Thyroid Injury and Effects on Growth and Development in Marshallese Children Accidentally Exposed to Radioactive Fallout

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Wat Sutow was involved for 25 years in the medical studies of the people of the Marshall Islands who were exposed to radioactive fallout. He was a dedicated member of the examination teams, participating on numerous occasions in carrying out pediatric and growth and development studies of the exposed Marshallese children. The results of his studies have added a great deal to our knowledge of the effects of radiation on children.

Wat won the respect and love of the Marshallese people with his careful, gentle examinations and treatment of the children. The many physicians and technicians who have worked with him over the years developed great respect and affection for him, and his participation in the program will be sorely missed.

To me, Wat was a close friend and advisor, and his passing leaves a void that will be hard to fill.—**RAC**

This report concerns the late effects of fallout exposure on the Marshallese people, particularly the effects on the thyroid gland and growth and development of children of Rongelap Atoll. A portion of the material and data reported here is excerpted from the Brookhaven National Laboratory report.[1]

During the weapons testing program in the Marshall Islands in 1954, an unfortunate accident occurred. Following experimental detonation of a large thermonuclear device, an unpredicted shift in winds caused deposition of radioactive fallout on 250 Marshallese, 23 American servicemen, and 23 Japanese fishermen aboard their fishing vessel, the "Lucky Dragon." Details of the accident and exposure data can be found in Brookhaven National Laboratory reports.[1,2]

The inhabitants of Rongelap Atoll were exposed to the greatest amount of fallout, those on Ailingnae Atoll to less, and those on Utirik Atoll to the least. The exposure included penetrating gamma radiation (whole-body exposure), deposits of radioactive fallout on the body (skin exposure), and internal absorption of radionuclides by inhalation and ingestion of contaminated food and water. The most serious internal exposure was from radioiodines, which produced significant doses to the thyroid gland. Table 1 lists the Marshallese populations involved, with estimated whole-body gamma doses and thyroid doses. It should be emphasized that the thyroid doses are rough estimates, and current reevaluation at Brookhaven National Laboratory indicates they are probably too low.

Early Effects

Early effects of exposure (transient nausea and vomiting, hematologic depression, development of "beta burns" of the skin) have been reviewed elsewhere and will not be presented here. No early deaths were attributed to exposure. The effects were more pronounced in the children, particularly those exposed on Rongelap. It is noteworthy also that no early

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Table 1. Estimated Radiation Doses in Exposed Populations

Atoll	No. Affected*	Estimated Whole-Body Gamma Dose (rem)	Estimated Thyroid Dose (rem) by Age at Exposure <10 yr	10–18 yr	>18 yr
Rongelap	67	175	810–1,800	334–810	335
Ailingnae	19	69	275–450	190	135
Utirik	164	14	60–95	30–60	30

*Includes in utero exposures (three on Rongelap, one on Ailingnae, and six on Utirik).

Table 2. Summary of Thyroid Nodularity in the Marshallese, 1981

Group	Age at Exposure	No.*	Estimated Dose	Total Nodules No. (%)	Carcinomat No. (%)
Rongelap	<10	22	810–1,800	17 (77.3)	1 (4.5)
	>10	45	335–810	6 (13.3)	3 (6.7)
Ailingnae	<10	7	275–450	2 (28.6)	0
	>10	12	135–190	4 (33.3)	0
Utirik	<10	64	60–95	5 (4.7)	1 (1.6)
	>10	100	30–60	12 (12.0)	2 (2.0)
Unexposed	<10	229		6 (2.6)	2 (0.9)
	>10	371		29 (7.8)	3 (0.8)

*Includes in utero exposures (three on Rongelap, one on Ailingnae, and six on Utirik).
†Carcinoma estimates may be low because all unoperated nodules were considered benign for these calculations.

effects of the internal absorption of radioiodines or other nuclides were noted. Indeed, nearly a decade passed before the effects of thyroid exposure could be documented.

Late Effects

Until about nine years after exposure—the time thyroid abnormalities were detected—the health status of the exposed people did not appear to be significantly different from that of unexposed people, with a few possible exceptions.[1] Examinations of the newborn did not reveal any detectable abnormalities in the children of exposed parents which might have been related to radiation exposure.

In 1972, a Rongelap man who had been exposed at 1 year of age died of acute myelogenous leukemia.[4] Relation to radiation exposure seemed probable.

