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

ROBERT E. ANDERSON, M.D.

(ATOMIC BOMB CASUALTY COMMISSION)

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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

ROBERT E. ANDERSON, M.D.
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LONGEVITY IN RADIATED HUMAN POPULATIONS, WITH PARTICULAR REFERENCE TO THE ATOMIC BOMB SURVIVORS
放射線被曝人口集団，特に原爆被曝者における寿命

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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. The reduction of life span is proportional to dose, in either a curvilinear or linear fashion depending on species and strain, and is closely related to age at the time of exposure. With single exposures, the radiobiologic effectiveness (RBE) of the various...
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. 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. 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. In general, the exposed animals die at an earlier age from the same general disease entities that affect their nonirradiated contemporaries. 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はほぼ同じであり、中性子はガンマ線より 2 倍に作用するのである。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、マウスでは被曝総量 100 rad 当たり約 5% の寿命縮短が起こるようである。入射な実験結果によると、発端効果、すなわち、これ以下の寿命縮短が見られない線量的存在を否定してもよい。

この寿命縮短反応は、特定の原因に基づくことのできないものであり、放射線被曝後の臓器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。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。この年齢特殊死亡率の増加というものはに対しては、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放射線照射を受けた人々がいくつかある。その中でも最も広範囲にわたって調査が行われたものの、おそらく広島・長崎の原爆被曝者であろう。被曝後 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 業務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ではない。そこで、今回の報告は次の三つの目的をもってある；(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、放射線に被曝した他の人口集団との関連研究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曝され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十分でなかったりするため、今回の報告の観点からは評価できない。そのほかの放射線被曝人口集団は、単独的に対応する「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, postmortem 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
### TABLE 1 SUMMARY: AGING PARAMETERS IN IRRADIATED HUMAN POPULATIONS

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

表1 総括: 放射線被験者群の加齢に関するパラメーター

<table>
<thead>
<tr>
<th>調査対象集団</th>
<th>放射線の種類</th>
<th>照射部位</th>
<th>調査対象者数</th>
<th>寿命</th>
<th>悪性新生物の有病率</th>
</tr>
</thead>
<tbody>
<tr>
<td>日本人原爆被爆者</td>
<td>ガンマ線と</td>
<td>全身</td>
<td>120,000人**</td>
<td>短絡あり</td>
<td>増加あり（白血病および関連疾患: 甲状腺癌; 主要唾液腺癌; 肺癌; 乳腺癌; 小児期被爆者の各種頭頸部癌)</td>
</tr>
<tr>
<td></td>
<td>中性子</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rongelap 住民</td>
<td>ガンマ線と</td>
<td>全身, ただし、</td>
<td>334人*</td>
<td>資料はまだない</td>
<td>順で異常あり（甲状腺癌)</td>
</tr>
<tr>
<td></td>
<td>放射性核種</td>
<td>甲狀腺の被爆</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>検体内放射線</td>
<td>が特に著しい</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>胸腺癌、その他の頭部および</td>
<td>X線</td>
<td>顱蓋内</td>
<td>24,004人**</td>
<td>増加あり（甲状腺癌, 白血病, 喉頭癌)</td>
<td></td>
</tr>
<tr>
<td>頭部の良性病変のために放射線</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>療法を受けた小児</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>強直性脊椎炎のために放射線</td>
<td>X線</td>
<td>脊髄</td>
<td>13,352人</td>
<td>資料なし</td>
<td>増加あり（白血病、リンパ腫)</td>
</tr>
<tr>
<td>療法を受けた小児</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>米国の放射線收費</td>
<td>X線, ラジウム</td>
<td>部分的ない</td>
<td>425-82,441人*</td>
<td>短絡あり</td>
<td>増加あり（白血病、リンパ腫, 皮膚)</td>
</tr>
<tr>
<td>放射線收費をした成人</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ラジウム塗装塩素工および関連</td>
<td>ガンマ線と</td>
<td>骨格</td>
<td>750人†</td>
<td>短絡あり</td>
<td>増加あり（骨髄腫骨および結核の</td>
</tr>
<tr>
<td>作業従事者: ラジウム療法を</td>
<td>中性子</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>受けた成人</td>
<td>アルファ射線</td>
<td>とベーター</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>骨格 (226Ra, 228Ra)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>診断用骨髄計測中に放射線療法</td>
<td>X線</td>
<td>全身</td>
<td>7,346人</td>
<td>資料なし</td>
<td>増加の疑いあり（白血病)</td>
</tr>
<tr>
<td>受けた小児</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*Includes comparable group of nonexposed ("control") individuals.  対照する非被爆 ['control'] 群を含む.
†May be some overlap in reported persons.  詳告の重複が若干あるかもしれません。
<table>
<thead>
<tr>
<th>Mortality apart from Neoplasms</th>
<th>Disease Entities Other than Malignant Tumors</th>
<th>Physiologic Functions</th>
<th>Biochemical &amp; Related Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not uniformly reduced to date (see text)</td>
<td>Increased (microcephaly and mental retardation of persons exposed in utero; retarded skeletal development; degenerative changes involving skin, testes, and ocular lens; benign skin tumors)</td>
<td>Probably altered (see text)</td>
<td>Probably no change from control values (see text)</td>
</tr>
<tr>
<td>No information</td>
<td>Increased (thyroid nodules with hypothyroidism; retardation of growth and development; increased incidence of miscarriages and stillbirths)</td>
<td>No significant differences between exposed and non-exposed groups</td>
<td>No significant differences between exposed and non-exposed groups</td>
</tr>
<tr>
<td>No information</td>
<td>Increased (thyroid adenomas, benign breast tumors; osteochondromas; neurilemmomas)</td>
<td>No information</td>
<td>No information</td>
</tr>
<tr>
<td>No information</td>
<td>No information</td>
<td>No information</td>
<td>No information</td>
</tr>
<tr>
<td>Reduced</td>
<td>No information</td>
<td>No information</td>
<td>No information</td>
</tr>
<tr>
<td>Reduced</td>
<td>Increased (osteomyelitis; dental abnormalities; aplastic anemia, osteosclerosis)</td>
<td>No information</td>
<td>No information</td>
</tr>
<tr>
<td>No information</td>
<td>No information</td>
<td>No information</td>
<td>No information</td>
</tr>
</tbody>
</table>

