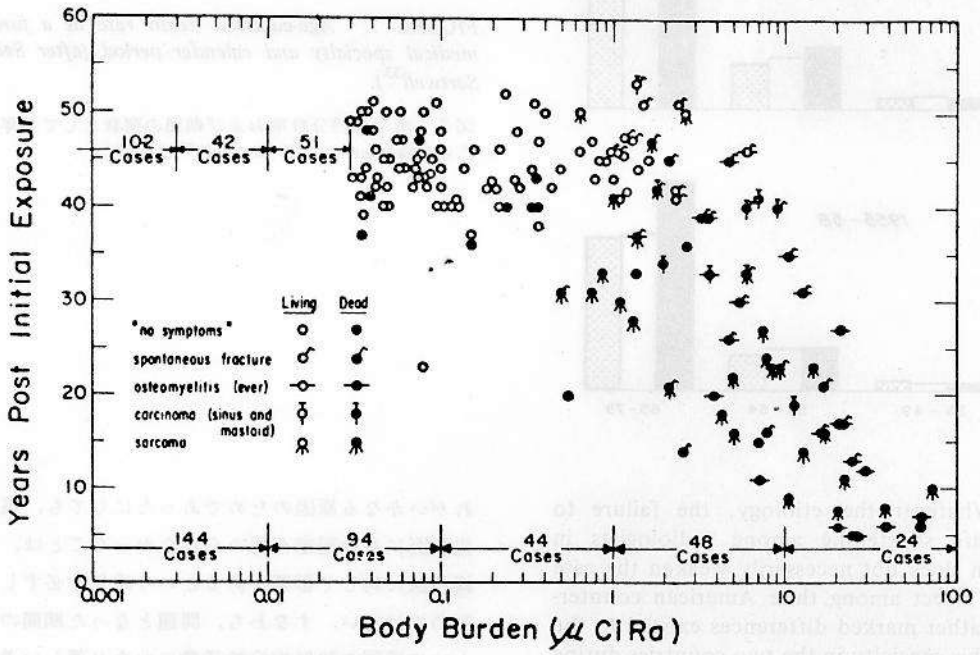

FIGURE 8. Estimate body-burden (as pure radium equivalent) as a function of survival time post initial exposure (after Evans as cited by Loutit[41]).

図8　初回被曝後の生存期間の関数としての推定身体負荷量（純粋なラジウムとして換算）（Loutit[41] が引用した Evans の研究による）．

BENIGN AND MALIGNANT NEOPLASMS

An increased prevalence of malignancies has been documented in all the radiated human populations, with the possible exception of the children radiated in utero during maternal pelvimetry. Leukemia is most often implicated in these populations, but carcinoma of the thyroid also has been frequently reported. Several additional malignancies appear to demonstrate an increased prevalence among the atomic bomb survivors.[41] Perhaps of equal

良性および悪性新生物

母体の骨盤計測の際に胎内被曝した者が例外と思われる他は，放射線照射を受けた人口集団のいずれにも悪性疾患の有病率の増加が認められている．これらの集団では，白血病の認められることが最も多いが，甲状腺癌の多発も報告されている．原爆被爆者では，その他に数種の悪性疾患の有病率の増加があることが認められている．[41] しかし，これと同等の重要性をもつと思われる所見は，今

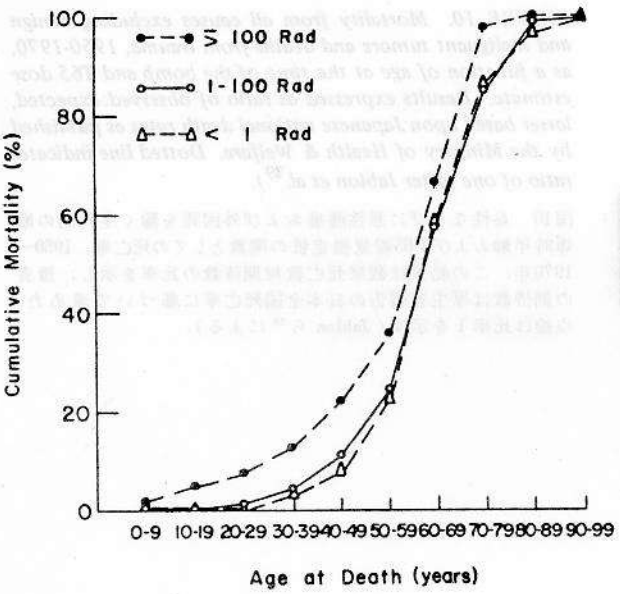

FIGURE 9. Age-specific cumulative mortality for individuals with malignant tumors by exposure category.

図9　悪性腫瘍を有する者の年齢特殊累積死亡率，被爆区分群別

importance, however, is the observation that all the radiation-related tumors specifically studied thus far appear to develop in the proximally located survivors at an earlier average age than in their nonexposed contemporaries.[42] As a corollary to the foregoing, the age-specific death rate for heavily exposed persons with malignant neoplasms is also displaced to the left as shown in Figure 9.

MORTALITY APART FROM NEOPLASMS

As noted, the pioneer American radiologists and radium dial painters demonstrate a reduced longevity which appears to be, at least in part, independent of the defined tumorigenic effect. The only other radiated population with available data in this regard is the atomic bomb survivors and here the picture is less clear cut. In the most recent ABCC study it was noted that life span is reduced in groups exposed to large doses, but a comparison of mortality from all causes versus mortality excluding benign and malignant neoplasms plus trauma (Figure 4 versus Figure 10) shows that the excessive mortality is primarily attributable to neoplasia and these investigators[29] conclude that "although late radiation effects on human mortality may to some degree manifest themselves in terms of disorders of many kinds and affecting many organs, the most notable effect is specifically the induction of cancer." In this connection, the relative risk of several major disease groupings in those exposed to ⩾ 200 rad versus those exposed to 0 to 9 rad is

までに特に検討の対象となった放射線関連腫瘍がいずれも非被爆者に比べて近距離被爆者において，その平均発病年齢が若いようであるということである.[42] 上記のことから推測されるように，悪性新生物を有する強度放射線被曝者の年齢特異死亡率も，図9に示したように，左方へ移動している.

