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THYROID HYPOFUNCTION APPEARING AS A DELAYED MANIFESTATION OF ACCIDENTAL EXPOSURE TO RADIOACTIVE FALL-OUT IN A MARSHALLESE POPULATION*

R.M. - Fallout - R.M. - long Term effect

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Abstract

THYROID HYPOFUNCTION APPEARING AS A DELAYED MANIFESTATION OF ACCIDENTAL EXPOSURE TO RADIOACTIVE FALL-OUT IN A MARSHALLESE POPULATION.

The increased incidence of thyroid nodularity and carcinoma appearing as a late effect after exposure of the human thyroid to ionizing radiation is well recognized. Despite the high prevalence of thyroid nodularity in Marshallese inadvertently exposed to fall-out in 1954,

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only two subjects, both about one year of age at exposure, have been found to have primary hypothyroidism. The recent availability of sophisticated immunoassay techniques for thyroxine (T_4) and thyrotropin (TSH) has allowed more thorough thyroid evaluation of the exposed population who do not have known thyroid abnormalities (43 Rongelap people). Initially, prophylactic T_4 was discontinued for two months in a sample group of exposed subjects and 10 U of bovine TSH were given intramuscularly. Plasma T_4 was measured before and 24 hours after TSH. The mean increment in T_4 was 2.4 ± 1.2 μg/dl (mean ± SD) in the exposed group, significantly less than the value of 4.2 ± 1.3 μg/dl in controls. This suggested a decrease in thyroid reserve in exposed subjects. Accordingly, prophylactic T_4 treatment was discontinued for two months, and basal plasma T_4 and TSH, as well as the increment in TSH after Thyrotropin Releasing Hormone (TRH) was measured. The upper limit of the normal basal plasma TSH was 3 μU/ml and of the TRH-induced TSH response was 22 μU/ml in control Marshallese subjects. Four of 43 Rongelapese had abnormally high basal TSH and TRH-induced TSH release on two such tests as opposed to only two of 214 controls. Plasma T_4 concentrations were low, or low-normal in these individuals. These results indicate the presence of early thyroid dysfunction. Several other subjects have shown at least one abnormal finding but have not had the required number of tests to meet the established criteria. In three quarters of these subjects the estimated thyroid exposure dose was < 400 rads. Hypothyroidism has been previously noted after therapeutic doses of ^{131}I for hyperthyroidism, but not in individuals exposed to the relatively low levels of thyroidal radiation (< 400 rads) estimated for these individuals.

BACKGROUND

This report concerns late radiation effects on the thyroid in a population in the Marshall Islands inadvertently exposed to fall-out. The accident occurred on 1 March 1954, during the United States atomic testing programme when an unexpected shift of winds, following detonation of a thermonuclear device at Bikini, caused radioactive fall out to be deposited on several inhabited islands to the east. Evacuation of exposed persons was accomplished by two days. The following were estimated whole body gamma doses in the Marshallese on three atolls. Rongelap (64 people), 175 rads; Ailingnae (18 people), 69 rads; and Utirik (158 people), 14 rads. (There were also 28 American servicemen on the island of Rongerik who received about the same exposure as the Ailingnae group.)

Acute effects of gamma exposure were noted in the Rongelap and Ailingnae groups, but not in the Utirik group. These consisted of early, transient anorexia, nausea and vomiting in a number of people followed by depression of white blood cells and platelets to about half normal levels. Fortunately the haematological depression was not great enough to result in detectable clinical signs of infection or bleeding. No specific therapy was necessary and no deaths occurred, and blood cells returned to near normal levels by one year. In addition, in the Rongelap and Ailingnae groups, beginning about two weeks post exposure, radiation burns ('beta' burns) and spotty epilation of the head developed where fall out material had been deposited on the skin. These burns were largely