Thyroid Abnormalities

The most widespread late effect in the Marshallese has been the development of thyroid abnormalities attributed to thyroid injury from exposure to radioiodines and gamma radiation at the time of the fallout. The effects of thyroid injury on growth and development of Rongelap children are presented below. The development of thyroid nodularities, benign and malignant, and of hypofunction are only briefly summarized here. Details can be found elsewhere.[1-3,5]

At nine years postexposure, when it was becoming apparent that growth retardation was occurring in some of the exposed Rongelap children, nodules began appearing in the thyroid glands of people who had been exposed in Rongelap, particularly the children. Varying degrees of thyroid hypofunction developed in some of the children, particularly in two boys, exposed at 1 year of age, who exhibited the most stunting of growth. They showed clinical evidence of myxedema with atrophy of the thyroid gland, puffy faces, dry skin, sluggish reflexes, and bony dysgenesis of the head of the humerus and femur. Thyroid nodules developed somewhat later in the groups exposed to lower doses of radiation on Ailingnae and Utirik.

The greatest incidence of thyroid nodularity has been noted in the high-dose Rongelap group, particularly in the children exposed at less than 10 years of age. Lower incidence was noted in the Ailingnae group, and the least incidence in the lower-dose Utirik group. Noteworthy has been the recent development of thyroid nodules in two of three children exposed in utero on Rongelap (Table 2).

Almost all the patients, including those who were not exposed, have had thyroid surgery in US hospitals. A wide spectrum of lesions has been found. Among the exposed patients, the ratio of benign lesions to carcinoma appears to be greater in children than in adults. The data are too few for definite conclusions, but they lead one to speculate that the higher thyroid doses in the children (due to the smaller sizes of their thyroid glands) could have produced an "overkill" effect.

As noted, a number of children who developed thyroid nodules showed evidence of hypofunction of the thyroid prior to surgery, primarily on the basis of elevation of serum thyroid stimulating hormone (TSH). More recently, six exposed adults without clinical evidence of thyroid lesions also have shown biochemical evidence of hypofunction.[5]

Preventive treatment with thyroid hormone was instituted in the exposed Rongelap people in 1965 and in the Ailingnae people in 1969.

Growth and Development Studies of Rongelap Children

The various anthropometric data on the Rongelap children have been tabulated periodically in annual reports,[1-3] and ongoing analyses have also been published in the literature.[6-9] Beginning several years after exposure it was noted that, for boys, the statural growth curve for the exposed group lagged behind the curve for the unexposed group. This lag appeared to be due primarily to the slowed growth in the group of boys exposed at <5 years of age. It was first thought that the growth retardation might be a direct radiation effect,[5] but, as noted, findings established radiogenic hypofunction of the thyroid gland as its cause.

Assessment of the pattern of growth and development of the individuals who were children (≤18 years old) on March 1, 1954, has been a consistent component of the pediatric examinations of the Rongelap people. Data interpretation has been complicated by radiation injury to the thyroid gland, partial or total thyroidectomies in the children who developed thyroid abnormalities, and administration of TSH suppressive doses of thyroid hormone to the exposed Rongelap population since September 1965 (when the youngest exposed child was 11 years old).

Analyses presented here are limited to the Rongelap Atoll population.

Methods

In 1957, the population repatriated to Rongelap included (in addition to the exposed returnees) a sizable number of children who had not been exposed to fallout radiation. Some were Rongelap natives who had been away at the time of fallout, and others were relatives of residents. Since these children were of the same stock (blood relations) and would live postreturn under the same environmental conditions as did the exposed population, they were selected as unexposed controls. During 1957, 1958, and 1959, the control population was carefully characterized. Examinations conducted on these children were the same as those conducted on the exposed population.

From the very first examination, growth data have been recorded. During the first three years, the measurements consisted of weight, standing height, sitting height, length of upper extremity, arm span, biacromial width, intercristal width, head circumference, abdominal circumference, and left calf circumference. In 1958, the battery of body measurements was standardized to include weight, stature, sitting height, head circumference, head width, head length, chest circumference, chest width, chest depth, buttock circumference, left calf circumference, biacromial diameter, and bicristal diameter. Standardized techniques[10-12] were used. The status of secondary sex characteristics was evaluated by inspection with the method described by Greulich et al,[13,14] Reynolds and Wines[15,16] and Shuttleworth.[17] History of menarche in girls, penile and testicular development in boys, hair distribution, and breast development were recorded during these examinations.