新生物以外の死因による死亡率

前述のように，初期の米国放射線科医やラジウム蛍光塗料工には寿命の短縮があり，少なくともその一部は既知の造腫瘍効果とは無関係であると思われる．この点について資料の入手されている放射線被曝人口集団としては，これらのほかに原爆被爆者があるだけであるが，この場合の状況はいっそう不明確である．最近のABCC調査によれば，高線量被曝群に寿命短縮が認められたが，全死因による死亡率と良性および悪性新生物ならびに外因死を除く死亡率との比較では（図4と図10），死亡率の増加が主として新生物に起因することが認められ，これらの研究者[29]は，「ヒトの死亡率に対する放射線の後影響は，多くの臓器に影響を及ぼす各種の障害として現われるであろうが，最も顕著な特異的な影響は発癌である」と結論している．この点に関して，数種の主要疾患について，200 rad 以上の群の0－9 rad 群に対する相対的危険率

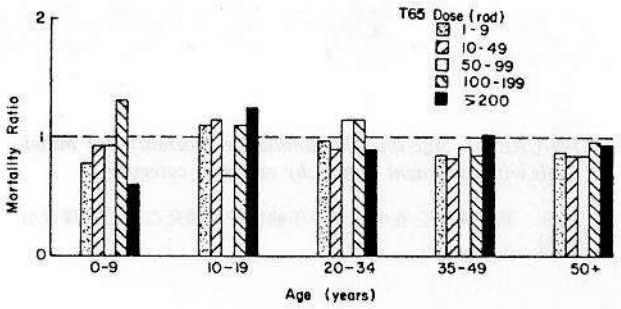

FIGURE 10. Mortality from all causes excluding benign and malignant tumors and deaths from trauma, 1950-1970, as a function of age at the time of the bomb and T65 dose estimate. Results expressed as ratio of observed:expected, latter based upon Japanese national death rates as published by the Ministry of Health & Welfare. Dotted line indicates ratio of one (after Jablon et al.[29]).

図10　良性ならびに悪性腫瘍および外因死を除く全死因の原爆時年齢およびT65線量推定値の関数としての死亡率，1950—1970年．この結果は観察死亡数対期待数の比率を示し，後者の期待数は厚生省報告の日本全国死亡率に基づいて求めた．点線は比率1を示す（Jablonら[29]による）．

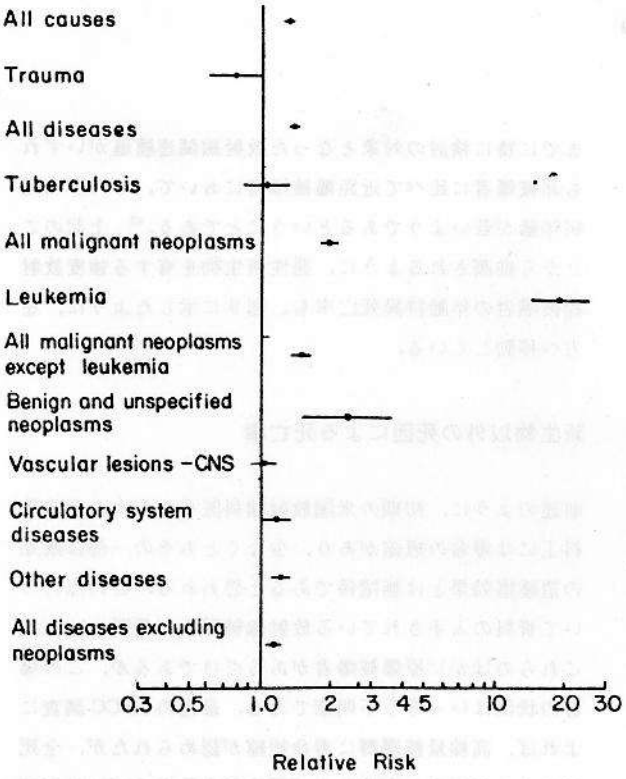

FIGURE 11. Relative risk and 80 percent confidence intervals ⩾ 200 rad versus 0 to 9 rad for major causes of death (after Jablon et al.[29]).

図11　200 rad以上の群の0—9 rad群に対する主要死因の相対的危険度および80%信頼区間（Jablonら[29]による）．

shown in Figure 11. Of particular importance in the present context is the category of "all diseases excluding neoplasms" which demonstrates a slight increase in relative risk. Specifically excluded from this category are both benign and malignant tumors, as well as deaths due to trauma for which no direct radiation effect is presumed to exist. Additional observations, based upon an analysis of these 15,842 deaths, include the following (see also Table 3);

を図11に示した．今回の報告の観点から特に重要であるのは「新生物を除く全病死」の分類項目であり，その相対的危険率に軽度の増加がみられる．この分類項目からは良性および悪性腫瘍のほかに放射線の直接的な影響があるとは思われない外因死も除外してある．その死亡者15,842人についての解析によって，さらに次のような観察結果が得られた（表3をも参照）：

TABLE 3 MORTALITY FROM ALL CAUSES EXCLUDING BENIGN AND MALIGNANT TUMORS AND DEATHS FROM TRAUMA, 1950-1970, AS A FUNCTION OF T65 DOSE ESTIMATE*