| 生物的機能 | 生化学的および関連パラメーター |
| 生物的機能 | 生化学的および関連パラメーター |

<table>
<thead>
<tr>
<th>新生物以外の死亡率</th>
<th>悪性腫瘍以外の疾病</th>
<th>生物的機能</th>
<th>生化学的および関連パラメーター</th>
</tr>
</thead>
<tbody>
<tr>
<td>下落なし</td>
<td>発育障害：皮膚、骨および髄液の退行性変化 (本文参照)</td>
<td>赤色変化あり</td>
<td>おそらく対照値と差なし</td>
</tr>
<tr>
<td>資料なし</td>
<td>良性腫瘍</td>
<td>赤色変化あり</td>
<td>おそらく対照値と差なし</td>
</tr>
<tr>
<td>資料なし</td>
<td>增加あり（甲状腺機能および甲状腺機能障害；成長）</td>
<td>被曝群と非被曝群</td>
<td>被曝群と非被曝群との間に</td>
</tr>
<tr>
<td>資料なし</td>
<td>増加あり（甲状腺機能および甲状腺機能障害；成長）</td>
<td>との間に有意差なし</td>
<td>有意差なし</td>
</tr>
<tr>
<td>資料なし</td>
<td>増加あり（甲状腺機能および甲状腺機能障害；成長）</td>
<td>資料なし</td>
<td>資料なし</td>
</tr>
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<td>資料なし</td>
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<td>資料なし</td>
</tr>
<tr>
<td>低下あり</td>
<td>資料なし</td>
<td>資料なし</td>
<td>資料なし</td>
</tr>
<tr>
<td>低下あり</td>
<td>増加あり（骨髄炎；髄液異常；再生不良性貧血？；骨軟化症？）</td>
<td>資料なし</td>
<td>資料なし</td>
</tr>
<tr>
<td>資料なし</td>
<td>資料なし</td>
<td>資料なし</td>
<td>資料なし</td>
</tr>
</tbody>
</table>

5
The magnitude of possible exposure by an unsheltered person as a function of the distance from the hypocenter is shown in Figure 1.\textsuperscript{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 $^{239}$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.\textsuperscript{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.