superficial and healed within several weeks with normal regrowth of hair. Slight scarring remained in some cases but no development of skin malignancy has been noted in subsequent years. Another source of exposure in all the island groups came from internal absorption of radionuclides from inhalation and ingestion of contaminated food and water. Radiochemical urinalyses run during the first few weeks showed the following estimated body burdens (μCi) of the principal radionuclides in the Rongelap population at one day post exposure: ^{89}Sr 1.6 2.2; ^{140}Ba 0.34 2.7; rare earth group 0 1.2; ^{131}I (in thyroid gland) 6.4 11.2; ^{103}Ru 0 0.013; ^{45}Ca 0 0.019; and fissile material 0 0.016 (μg). No acute symptoms were noted from this internal absorption of radionuclides, and by six months urinalyses indicated they were virtually completely eliminated. Nevertheless, the early exposure to radioiodines resulted in serious injury to the thyroid glands with late effects to be described below. The thyroid dose was estimated to be considerably higher in the children because of the smaller size of the thyroid glands. In the Rongelap people the thyroid dose from gamma radiation and radioiodines (principally ^{131}I, ^{132}I, ^{133}I and ^{135}I) was estimated to be about 335 rads in the adults whereas in small children the doses ranged up to 700–1400 rads. The thyroid doses in the Ailingnae and Utirik groups were extrapolated from the Rongelap estimates assuming the ratio of whole body gamma and iodine doses were the same as in the Rongelap people.

Following the initial studies, annual examinations and, more recently, quarterly examinations of the exposed people, as well as an unexposed control Marshallese population, have been carried out, and results of these examinations have been published [1–4].

In the first ten years after the accident few findings were noted that could be related to radiation exposure. An increase in miscarriages and stillbirths in the exposed Rongelap women was thought to be possibly related to exposure.

During the second decade, however, serious late effects developed related primarily to the thyroid gland. In addition a Rongelap man who had been exposed at one year of age, died of acute myelogenous leukaemia which was likely related to radiation exposure [3].

Before thyroid abnormalities became apparent, it was noted that about five children exposed at less than five years of age showed some degree of growth retardation [4]. In two boys growth retardation was marked and frank myxoedema developed. Thyroid hypofunction related to thyroid injury later became apparent with more sophisticated techniques for determining thyroxine levels. It was not detected early in the children by PBI determinations because of masking of true thyroxine levels by unusually high levels of iodoprotein, later found to be characteristic of the Marshallese people [5].

Nodules of the thyroid gland began to appear in Rongelap children and to a lesser extent in adults beginning about nine years post exposure. These nodules have continued to appear over the subsequent 15 years, and virtually all of these

TABLE I. THYROID LESIONS IN MARSHALLESE, SEPTEMBER 1977

Group	Age at exposure	Est. thyroid dose[a] (rads)	% Subjects[b] with thyroid lesions	No. subjects with surgery	% Subjects[b] with malignant tumor
Rongelap exposed	<10	810–1150	89.5 (17/19)	15	5.3 (1/19)
(175 rads)	10–18[c]	335–810	25.0 (3/12)	2	8.3 (1/12)
	>18	335	12.1 (4/33)[d]	4	6.1 (2/33)
	All	556[e]	37.5 (24/64)	21	6.3 (4/64)
Ailinginae exposed	<10	275–450	33.3 (2/6)	1[f]	
(69 rads)	10–18	190	0.0 (0/1)	0	
	>18	135	36.4 (4/11)	3	
	All	217[e]	33.3 (6/18)	4	
In utero exposed		175+[g]	33.3 (1/3)	1	
		69+[g]	0.0 (0/1)	0	
Rong. + All	All	135–153	36.0 (31/86)	26	4.7 (4/86)
Utirik exposed	<10	60–95	1.7 (1/58)	1	1.7 (1/58)
(14 rads)	10–18	27–60	14.3 (3/21)	2	4.8 (1/21)
	>18	30	7.6 (6/79)	5	1.3 (1/79)
	All	50[e]	6.3 (10/158)	8	1.9 (3/158)
Rong. + All + Utirik	All	30–1150	16.8 (41/244)	34	2.9 (7/244)

[a] Dose from ^{131}I, ^{132}I, ^{133}I and ^{133}Te plus gamma. mean dose extrapolated from calculations for adults and three-year-olds

[b] Based on number of people exposed. excluding those in utero (number of cases/total number in group)

[c] The thyroid is considered to be fully developed by about age 18

[d] One additional case of adenoma. found at autopsy, not included here

[e] Weighted mean dose

[f] Pathologists differed as to whether this lesion was malignant. It was scored as benign

have been resected surgically. The incidence of thyroid nodularities and estimated thyroid doses in the various age groups exposed to fall out are depicted in Table I. It is apparent that more than two-thirds of those individuals in the combined Rongelap and Ailinginae groups, who were under the age of ten at the time of exposure, and over 15% of those exposed over the age of ten have developed thyroid lesions. Four Rongelap children were exposed in utero. One of these, a boy exposed at 22–24 weeks gestation (at which time the thyroid was functional), had benign nodules of the thyroid removed at age 20. A much smaller proportion of the Utirik group of either age has developed thyroid abnormalities. The occurrence of three thyroid cancers in the exposed Utirik population (compared with four in the Rongelap group) appears to implicate radiation exposure in the aetiology, but the high incidence is puzzling since it is greater than would be predicted based on Rongelap and Japanese data, and there does not appear to be any increase in benign thyroid tumours in that group compared with the much greater prevalence in the Rongelap group.