表3　良性ならびに悪性腫瘍および外因死を除く全死因のT65線量推定値の関数としての死亡率，1950－1970年

T65 Dose Estimate (rad)	Period of Observation				
	1950-1954	1955-1959	1960-1964	1965-1970	1950-1970
0- 9	0.873	0.933	0.873	0.837	0.876
10-49	0.800 (0.06)	0.947 (0.38)	0.836 (0.19)	0.838 (0.50)	0.856 (0.17)
50-99	0.697 (0.01)	0.841 (0.13)	1.057 (0.01)	0.881 (0.26)	0.881 (0.45)
100-199	1.119 (0.01)	0.934 (0.50)	0.908 (0.37)	0.896 (0.24)	0.951 (0.05)
⩾200	0.939 (0.30)	1.077 (0.10)	0.950 (0.23)	0.970 (0.07)	0.983 (0.02)

**Results expressed as ratio of observed to expected deaths; expected data derived from concurrent Japanese national rates. Significance values in parentheses are based upon a comparison with related 0-9 rad group and are derived from one tail test taken in the direction of the observed discrepancy.*

この結果は観察死亡数と期待死亡数との比率として示した；この期待数の資料は当時の日本全国死亡率から求めた．括弧内の有意性値は該当する0－9 rad群との比較に基づくものであり，差が観察された方向での一側検定から求めた．

(1) The groups exposed to an estimated dose of ⩾ 200 rad exhibit a higher mortality than those exposed to an estimated dose of 0 to 9 rad in every time period examined, but the difference is significant only for the 20-year period as a whole and not for any of the subperiods.

(2) With respect to age at the time of exposure, survivors aged 10 to 19 years at the time of the bomb, unlike those in the other age groups, demonstrate higher than expected mortality in comparison with national death rates in Japan.

(3) Surprisingly, mortality in Hiroshima is very low (82% of standard) whereas in Nagasaki it is almost 8% higher than would be expected on the basis of the national death rates.

(4) In Hiroshima, the observed:expected ratios for both the groups exposed to 100 to 199 and ⩾ 200 rad estimates are generally higher than the comparable figure for the group exposed to 0 to 9 rad; however, these differences are not statistically significant.

(5) In Nagasaki, the people exposed to 100 to 199 rad do not demonstrate a higher mortality than those exposed to 0 to 9 rad, and even for survivors exposed to an estimated dose of ⩾ 200 rad the differences are neither impressive nor statistically significant.

(6) In comparison with national death rates, the expected mortality in both men and women is

(1) いずれの調査期間においても推定線量が200 rad以上の群の死亡率は0－9 radの群よりも高いが，20年間全体をみた場合にのみその差は有意であり，期間別にみれば有意ではない．

(2) 原爆時年齢別にみると，年齢10－19歳の被爆者は，その他の年齢群とは違って死亡者数が日本全国の死亡率に基づく期待数よりも多い．

(3) 広島における死亡が非常に少ないこと（標準値の82％）は意外であったが，長崎における死亡数は日本全国の死亡率に基づく期待数に比べてほぼ8％も多い．

(4) 広島では，推定線量100－199 radおよび200 rad以上の両群における観察死亡者数の期待数に対する比率は，全般的に0－9 rad群よりも高い．しかし，その差は統計的に有意ではない．

(5) 長崎では，100－199 rad群における死亡率が0－9 rad群よりも高いとは認められない．推定線量200 rad以上の群においてさえも差は顕著でなく，統計的に有意ではない．

(6) 日本全国死亡率との比較では，男女とも死亡率は期待

lower than expected (83% of standard for women and 91% for men); however, for both sexes, the observed:expected ratios are higher in those exposed to ⩾ 200 rad versus those exposed to 0 to 9 rad.

値よりも低い(女性では標準値の83%，男性では91%)；しかし，男女とも 200 rad 以上の群における観察死亡者数の期待数に対する比率は 0 — 9 rad 群よりも高い．

OTHER DISEASE ENTITIES

Some of the entities implicated in this regard are listed in Table 1. Retardation of growth and development in children exposed in whole body fashion correlates well with similar experience in the experimental situation, although alternative explanations which do not implicate radiation have been advanced with respect to the ABCC data. In a fashion comparable to that noted previously in respect to malignancies, proximally located atomic bomb survivors demonstrate not only an increased prevalence but also an accelerated appearance of benign tumors of the skin in comparison with their more distally located counterparts.[43]

その他の疾病項目

これに関連があると思われるいくつかの疾病項目を表1に示した．全身照射を受けた子供にみられる成長・発育の遅滞は，実験的状況下における同種の経験とよく一致している．ただし，ABCC の資料に関しては，放射線とは無関係の別の説明も示唆されている．前述の悪性腫瘍の場合と同様に，皮膚の良性腫瘍も，近距離原爆被爆者では遠距離被爆者に比べて有病率が増加しているばかりでなく，その発生の促進もみられる．[43]

PHYSIOLOGIC FUNCTIONS

Some of the intrinsic problems in this type of approach have been alluded to previously. The only meaningful information in this regard relates to the Japanese and the Marshallese survivors. To define a composite "physiologic" age, Hollingsworth et al[24] evaluated the following age-related functions among the Japanese: skin elasticity, systolic blood pressure, vital capacity, hand (grasp) strength, light extinction time, vibratory perception, visual acuity, auditory perception and serum cholesterol. The resultant composite appeared to be age-dependent for persons age 35 or over. Unfortunately, these investigators were unable to apply this approach to a controlled sample of exposed and nonexposed persons of sufficient size. However, some preliminary observations in this regard disclosed no radiation-related discrepancies with respect to hearing loss, skin retractibility, hair graying and subjective estimation of age.[24,44,45]

More recently, Johnson et al[43] reexamined several of these parameters with particular emphasis on the integument. Of interest in the present context is the observation of a tendency toward an increased prevalence and accelerated appearance of hair graying, and senile elastoses among proximally exposed survivors of Hiroshima and Nagasaki in comparison with distally located persons.