In 1958, apparent discrepancies regarding birth dates were noted in the charts of many children. The absence of recorded birth information in the Marshall Islands seriously complicated the verification of ages. Detailed genealogic and biologic histories were compiled for the Rongelap population in 1958–1960. The reconstruction of birth chronologies was based on intensive evaluation of frequently contradictory information derived from the following sources: (1) dates of birth reported by parents; (2) dates of birth recorded occasionally in ledgers kept by the village magistrate; (3) limited number of birth certificates (not always accurate) on file at the courthouse in Majuro; (4) birth order of children within each family unit; (5) ranking of childhood population in terms of age by parents; and (6) ranking of childhood population in terms of age by the children (particularly age peers), by relatives, and by friends living in the village.

A table of most probable birth dates was derived for the Rongelap childhood population. Biologic compatibility of the birth dates within each family was carefully checked, and the compatibility of physiologic status with age was also determined for each child. The presumptive dates of birth have been used in the calculations of chronologic ages for analyses of growth and development.

Roentgenographic documentation of osseous maturation (x-rays of the left hand and wrist) was initiated in the exposed children in 1957. A major effort was made in 1958 to examine the skeletal maturation of exposed and unexposed children. Unfortunately, these valuable base-line films were lost at sea during transport. This created a gap of almost three years when no radiographs were available on a number of children in the spurt phase of growth. Thereafter, roentgenographic studies of the left hand and wrist were included at irregular intervals. These were particularly difficult under field conditions and presented many technical problems, but the minimal number of roentgenograms eventually obtained permitted a reasonable assessment of the longitudinal skeletal development of each child through the chronologic age of 16 or 17 years in the girls and 18 in the boys.

Skeletal age determinations were made by inspection with the techniques and standards published by Greulich and Pyle.[14] Early analyses of the skeletal age data were included in the reports of previous surveys.[3] Comparisons between the exposed and unexposed children were made primarily in the group who were <10 years old on March 1, 1954. This group was further subdivided into two categories: those <5 years old on March 1, 1954, and those aged 5 to 10.

The data on children >10 years old on March 1, 1954, could not be analyzed in detail. The number of children (particularly in the exposed group) in each age category was extremely small, and by the time satisfactory roentgenograms were obtained for most of them (1961 to 1963), even the youngest members of this group were already approaching skeletal maturity.

Statural Growth

Detailed data are given elsewhere.[1] Three age groupings were used: 0 to 5, 5 to 10, and 10 to 18 years of age as of March 1, 1954. The two younger groups were combined (age 0 to 10) for some of the analyses. The numbers of exposed subjects in the 10- to 18-year-old age groups were extremely small.