The high incidence of thyroid nodularity in the irradiated subjects is in agreement with previous data linking irradiation of the gland with subsequent development of thyroid nodules or carcinoma [6]. Since ^{131}I is considered much less tumorigenic for thyroid tumours than X-rays, it is rather surprising that, in view of the large contribution of radionodines to the thyroid dose in the Marshallese, the risk factor (risk/rad) is comparable with that noted following X-ray exposure. This may be related to the presence of more potent short-lived isotopes of iodine present in fall-out which accounted for two to three times the dose from ^{131}I.

Aside from the two subjects with frank hypothyroidism, there has been an increasing suspicion of possible hypothyroidism in other cases. The evidence supporting this conclusion is summarized in Table II. The two boys who developed myxoedema had received an estimated thyroid dose of 1150 rads. In addition at least five of the Rongelap population, who had appropriate testing before surgery, had either hypothyroidism or decreased thyroid reserve [7]. In addition a number of subjects with sub-total thyroidectomy have shown elevation in serum TSH concentrations and reduction in serum I_4 when their thyroid replacement schedule was not rigorously adhered to. This is significant since in general subtotal, thyroidectomy or lobectomy is not associated with frank hypothyroidism, since the remaining thyroid lobe may often hypertrophy to supply the needed thyroid hormone requirements of the individual. All the subjects so tested and listed in Table II were irradiated at a young age, and therefore received thyroidal dosage of about 800–1150 rads. Because of the suspicion of possible hypothyroidism in individuals to even lower calculated doses, a series of studies of thyroid reserve in previously unoperated exposed Marshallese was initiated in 1974, and the following report summarizes the data obtained in this study up to the present time.

TABLE II. PRIOR EVIDENCE OF THYROID HYPOFUNCTION AND CALCULATED THYROID EXPOSURE

Description	Subject identification number	Thyroid estimated dose (rads)
1. Two subjects with frank hypothyroidism 10 years after exposure	3	1150
	5	1150
2. Five subjects with hypothyroidism or decreased thyroid reserve pre-operatively	2	810–1150
	20	810–1150
	33	810–1150
	42	810–1150
	65	810–1150
3. Three subjects with impaired thyroid function following subtotal thyroidectomy	17	810–1150
	21	810–1150
	69	810–1150

TABLE III. RESULTS OF TSH STIMULATION TESTS IN EXPOSED RONGELAP SUBJECTS AND CONTROLS
Mean ± SD

	Mean serum T_4 prior to TSH (10 U IM) (μg/dl)	Mean serum T_4 increment 24 h after TSH (μg/dl)
Controls	6.0 ± 1.7	4.2 ± 1.3
Exposed Rongelapese (n = 26)	6.6 ± 1.7	2.4 ± 1.2

METHODS

Studies were performed during the annual or semi annual visits of the Brookhaven medical team to the Marshall Islands. Subjects were instructed to discontinue thyroid medication for two months before the studies of thyroid function which are described below. Occasionally, this instruction was not followed. However, the nature of the tests performed was such that this circumstance would result in an underestimation (rather than an overestimation) of the frequency of abnormalities in thyroid function.

Plasma was separated by allowing the red cells to sediment and was frozen within eight hours after obtaining the specimen. Serum Thyroid Stimulating Hormone (TSH) and thyroxine (T_4) were measured as previously described [8]. The normal range for serum TSH in our laboratory is from < 0.05 to 3 μU/ml in the United States population (mean 2.0 μU/ml). Thyrotropin Releasing Hormone (TRH) stimulation tests were performed by infusion of 500 μg of TRH intravenously, plasma samples were obtained at 0 and at 20 minutes after the infusion. TSH stimulation tests were performed by administration of ten units of bovine TSH intramuscularly with plasma obtained for T_4 determinations before injection and 24 hours later. The normal range for serum T_4 concentrations is 5–10 μg/dl. Estimation of the free fraction of T_4 was obtained by a T_3 charcoal uptake method developed in our laboratory (TBG Index). Twenty five μl of plasma are incubated in 1 ml of glycine acetate buffer, pH 8.6, containing ^{125}I-T_3. Dextran coated charcoal is added at 4°C with subsequent centrifugation to sediment the charcoal. The fraction of the total ^{125}I-T_4 bound to charcoal is determined and this result is normalized to the results of simultaneously assayed quality control samples containing normal quantities of T_4 and thyroxine-binding globulin (TBG). The normal range for the test is 0.85–1.10. The TBG Index increases parallel to the free fraction of the serum T_4 and T_3 and is therefore elevated in hyperthyroidism or TBG deficiency.