生理学的機能

この種の調査に伴っている本質的な問題のいくつかについてはすでに言及した．この分野における意味ある資料としては，僅かに日本ならびに Marshall 群島の被曝者に関するものがあるだけである．Hollingsworth ら[24]は，総合的な「生理学的」年齢を定義する目的で日本人における次の年齢関連機能の評価を行った：皮膚弾性，収縮期血圧，肺活量，握力，消灯反応時間，振動感覚，視力，聴力ならびに血清コレステロール値であった．この総合判定の結果では，35歳以上の者においては年齢依存性を示すようであった．残念ながら，この著者らは，被爆者と非被爆者を含む十分な規模の，よく管理された集団にこの方法を適用することができなかった．しかし，これらの調査項目について行われた若干の予備的観察によれば，聴力減退，皮膚退縮性，白髪化，および主観的年齢評価に関して放射線関連の食違いは認められなかった．[24,44,45]

Johnson ら[43]は，皮膚を特に重点的に取り上げて，これらの調査項目のいくつかについての再検討を最近行った．ここで興味ある観察所見として，広島・長崎の近距離被爆者は，遠距離被爆者に比べて白髪化および老年性弾力線維症の有病率が高く，その発生が促進されているという傾向が認められた．

A similar approach has been applied by Conard and co-workers to the Marshallese.[46] As noted by these investigators, the studies were hampered by the small number of people involved, a language barrier, an uncertainty with respect to the age of some of the older persons and a lack of vital statistics pertinent to this population. However, no significant discrepancies were noted between the exposed and nonexposed segments of the study population, and it was postulated that if radiation-related aging effects were present, more sensitive tests would be necessary to demonstrate them.

MORPHOLOGIC, BIOCHEMICAL AND RELATED PARAMETERS

Again, the majority of the relevant data in this regard have eminated from ABCC. The following parameters have been evaluated:

(1) Cardiac lipofuscin. This pigment accumulates in the cytoplasm of myocardial cells in a linear fashion at the rate of approximately 0.3% per decade in persons over age 10.[47] In a comparison of carefully matched proximally exposed versus nonexposed persons, no radiation-related discrepancy was found with respect to the rate of lipofuscin accumulation, the amount of pigment acquired by an involved cell or the histologic characteristics of this substance in situ.[48]

(2) Extensibility of isolated segments of aorta. One of the early ABCC aging studies involved an evaluation of the mechanical extensibility of standardized portions of aorta removed at postmortem examination from exposed and nonexposed persons. No significant difference was noted between the two groups with respect to this age-dependent parameter.[49]

(3) Hexosamine:collagen ratio. In connective tissue, the ratio of collagen to the mucopolysaccharide ground substance appears to vary with age in a predictable fashion. A significant discrepancy was found between proximally exposed survivors matched by age and sex with persons not in the city at the time of the bombing.[50]

(4) Soluble:insoluble collagen ratio. The ratio between the acid (or heat) soluble and insoluble fractions of collagen is an extremely reliable parameter of aging in rodents. Application of this parameter to 261 proximally exposed survivors of Hiroshima and to persons away from the city at the

Conard らは，Marshall 群島住民について同様な調査を試みた.[46] これらの研究者が指摘しているように，調査対象者が少ないこと，言語上の障壁があること，高齢者の一部は年齢が不確実なこと，およびこの集団についての人口動態統計資料がないことのために調査は困難であった．しかし，この調査集団では，被曝群と非被曝群との間に有意差は認められなかったので，放射線に関係ある加齢影響があるとすれば，その検索に感度のより高い検査が必要であろうと思われた．

形態学的，生化学的ならびにその他の関連ある調査項目

この分野における資料の大部分もABCCで求められたものである．次の項目についての評価が行われている．

(1) 心臓リポフスチン沈着．この色素の心筋細胞原形質内沈着は，年齢10歳以降に10年について約0.3％の割合で直線的に増加すると認められている.[47] 近距離被爆者と非被爆者を注意深く組み合わせて比較した結果によれば，リポフスチン沈着率，被検細胞内の色素沈着量および沈着物質の組織学的特性において放射線との関係を示す差異は認められなかった.[48]

(2) 摘出大動脈管の弾性．ABCCにおける初期の加齢調査の一つとして，剖検時に被爆者および非被爆者の大動脈の標準的な一部分を摘出してその機械的伸展性の評価が行われた．この年齢依存性の調査項目では，両群間に有意差は認められなかった.[49]

(3) ヘクソサミン対コラゲン比．結合組織におけるコラゲンのムコ多糖類基礎物質に対する比率は，予想可能な形式に従って年齢変化を示すようである．年齢・性別構成が一致するように組み合わせた近距離被爆者と原爆時に市内にいなかった者との間に有意な差が認められた.[50]

(4) 可溶性対不溶性コラゲン比．酸（または熱）処理におけるコラゲンの可溶性および不溶性分画の比率は，齧歯動物では加齢のきわめて信頼できるパラメーターである．このパラメーターを広島の近距離被爆者および原爆時に

time of the explosion revealed no consistent radiation-related differences.[51]

(5) Spleen index. Ratio of the weight of the spleen to the entire organism has been shown to represent an effective parameter of autoimmune phenomena and is the basis of the Simonsen assay.[52] More recently, Walford[53] has noted the relationship between this function and chronologic age in man. However, no radiation-related difference could be documented when this parameter was applied to a portion of the ABCC autopsy series.[54]

(6) Pyrinophilic spleen cells. In most populations, serum gamma globulin levels increase with age. The corresponding tissue equivalent is the relative number of pyrinophilic cells in the spleen. The ratio of positive:negative cells in two mtached populations, one of which was exposed to significant amounts of radiation, was not significantly disparate.[55]

(7) Giant hepatic nuclei. The frequency of very large liver nuclei increases with age. Preliminary analysis suggests no consistent radiation-related difference between two segments of the ABCC study population in this regard.[55]