Figure 1 shows that there was a consistent retardation of

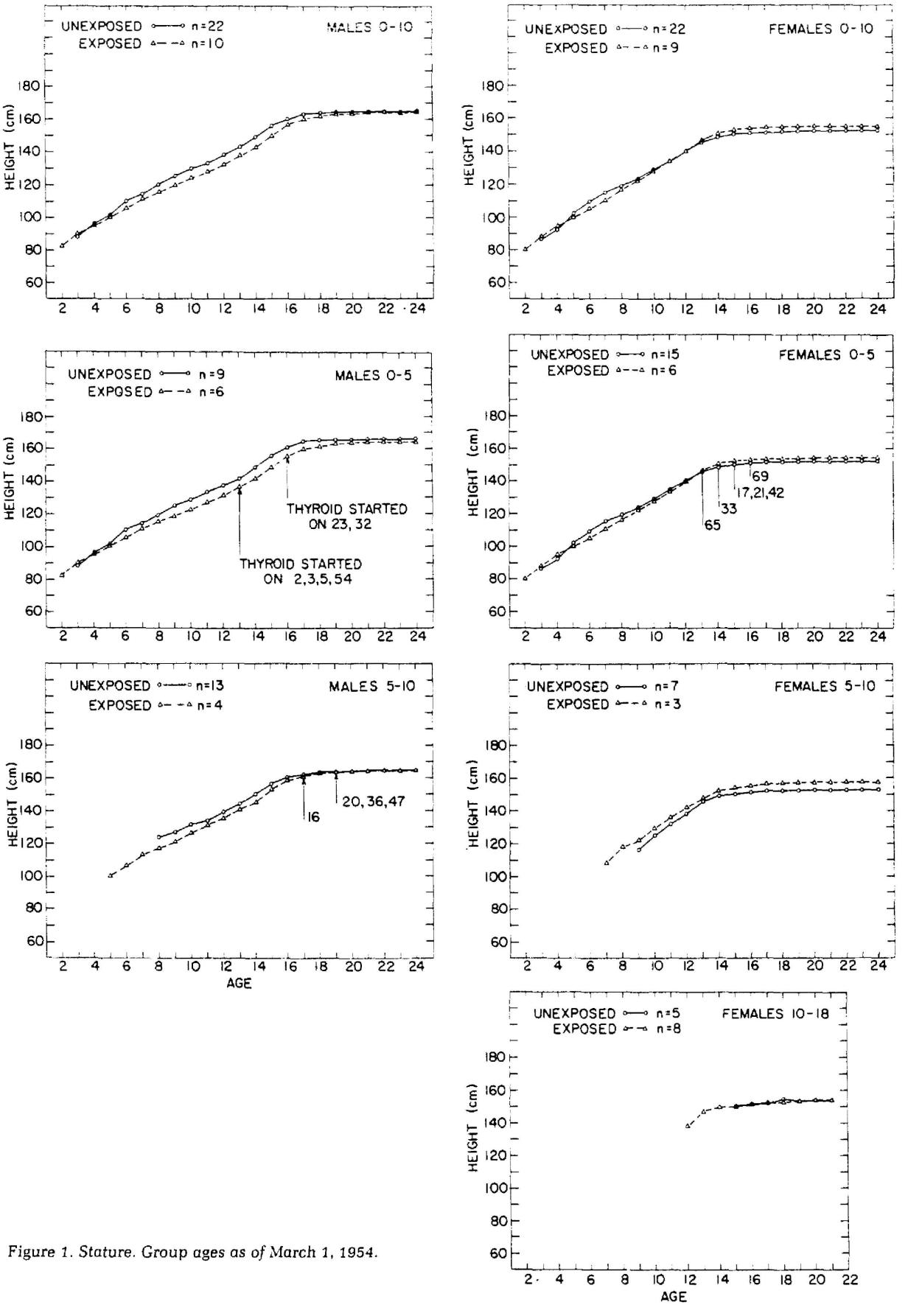

Figure 1. Stature. Group ages as of March 1, 1954.