正確な線量資料の最近の人手以前には、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、拡散性の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の主要試験対象である寿命調査集団は、元来、被爆距離区分別に決定されたものである。
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-
continue 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 non-specific 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 quantify 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.
Probably the most satisfactory information in this regard will emanate 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 evaluation27 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, Ciocco28 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、日本の戦の制度を通じて各被爆生存者についての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、一般に出土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。戸籍における年齢設定の記載は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率が遠距離被爆者よりも高いことを認めた。これは1950-52年の期間において特に著しかった（男性では期待値よりもほとんど50％多く、女性では50％程度であった）。増加していると認めたのは全死因、全病死、白血病、白血病を除くすべての悪性新生物、ならびに核爆破による死亡であり、この最後の結果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層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、期間の生存者よりも有意に高かった。その後行われた評価27では、1950-54年に作用していた被爆素を解明できなかったが、この期間にみられた死亡率の增加は「後発」急性効果のためである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衰して1950年代の半ばには基準水準に達したのであった。

1955年にCiocco28は、前述の調査の延長として、寿命調査対象集団中、病状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的に近づいていた原爆的被爆群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の差が認められ、その差は長崎よりも広島でおろしい。これは寿命調査対象集団中の女性において特に著であり、2％の水準で有意であった。

最近の調査27では、1950-70年の死者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価
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). 

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 Lombard34 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.
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
Jablons et al.29).

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
Jablons et al.29).

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

<table>
<thead>
<tr>
<th>Source of data</th>
<th>Dublin and Spiegelman 29-31</th>
<th>Warren 34</th>
<th>Seltser and Sartwell 23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period of observation</td>
<td>1938-1942</td>
<td>1930-1954</td>
<td>1935-1958</td>
</tr>
<tr>
<td>Comparison groups</td>
<td>Other specialists</td>
<td>Other specialists; all physicians; males over 25 years</td>
<td>Internists; ophthalmologists-otolaryngologists</td>
</tr>
<tr>
<td>Sample size</td>
<td>37,010 (2,020 deaths)</td>
<td>82,441 deaths</td>
<td>16,808 (3,421 deaths)</td>
</tr>
<tr>
<td>Estimated reduction of life span</td>
<td>1-3 years</td>
<td>5.2 years</td>
<td>4.8 years (1935-1944, less later)</td>
</tr>
<tr>
<td>Remarks</td>
<td>Mortality among dermatologists and persons interested in chest disease also elevated</td>
<td>Other specialists exposed to radiation also showed reduced life span</td>
<td>Variety of disease processes implicated in reduced life span</td>
</tr>
</tbody>
</table>

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 comparison.
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. 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...
dial painters in New Jersey has been recognized since the early reports of Martland. Only in the past several years, however, and primarily via the reports of Loutit, 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. This effect, summarized in Figure 8, persists even when cases with malignant tumors of the bone and adjacent epithelium (e.g., nasal sinuses, mastoid) are excluded.

Martland's initial reports, radium (およびメソトリウム) and bone tumors, but other cancers, have been reported more recently. However, the association of bone tumors with exposure to radium is well established. Loutit's observations, that mortality rates are increased in persons with estimated body burdens of 10 μCi (および1 μCi), supported by further studies, have been confirmed. 

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

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. Perhaps of equal concern are the increases in other solid tumors, such as lung cancer. The increased incidence of these tumors has been attributed to the exposure to radon and other radioactive gases. 

良性和悪性新生物

母体の懸念を除く他の放射線障害の例で、皮膚癌の増加が確認されている。これらの集団では、時期を問わず、母体の照射が行われた場合でも、皮膚癌の増加が確認されている。母体の照射では、時期を問わず、皮膚癌の増加が確認されている。母体の照射では、時期を問わず、皮膚癌の増加が確認されている。
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.\textsuperscript{92} 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\textsuperscript{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

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure9.png}
\caption{Age-specific cumulative mortality for individuals with malignant tumors by exposure category.}
\end{figure}

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曝者に比べて近距離被曝者において、その平均発病年齢が早いということがあつた。\textsuperscript{92}更にこのことから推測されるように、悪性新生物を有する重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塗装料工は寿命の短縮があり、少なくともその一部は既知の虚腫果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、これらは中には原爆被曝者がいるだけであるが、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、全死亡原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\textsuperscript{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表現されるであろうが、最も顕著な特異的な影響は発ガンである」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群に対する相対的検査率
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).