(8) Isoantibodies. Following a peak early in life, the titer of naturally-occurring anti-A and anti-B declines in linear fashion as a function of age in man with a correlation coefficient of -0.72.[56] An evaluation of 1042 serum specimens showed no difference among the following exposure categories: persons located 0 to 1999 m from the hypocenter with symptoms of acute radiation injury; persons similarly located but without such symptoms; persons more distally located (3000 to 3499 m); and persons not in the city at the time of the explosion.[56]

In summary, with respect to this subsection, quantifiable morphologic and biochemical parameters have been applied to the exposed populations of Hiroshima and Nagasaki. Of the eight parameters thus far evaluated, only one shows a significant difference between exposed and nonexposed persons. As discussed in more detail elsewhere,[57] several factors may account for the apparent negative relationship between these measurements and exposure status: the demographic heterogeneity of the study population; the marked variations in exposure status among the involved persons including the magnitude of exposure and the degree of shielding; and the poor sensitivity of the parameters employed. With respect to the latter point, a

市内にいなかった者261人に応用してみた結果，放射線との関係を示す一貫した差は認められなかった.[51]

(5) 脾臓指数．脾臓重量の総体重に対する比率は，自己免疫現象の効果的なパラメーターであると認められており，Simonsen 分析法の基礎である.[52] 最近，Walford[53] はこの関数とヒトの実年齢との間に関係があることを認めている．しかし，このパラメーターをABCC剖検例の一部に適用してみた結果によれば，放射線との関係を示す差異は認められなかった.[54]

(6) 好ピリン性脾細胞．大部分の集団では，血清ガンマ・グロブリン値が年齢とともに上昇すると認められている．組織の中でこれに相当するものは脾臓に含まれる好ピリン性細胞の相対的数量である．有意な放射線に被曝した者とそうでない者とを組み合わせて陽性細胞と陰性細胞との比率をみたところ，両群間に有意な差はなかった.[55]

(7) 巨大肝細胞核．きわめて大きな核を有する肝細胞の頻度は年齢とともに増加する．この点については，ABCC調査対象集団中の二つの副次群における予備的解析によれば，放射線との関係を示す一貫した差があることは示唆されなかった.[55]

(8) 同種抗体．ヒトにおける自然発生の抗A および抗B 抗体値は，若年期に頂点に達し，以後，年齢の関数として直線的下降を示し，その相関係数は-0.72である.[56] 次の被爆区分群に属している1042人の血清を検査した結果，各群間に差は認められなかった．なお，その被爆区分群というのは，爆心地から0－1999 mで被爆して急性放射線傷害の症状を呈した者，同距離であるがこの種の症状がなかった者，もっと遠距離(3000－3499 m)であった者，ならびに原爆時に市内にいなかった者である.[56]

本項を要約すると，広島・長崎の被爆者集団に対しては定量測定の可能な形態学的ならびに生化学的パラメーターが適用された．現在までに評価の行われたパラメーター8項目の中でわずかに1項目に被爆者と非被爆者との間に有意差が認められているにすぎない．別の報告[57]で詳細に論じているように，これらの測定と被曝状態との間の関係が陰性であることは，次のいくつかの要因によって説明できるであろう．すなわち，調査集団が人口統計学的に不均一であること，被曝の程度や遮蔽の程度など，各被検者の被爆状態が著しく異なること，ならびに使用したパラメーターの感度が不良であることなどである．

difference of 2.7 years of total life span (from birth) between exposure categories would be detected with only a 50% probability in the study dealing with naturally-occurring anti-A and anti-B.[56] Assuming that aging in man is accelerated by 5 to 10 days per absorbed rad, the eventual mean constriction of life span in a subsample with an average exposure of 200 rad might amount to only 1.28 to 3.85 years in the complete lifetime experience of the subsample. Thus, a strong suspicion exists that the parameters thus far applied are not sufficiently sensitive to detect the magnitude of change expected.

COMMENTS

An evaluation of radiation-induced life shortening is complicated by the paucity of meaningful data concerning the fundamental mechanisms involved in irreparable radiation injury and in spontaneous aging. Thus, it is often difficult to separate effect from cause, primary manifestations from secondary complications. Consequently, comparisons between radiation-related and spontaneous aging must be made on the basis of overt manifestations of undefined basic mechanisms. As might be expected, considerable uncertainty exists as to which pathologic processes warrant designation as hallmarks of aging.

Experience to date does not support the somewhat oversimplified postulate that a portion of radiation injury is qualitatively and quantitatively identical to the effects which transpire with the passage of time. Such a situation might pertain with respect to an agent which accelerates aging but has no other action; radiation does not fall into this category. In this connection, Casarett[58] has pointed out that aging purists who require equal temporal advancement of all events common to the control population ignore important radiobiologic variations in host responsiveness including the degree of age-dependence of specific disease entities.

As already noted, considerable controversy exists as to the appropriateness of the various putative parameters of aging. Possibly the only area of general agreement is that accelerated or precocious aging should be associated with decreased longevity even when appropriate corrections are made for the increased incidence and/or accelerated appearance of tumors. Reference to Table 1 reveals that this information is available for only three of the seven populations listed and, of the former, the largest group (Japanese survivors) shows an equivocal effect.