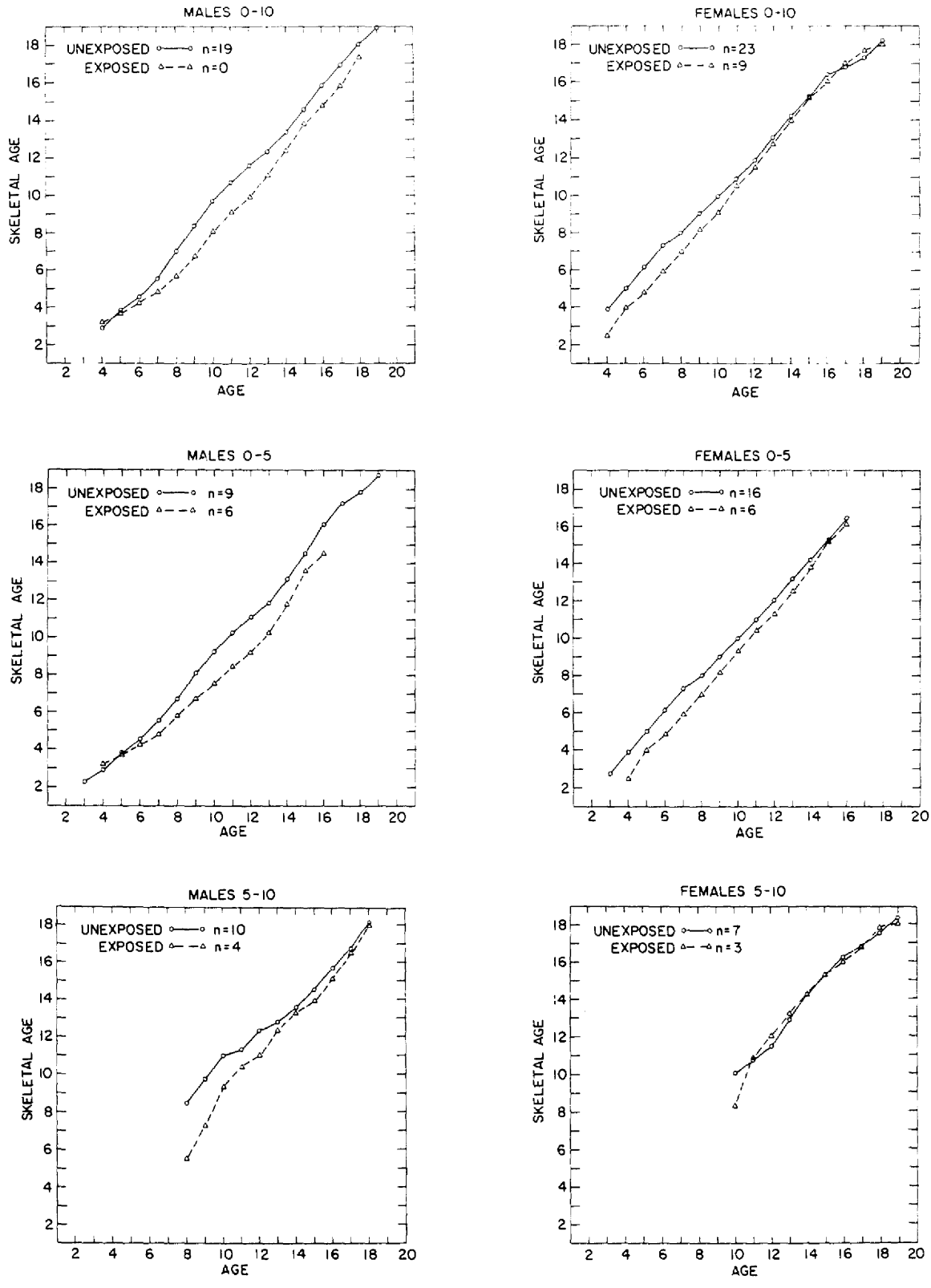

Figure 2. Skeletal age. Group ages as of March 1, 1954.

stature among the boys exposed at less than 10 years of age. The differences are statistically significant only between ages 9 and 16, apparently because thyroid medication was administered to the exposed people on Rongelap after 1963. Figure 1 also shows that statural retardation occurred in both subgroups (age 0 to 5 and 5 to 10 at exposure) but was more marked in the younger subgroup. Statural growth in the few boys exposed at greater than 10 years of age showed no differences from that in unexposed boys.

Among the girls, the statural growth curve (Figure 1) for those exposed to fallout at age 0 to 10 was significantly retarded at chronologic ages of 6 to 7 years, compared with that for the unexposed girls. Figure 1 also shows that the statural retardation occurred in girls exposed at less than 5 years of age but not in those exposed at age 5 to 10, and disappeared by about age 9. The curves for girls exposed at age 10 to 18 are quite similar to those for unexposed girls. These findings suggest that retardation in stature among the exposed girls occurred earlier and was less prominent and of shorter duration than that among the exposed boys.

Osseous Maturation

Osseous maturation among exposed boys was significantly retarded compared with that in unexposed age peers (Figure 2). This retardation was particularly prominent when the boys were 14, 15, and 16 years of age, and as can be seen in Figure 2, retardation occurred in both age groups (those age <5 and age 5 to 10 in 1954).

Figure 2 also shows a similar comparison among girls. For the entire group exposed at less than 10 years of age, skeletal maturation lagged significantly behind that in the unexposed girls until about age 10, and thereafter the gap progressively narrowed. Figure 2 suggests that this retardation in osseous maturation among exposed girls occurred primarily among those exposed at less than 5 years of age and to a very limited degree in those exposed at age 5 to 10.

Comments

Growth studies on young people exposed to radiation from atomic bombs in Hiroshima and Nagasaki showed that their adult heights were significantly lower than those of the controls.[16] Similar analyses were carried out on statural data from inhabitants of Rongelap and Ailingnae Atolls who were exposed as children to fallout radiation. The presumptive adult (final) stature is either the plateau value when several measurements remained the same, or the latest measurement (made when the subject was ≥20 years of age) if the latest prior measurement had continued to show increase.