RESULTS

TSH stimulation tests

To determine whether or not there was impaired thyroid reserve in the exposed subjects, TSH stimulation tests were carried out using an increase in serum T_4 as the response endpoint. In normal subjects in the United States of America, the mean increment in plasma T_4 was 4.7 ± 1 μg/dl (mean ± SD) in 13 subjects following injection of 10 U of TSH. In Table III are shown data for the Marshall Islands population. The control subjects who had not been exposed to radiation were given TSH, and the mean increment in T_4 was 4.2 ± 1.3 (SD) not statistically different from the results in the United States population. However, in 24 exposed Rongelap subjects, a mean increment of only 2.4 ± 1.2 μg/dl was obtained, which was significantly less ($p < 0.001$) than in the control subjects.

TABLE IV. BASELINE SERUM TSH CONCENTRATIONS AND RESPONSE TO 500 μg THYROTROPIN RELEASING HORMONE (TRH) IN CONTROL MARSHALLESE SUBJECTS
Mean ± SD

		μU/ml
Basal TSH	Mean ± SD	2.0 ± 0.73
	Range	0.5 – 3.0
TSH 20 min after TRH		11.5 ± 4.5
	Range	4.7 – 20

TABLE V. CRITERIA FOR THE DIAGNOSIS OF BIOCHEMICAL THYROID DYSFUNCTION

1.	Basal plasma TSH	> 5 μU/ml	on two occasions
	or		
2. a.	Basal plasma TSH	> 3 μU/ml	on two occasions
b.	Plasma TSH after TRH	> 22 μU/ml	

TABLE VI. FREQUENCY OF AT LEAST A SINGLE ELEVATED BASAL SERUM TSH CONCENTRATION IN THE MARSHALLESE POPULATION

	Number tested	Number > 3.0 μU/ml	%
Control unexposed	115	11	10
Utrik exposed (Thyroid dose < 95 rads)	99	12	12
Rongelap and Ailingnae exposed (Subjects without surgery and excluding Nos 3 & 5)	43	11	26

Basal serum TSH concentrations and response to TRH

Since the most sensitive index of impaired thyroid function is an elevation in serum TSH which occurs through the hypothalamic-pituitary-thyroid feedback axis, serum TSH concentrations and their response to TRH were measured in both the control and the exposed Rongelap population. In primary hypothyroidism, the response of the pituitary to TRH is excessively great [8]. Mean basal TSH was 2 μU/ml in 25 non-exposed euthyroid Marshallese, and the range was from undetectable (< 0.05 μU/ml) to 3 μU/ml (Table IV). Serum TSH 20 minutes following TRH was increased in all control subjects. The mean increment was 11.5 ± 4.5 (SD) with a range of from 4.7 to 20 μU/ml. These results are not significantly different from those previously reported in other populations [9].

On the basis of these studies, criteria were established for classification of patients as having biochemical evidence of impaired thyroid function. These criteria are summarized in Table V, and include either two basal TSH determinations greater than 5 μU/ml (> 4 standard deviations above the mean) or basal plasma TSH > 3 μU/ml (but < 5 μU/ml) and plasma TSH after TRH > 22 μU/ml. Consistent observations in these ranges were required on two occasions to meet the criteria for biochemical evidence of thyroid dysfunction. While serum T_4 concentration is an important determinant in the thyroid status of the individual, previous studies have indicated that evidence of impaired thyroid function can be elicited by these tests before serum T_4 concentrations have fallen below the normal range [10]. Therefore, the serum T_4 concentration was not used as a criterion in establishing the diagnosis of impaired thyroid function.