この最後の点に関しては，自然発生の抗Aおよび抗B抗体値の調査では，各被爆区分群の（出生時以降の）総寿命に2.7年の差が検出される確率はわずかに50%にすぎなかった.[56] ヒトの場合に吸収線量1 rad当たり5－10日の加齢促進があると仮定すれば，平均被曝線量が200 radの集団における究極的な平均寿命短縮は，その一生を通じてわずかに1.28－3.85年にすぎないであろう．したがって，現在までに適用された各パラメーターでは，起こりうると予想されるこの程度の変化の検出には感度不十分である疑いが強い．

考　察

回復不可能の放射線傷害や自然加齢に関与する基礎的機序について意味のある資料が少ないために，放射線誘発性寿命短縮の評価は困難である．したがって，原因と結果あるいは原発性発症と続発性併発症との区別が困難であることが多い．そのために，基礎的機序が不明確な発症現象に基づいて放射線関連の加齢と自然加齢との比較をしなければならないことになる．また，予想されるように，いずれの病的過程を加齢の指標として指定すべきかもかなり不明確である．

今日までの経験からすると，放射線傷害の構成部分は，時の経過とともに発生する効果と質的，量的に等しいであろうという簡略化しすぎた仮説は支持されるものではない．加齢促進を誘発してもその他の作用を全くもたない因子であれば，そのような状況を示すかもしれない．放射線は，そのような部類のものではない．この点に関しては，対照人口に共通するすべての事象の発生が時間的に平等に促進されなければならないとする加齢純粋主義者の考え方は，各特定疾病項目における年齢依存性の程度をも含めて，宿主反応に重大な放射線生物学的差異があることを無視するものであるとCasarett[58]は指摘している．

前述のように，加齢のパラメーターと考えられているものの妥当性には相当の議論がある．一般に意見の一致がみられるのは，加齢促進または早期加齢では，腫瘍発生率の増加あるいはその発生の促進に対して適当な補正を行った後においても寿命の短縮がある筈であるという点についてだけである．表1をみれば，ここに記載した7集団中のわずかに三つについてこの種の情報が入手されているにすぎないことが分るが，その中で最も大規模な集団（日本における原爆被爆者）ではその影響は不確実である．

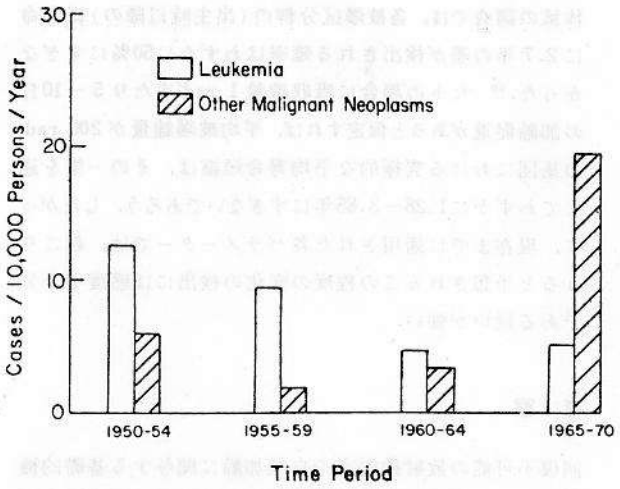

FIGURE 12. Excess mortality from leukemia versus other malignant neoplasms, 1950-1970 in group exposed to ⩾200 rad as a function of time period (after Jablon et al[29]).

図12　200 rad 以上の群における白血病およびその他の悪性新生物の期間の関数としての過剰死亡，1950－1970年（Jablon ら[29]による）．

Evidence exists to suggest a decreased life span among the early American radiobiologists and the radium dial workers, a response which appears to be independent of the defined tumorigenic effect. The absence of a similar effect among the Japanese survivors, with the possible exception of the 1950-54 period, is somewhat unexpected and demands an explanation since most of the currently popular theories that approach aging from a molecular standpoint (somatic mutation theory, cross-linking theory, various DNA theories, immune theory) are in serious difficulty if radiation does something which is quite different from accelerating the onset and progress of senescence.[53] Possible explanations for this apparent discrepancy include the following:

(1) The concept of accelerated aging does not pertain to humans. This is considered unlikely based upon the reported experience relevant to the pioneer American radiologists and radium dial workers.[33,39]

(2) Accelerated aging is only associated with chronic exposure. Duration of exposure clearly distinguishes the Japanese survivors versus radium dial painters and American radiologists. However, the available experimental experience suggests that continuous or protracted exposures have a less pronounced effect on life shortening than does the same amount of radiation given in a single dose.

(3) Accelerated aging among the Japanese survivors will be shown at some future date to be confined to the youngest age groups and, since the youngest survivor today is only 27 years of age, it is too early to expect definitive evidence of such an

初期の米国放射線科医およびラジウム蛍光塗料工に寿命短縮を示唆する知見が認められており，その影響は既知の腫瘍発生効果とは独立しているようであった．日本における原爆被爆者では，1950－54年の期間が例外であろうということを除けばこの種の影響の認められないことはやや意外であり，放射線の作用が老衰の発現や進行とは全く異なる効果をもたらすものであるとすれば，分子の見地から加齢を取り上げている現在の種々の人気ある学説（体細胞突然変異説，交叉連鎖説，各種のDNA説，免疫説）の多くは重大な困難に直面することになるので，この所見の原因説明が是非必要である．[53] この明らかな矛盾については次のような説明が考えられるであろう：

(1) 加齢促進の概念はヒトに当てはまらない．初期の米国放射線科医やラジウム蛍光塗料工について報告されている経験[33,39]を考えれば，この説明は可能性が少ない．

(2) 加齢促進は慢性被曝にのみ伴っている．被曝期間には，日本における原爆被爆者とラジウム蛍光塗料工や米国放射線科医との間で明らかな差がある．しかし，実験によって得られた経験によれば，連続的または長期被曝の寿命に対する短縮効果は，同一線量の1回照射の場合よりも少ないことが示唆されている．

(3) 日本における原爆被爆者の加齢促進は，若年齢層に限定されることが今後判明するであろうが，最も若い被爆者は現在27歳にすぎないので，この種の影響の明確な証拠が現われるにはまだ早すぎる．これは魅力ある説明で，

effect. This is an attractive explanation which would correlate with the experimental situation. However, as reflected in the mortality data reviewed herein, and particularly Figure 10, there is no evidence at the moment to support such an hypothesis with the possible exception of persons who were between 10 and 19 years of age at the time of the explosion. The absence of a similar effect in the youngest group (0 to 9 years) is particularly disquieting, although the data here are undoubtedly influenced by the marked prevalence of leukemia.