It is generally assumed that adult height is attained when the skeletal age is 17 to 18 years in girls and 18 to 19 in boys,[13,15,19] but actual measurements on the Marshallese population showed that many subjects continued to increase in stature with advancing chronologic age, even after age 30, although the late increments were almost always very small. After the Marshallese reached 16 years of age, absences from the island at the time of survey became more frequent; therefore, the time when adult stature was actually attained is uncertain for many individuals.

Statistical analyses of the data on adult (final) stature of the Rongelap inhabitants who were in the pediatric age group on March 1, 1954, gave the following results:

- In the unexposed group, for both boys and girls, there was no significant difference in mean adult stature between those born after 1944 (≤10 years old on March 1, 1954) and those born before 1945 (>10 years old on March 1, 1954).
- In the exposed group, for both boys and girls, there was no significant difference in mean adult stature between those born after 1944 and those born before 1945.
- For both boys and girls, there was no significant difference in mean adult stature between those who were exposed to fallout radiation on Rongelap and Ailingnae and those who were not.

Since osseous maturation is dependent on normal thyroid function, it is reasonable to assume that its retardation in exposed children was due to radiation damage to the thyroid glands. The marked retardation of skeletal maturation followed by dramatic improvement after the administration of thyroid hormone has been documented in the children who were clinically hypothyroid.[3] The catch-up phenomenon in osseous maturation can reasonably be attributed to the administration of thyroid hormone to the exposed populations, many of whom were subclinically hypothyroid.

Acknowledgments

The submitted manuscript has been written under contract DE-AC02-76CH00016 with the US Department of Energy. Accordingly, the US Government retains a nonexclusive, royalty-free license to publish or reproduce the published form of this contribution, or allow others to do so, for US Government purposes.

The authors wish to thank the many physicians and technicians, from both the United States and the Trust Territory of the Pacific Islands, for their assistance, and particularly the Marshallese people, for their cooperation in the performance of the examinations.

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Dr. Sutow's Contribution to Japanese Pediatrics in the Early Days of the Atomic Bomb Casualty Commission

—Personal Note From Atsuyoshi Takao, MD, The Heart Institute, Tokyo Women's Medical College

During the time of confusion and chaos that followed the Second World War, the practice of medical pediatrics in Japan had lagged far behind in many respects, as compared with that in the United States. We were introduced to Dr. Wataru W. Sutow, who came to Japan as a medical investigator and officer to administer the activities of the Atomic Bomb Casualty Commission (ABCC). We Japanese physicians were to help study the effect of atomic bomb radiation on the growth and development of exposed children and to compare the results with the norms for a control group of children not exposed to radiation.

The first thing Dr. Sutow did was to recruit young Japanese physicians seeking new knowledge in pediatrics from various medical schools all over Japan. This recruitment policy removed the interscholastic fence. We gathered to work and study with US physicians at ABCC headquarters in Hiroshima and Nagasaki. The spirit of international, interscholastic, and interindividual cooperation and mutual education was high. The interdisciplinary approach, now considered standard procedure, was also learned by the Japanese members.

The introduction to the American approach to pediatric medicine, represented by Nelson's or Holts' textbook, was exciting. Educational programs, seminars, and conferences conducted at the ABCC as well as the American routine of working opened a new world for young Japanese members. Every moment was precious and we learned with gusto, as dried fields absorb long-needed water. The nurturer was Dr. Sutow. We admired him as a truly well-rounded physician who knew everything in pediatrics. We were overwhelmed with his knowledge and ability, qualities that were lacking in Japanese professors. Of all his contributions at the ABCC, I personally believe the most important was that he taught that the principles of growth and development were the essence of pediatrics, the foundation on which pediatric medicine was based.

Dr. Sutow won the respect and admiration not only of many Japanese disciples but also of many friends in various Japanese medical circles through his teaching, training, and collaboration. He built a bridge across the Pacific by sharing his knowledge and with his favorite pastime, the collection of seashells of the Pacific coasts.

From the land he nurtured and learned to love now have sprung many Japanese physicians and scientists, actively participating in works for the welfare of all human beings. Dr. Sutow is beloved and praised for his unforgettable great contribution. He will continue to live in the memories of those who learned with him, not only for his contributions to the children of Japan, including his great works in pediatric oncology, but also for his philanthropic works in other areas of benefit to the Japanese people.