图10 本例における良性および悪性腫瘍および外因死を除く全死亡の年齢と被曝時の放射線線量の関係を示す。1950-1970年当時の結果を示し、点線は1を示す (Jablonらによる)。

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

図11 200rad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);
### Table 3: Mortality from All Causes Excluding Benign and Malignant Tumors and Deaths from Trauma, 1950-1970, as a Function of T65 Dose Estimate*

<table>
<thead>
<tr>
<th>T65 Dose Estimate (rad)</th>
<th>Period of Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>0.873</td>
</tr>
<tr>
<td>10-49</td>
<td>0.800 (0.06)</td>
</tr>
<tr>
<td>50-99</td>
<td>0.697 (0.01)</td>
</tr>
<tr>
<td>100-199</td>
<td>1.119 (0.01)</td>
</tr>
<tr>
<td>≥200</td>
<td>0.939 (0.30)</td>
</tr>
</tbody>
</table>

*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.

(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はどの差は有意であり、期間別にみれば有意ではない。

(2) 原爆発時年齢別にみると、年齢10-19歳の被爆者は、その他の年齢群と比べ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（標本値の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-expectected ratios are higher in those exposed to $\geq 200$ rad versus those exposed to 0 to 9 rad.

**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, proximaly 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.\(^{24}\)

**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 Marshalllese 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 elastomas among proximally exposed survivors of Hiroshima and Nagasaki in comparison with distally located persons.

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病気項目を表1に示した。全身照射を受けた子育にみられる成長・発育の遅延は、実験的状況下における同様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、遠距離線量被曝者では遠距離被曝者に比べて有病率が増加しているばかりでなく、その発生の速度もみられる。\(^{14}\)

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を指してすでに言及した。この分野における意味ある資料としては、例えば日本ならびに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大脳機能の評価を行った：皮膚弾性、収縮期血圧、肺活量、筋力、視力、聴力ならびに血清コレステロール値であった。この統合判定の結果では、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、被曝者と非被曝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、聴力障害、皮膚退化症、白髪症、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、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・長崎の近距離被曝者、遠距離被曝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い、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. 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 emanated 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. 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.

(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 post-mortem examination from exposed and nonexposed persons. No significant difference was noted between the two groups with respect to this age-dependent parameter.

(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.

(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。これらの研究者が指摘しているように、調査対象者が少なくないこと、言語上の障壁があること、高齢者の一部が年齢が不確定であること、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思われ、その検証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) 心筋リポフコースチン沈着。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。1近距離被曝者と
非被曝者を注意深く組み合わせて比較した結果によれば、リポフコースチン沈着率、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。

(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、剖検時に被曝者および非被曝者の大動脈
の段階的である一部を摘出してその機械的弾性の評価が
行われた。この加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。

(3) ベクサミン対コラーゲン比。結合組織におけるコラゲ
ンのムコ多糖類基質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曝者と原爆時
に市内にいなかった者との間に有意な差が認められた。

(4) 可溶性対不溶性コラーゲン比。酸（または熱）処理におけ
るコラーゲンの可溶性および不溶性分画の比率は、聴覚動
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対象の近距離被曝者および原爆時に
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 matched 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.\(^{56}\)

(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 \(-0.72.\)\(^{57}\) 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.\(^{58}\)

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,\(^{59}\) 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) 肝臓指数。肝臓重量の総重量に対する比率は、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) 好ビリオン性脾細胞。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ビリオン性細胞の相対的数骨で、有意な放射線に被爆した者とそうでない者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、両群間有意の差はなかった。\(^{55}\)

(7) 巨大肝細胞核。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。\(^{56}\)

(8) 同種抗体。ヒトにおける自然発生のAおよびB抗原体価を、若年期に高点に達し、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。\(^{57}\) 次の被爆区分群に属している1042人を検査した結果、各群間差は認められなかった。なお、その被爆区分群ということは、被災地から0～1999mで被爆して急性放射線障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、もと被爆者（3000～3499m）であった者、ならびに崩壊時に市内にいなかった者である。\(^{58}\)

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。現在のところ、特に実行されたパラメター8項目の中でもわずかに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。別報で詳細に論じているように、これらの測定と被爆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、報告集団が人口統計学的に不均一であること、被爆の程度や被爆の程度など、被爆者間の被爆状態が著しく異なること、さらに使用したパラメーターの精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. 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 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.
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. 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.

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 effect.

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 people 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.

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 ABCD 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をみると限りでは、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速された老化がまだ現れていない。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腫瘍発生との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受傷者には過去20年間に白血病以外のすべての悪性腫瘍の発症率増加があり、最近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。

要するに、腫瘍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他の動物とは異なっているようである。この差があるので、ABCD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を控えることが賢明であろう。
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