(4) An insufficient period of time has elapsed after exposure for accelerated aging to become manifest. This represents possibly the most reasonable explanation. The apparent relationship between reduced life span and the tumorigenic effects of ionizing radiation has been alluded to previously. Among survivors exposed to large dose estimates, the prevalence of all malignant tumors excluding leukemia has increased over the past 20 years with a particularly sharp rise evident recently (Figure 12), especially among persons who were less than 10 years of age at the time of exposure.[29]

In summary, tumor-independent life shortening effect is only equivocally apparent with respect to the atomic bomb survivors, an observation which appears to be at variance with other reported experience in man. Because of this discrepancy it would appear prudent to reserve judgment on the interpretation of the ABCC data until additional information is available.

実験成績とよく一致する．しかし，ここで再検討した死亡資料，特に図10をみる限りでは，原爆時年齢10—19歳の者を除けば，この種の仮説を支持する証拠は今のところ認められない．年齢の最も若い群（0—9歳）にこの種の影響がないことに特に不安が感じられるが，この資料は白血病有病率が顕著であることの影響を受けている点に疑問の余地はない．

(4) 被爆後の経過期間が不十分であるために加齢促進がまだ現われていない．この説明がおそらく最も合理的であろう．寿命短縮と電離放射線の造腫瘍効果との間にみられる関係についてはすでに言及した．推定線量の高い原爆放射線被曝者には過去20年間に白血病以外のすべての悪性腫瘍の有病率増加があり，最近は特に急激な上昇がみられ（図12），これは原爆時年齢10歳未満の者において特に顕著である．[29]

要するに，腫瘍とは独立した寿命短縮効果が原爆被爆者に不確実に認められているにすぎないが，これはヒトについて報告されたその他の経験とは異なっているようである．この差があるので，ABCC資料の解釈に関する判断はさらに情報が入手されるまで差控えることが賢明であろう．

REFERENCES

参考文献

1. UPTON AC: Ionizing radiation and the aging process. J Gerontol 12:306, 1957

2. UPTON AC, KIMBALL AW, FURTH J, CHRISTENBERRY KW, BENNETT WH: Some delayed effects of atomic bomb radiation in mice. Cancer Res 20:1, 1960

3. STORER JB, SANDERS PC: Relative effectiveness of neutrons for production of delayed biological effects. 1. Effect of single doses of thermal neutrons in life span of mice. Radiat Res 8:64, 1958

4. LINDOP PJ, ROTBLAT J: Long-term effects of a single whole body exposure of mice to ionizing radiations. 1. Life shortening. Proc Roy Soc (London) 154:332, 1961

5. LINDOP PJ, ROTBLAT J: The age factor in the susceptibility of man and animals to radiation. 1. The age factor in radiation sensitivity in mice. Brit J Radiol 35:23, 1962

6. JONES DCL, KIMELDORF DJ: Effects of age at irradiation on life span in the male rat. Radiat Res 22:106, 1964

7. STORER JB, GRAHN D: Vertebrate radiobiology: late effects. Ann Rev Nucl Sci 10:561, 1960

8. VAN CLEAVE CD: Late somatic effects of ionizing radiation, TID-24310, Washington, D.C., Division of Technical Information, U.S. Atomic Energy Commission, 1968, p 25.

9. ALEXANDER R, CONNELL DI: Shortening of life span of mice by irradiation with X-rays and treatment with radiometric chemicals. Radiat Res 12:38, 1960

10. UPTON AC, FURTH J, CHRISTENBERRY KW: Late effects of thermal neutron irradiation in mice. Cancer Res 14: 682, 1954

11. LAMSON BG, BILLINGS MS, MEEK RA, BENNETT LR: Late effects of total body roentgen irradiation. Arch Path 66:311, 1958

12. ALEXANDER P: Accelerated aging: long term effect of exposure to ionizing radiations. Gerontologia (Basel) 1: 174, 1957

13. KALLMAN RF, KOHN HI: Life-shortening by whole and partial-body X-irradiation in mice. Science 128:301, 1958

14. BOONE IU: Effects of partial-body and whole-body X-irradiation on life span and tumor incidence of CF_1 mice (abstract). Radiat Res 11:434, 1959

15. LAMSON BG, BILLINGS MS, BENNETT LR: Late effects of total-body roentgen irradiation. V. Longevity and incidence of nephrosclerosis as influenced by partial-body shielding. J Nat Cancer Inst 22:1059, 1959

16. MAISIN JA, DUNJIC A, MALDAGUE P, MAISIN H: Delayed effects observed in rats subjected to a single dose of X-rays. Proceedings of the Second United Nations International Conference on the Peaceful Users of Atomic Energy, United Nations, New York. Geneva 22:57, 1958

17. DUNJIC A, MAISIN J, MALDAGUE H, MAISIN H: Incidence of mortality and dose-response relationship following partial-body X-irradiation of the rat. Radiat Res 12:155, 1960

18. CONRAD RA, MEYER LM, SUTOW WW, MOLONEY WC, LOWREY A, HICKING A, KIKLON E: Medical survey of Rongelap people eight years after exposure to fallout, USAEC Report BNL-780, Brookhaven National Laboratory, 1963

19. OUGHTERSON AW, WARREN S, eds: Medical Effects of the Atomic Bomb in Japan, 1st ed, New York, McGraw-Hill, 1956. p 86

20. AUXIER JA, CHEKA JS, HAYWOOD FF, JONES TD, THORNGATE JH: Radiation dose distributions from Hiroshima and Nagasaki bombings. Health Phys 12:425, 1966

21. CHEKA JS, SANDERS FW, JONES TD, SHINAPAUGH WH: Radiation in Japanese residential structures. USAEC Report CEX 62:11, 1965

22. MILTON RC, SHOHOJI T: Tentative 1965 dose estimation for A-bomb survivors, Hiroshima and Nagasaki. ABCC Technical Report 1-68

23. JABLON S, FUJITA S, FUKUSHIMA K, ISHIMARU T, AUXIER JA: RBE of neutrons in atomic bomb survivors Hiroshima-Nagasaki. ABCC Technical Report 12-70

24. HOLLINGSWORTH JW, HASHIZUME A, JABLON S: Correlations between tests of aging in Hiroshima subjects–an attempt to define "physiologic age". Yale J Biol Med 38:11, 1965

25. STEER A: Neoplasia–introduction and overview. Hum Path 2:501, 1971

26. JABLON S, ISHIDA M, YAMASAKI J: Mortality, October, 1950–September, 1960. ABCC Technical Report 15-63

27. BEEBE GW, KATO H, LAND CE: Mortality and radiation dose, October, 1950-September, 1966. ABCC Technical Report 11-70

28. CIOCCO A: Mortality 1950-64 and disease and survivorship 1958-64 among sample members aged 50 years or older, October 1, 1950. ABCC Technical Report 18-65

29. JABLON S, KATO H: Mortality among A-bomb survivors, 1950-70. ABCC Technical Report 10-71

30. DUBLIN LI, SPIEGELMAN M: The longevity and mortality of American physicians, 1938-1942. JAMA 134:1211, 1947

31. DUBLIN LI, SPIEGELMAN M: Mortality of medical specialists–1938-1942. JAMA 137:1519, 1948

32. WARREN S: Longevity and causes of death from irradiation in physicians. JAMA 162:464, 1956

33. SELTSER R, SARTWELL PE: The influence of occupational exposure to radiation on the mortality of American radiologists and other medical specialists. Amer J Epidem 81:2, 1965

34. WARREN S, LOMBARD OM: New data on the effects of ionizing radiation on radiologists. Arch Environ Health 13: 415, 1966

35. COURT BROWN WM, DOLL R: Expectations of life and mortality from cancer among British radiologists. Brit Med J 2:181, 1958

36. PIFER JW, TOYOOKA ET, MURRAY RW, AMES WR, HEMPELMAN LH: Occupational poisoning of manufacture of luminous watch dials. J Nat Cancer Inst 31:1333, 1963

37. MARTLAND HS: Occupational poisoning in manufacture of luminous watch dials. General review of hazard caused by ingestion of luminous paint with special reference to the New Jersey cases. JAMA 92:466, 1929

38. MARTLAND HS: The occurrence of malignancy in radioactive persons. Amer J Cancer 15:2435, 1931

39. LOUTIT JF: Malignancy from radium. Brit J Cancer 24:195, 1970

40. EVANS RD, KEANE AT, KOLENKOW RJ, NEAL WR, SHANAHAN MM: Report Mass Inst Technol 195-5:1, 1968

41. ANDERSON RE, STEER A, KEY CR, TROUP GM, CIHAK RW, YAMAMOTO T, JORDAN SW: The delayed consequences of exposure to ionizing radiation - pathology studies at the Atomic Bomb Casualty Commission, Hiroshima and Nagasaki, 1945-1970. Hum Path 2:469, 1971

42. ANDERSON RE, KEY CR, YAMAMOTO T, THORSLUND T: ABCC Technical Report (in preparation).

43. JOHNSON MT, GREGORY PT, LAURA T, MILTON RC, LAND CE: Effects of ionizing radiation on the skin. ABCC Technical Report 20-69

44. HOLLINGSWORTH JW, ISHII G: Audiometric changes with age, Hiroshima: a statistical study. ABCC Technical Report 20-60

45. HOLLINGSWORTH JW, ISHII G, CONARD RA: Skin aging and hair graying. Hiroshima. ABCC Technical Report 7-60

46. CONARD RA, LOWREY A, EICHER M, THOMPSON K, SCOTT WA: Aging studies in a Marshallese population exposed to radioactive fall-out in 1954, Radiation and Aging (Kindop PJ, Sacher GA, eds), London, Taylor and Francis Ltd., 1966, p 345

47. STREHELER BL, MARK DD, MILDVAN AS, GEE MV: Rate and magnitude of age pigment accumulation in the human myocardium. J Geront 14:430, 1959

48. ANDERSON RE, YAMAMOTO T, ISHIDA K, THORSLUND T: Aging in Hiroshima and Nagasaki atomic bomb survivors. Accumulation of cardiac lipofuscin. J Amer Geriat Soc 19:193, 1971

49. NISHIMURA ET, MATSUOKA M, ISHII G, MADDEN SC: Effect of age upon extensibility of isolated aortic segments of Japanese. ABCC Technical Report 6-60

50. ANDERSON RE: Aging in Hiroshima atomic bomb survivors. Arch Path 79:1, 1965

51. ANDERSON RE, ISHIDA K, THORSLUND T: Aging in Hiroshima and Nagasaki atomic bomb survivors: soluble-insoluble collagen ratio. J Gerontol (submitted).

52. SIMONSEN M: Graft versus host reactions: Their natural history and applicability as tools of research. Progr Allerg 6:349, 1962

53. WALFORD RL: The Immunologic Theory of Aging. Baltimore, Williams & Wilkins, 1969. p 31

54. DOUGHTY WE, ANDERSON RE, YAMAMOTO T, THORSLUND T: Spleen index in atomic bomb survivors. Arch Path (in press)

55. ANDERSON RE, YAMAMOTO T, THORSLUND T: Unpublished results.

56. HOLLINGSWORTH JW, HAMILTON HB, BEEBE GW, YAMASAKI M: Blood group antibody levels in Hiroshima. Blood 17:462, 1961

57. ANDERSON RE: Aging in atomic bomb survivors. Hum Path 2:567, 1971

58. CASARETT GW: Similarities and contrast between radiation and time pathology. Advances Geront Res 1:109, 1964