In Table VI is shown the frequency of at least a single elevated basal TSH concentration in various Marshallese populations. In a control group of 115 who were not exposed to radiation, 11 subjects or 10% of the population had a serum TSH greater than 3 μU/ml. In ten of these, serum TSH was only minimally elevated (4.0 μU/ml or less), the remaining value was 6.1 μU/ml. None of these patients had detectable clinical hypothyroidism or thyroid enlargement, but serum T_4 concentrations were generally in the low normal range.

In the exposed Utrik population, 12 of 99 subjects tested had at least one basal serum TSH greater than 3 μU/ml, though none of these was in excess of 5 μU/ml. The incidence of elevated TSH in this population is not significantly different from that of the unexposed group. In the Rongelap and Ailingnae population, 11 of 43 subjects were found to have at least a single elevated basal serum TSH greater than 3 μU/ml, and in two cases serum TSH was in excess of 7 μU/ml, and in two cases serum TSH was in excess of 7 μU/ml. This is a significantly higher prevalence than in the other two groups pooled ($p < 0.05$). In Fig. 1 are shown the responses to TRH of the four individuals who met the criteria given in Table V. The normal basal TSH and response to TRH are shown in the shaded bars. In these four individuals, the basal serum TSH was elevated,

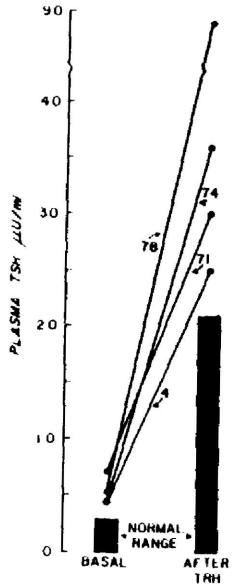

FIG 1. Basal plasma TSH and TRH-stimulated TSH in euthyroid Marshallese and in four exposed subjects with biochemical evidence of impaired thyroid function. Plasma was obtained 20 min after infusion of 500 μg TRH. The upper limits of the normal range are indicated by the shaded bars.

TABLE VII. CHARACTERISTICS OF MARSHALLESE WITH BIOCHEMICAL EVIDENCE OF THYROID DYSFUNCTION

Subject	Age at exposure	Estimated thyroid dose (rads)	Serum T_4 (μg/dl)	TBGI units	T_4 increment 24 h p TSH (μg/dl)
Normal values			5 10.2	0.85 1.10	1.6 6.8
74	16	335 810	5.8	0.97	0.8
71	28	335	5.2	0.98	N.T.*
78	37	335	6.1	0.82	0.8
4	38	335	7.4	0.79	0.9

* Not tested.

and the TSH response to TRH was also significantly increased, indicating the presence of impaired thyroid function.

Characteristics of Marshallese with biochemical evidence of thyroid dysfunction

In Table VII are presented the results of other studies in the four individuals with biochemical evidence of impaired thyroid function. At present, these are the only individuals who have fulfilled the criteria described in Table V, though several other subjects have shown at least one abnormal finding but have not had the required number of tests to meet the established criteria. The age at exposure varied from 16 to 38 years and the estimated thyroid dose was thought in three or four to be less than 400 rads. Serum T_4 concentrations in all four subjects are in the low normal range when considered in the light of their estimated serum Thyroxine-Binding Globulin (TBG). Subjects 74 and 71 have approximately normal serum TBG concentrations, whereas subjects 78 and 4 apparently have a modestly elevated serum TBG. In the last column of Table VII are shown results of the TSH stimulation tests of these subjects performed in 1974. In all three, the serum T_4 response to TSH was impaired, suggesting decreased thyroid reserve.

DISCUSSION

An association of thyroid nodularity and cancer with prior radiation of the thyroid gland, particularly in younger patients, is well recognized and the association has recently been reviewed [11]. In addition, it has been recognized that radiation to the thyroid delivered in the course of treatment of patients with thyroid dysfunction is associated with hypothyroidism in a significant fraction of the patients (as high as 50%) at the higher dosage levels [12]. The lowest dosage considered in previous studies of this type has been approximately 3400 rads estimated dose to the thyroid which was associated with a 6% probability of hypothyroidism within one year and a 13% probability in 13 years [13].

There are few data available in the literature relative to the possibility of hypothyroidism following ^{131}I dosages of less than 2500 rads. Preliminary results of Hamilton and Thompkins indicated that eight of 443 subjects (1.8%) subsequently became hypothyroid after diagnostic ^{131}I tests at less than 16 years [13]. A summary of these preliminary data has been presented. None of 146 subjects with an estimated thyroid absorbed dose of 30 rads developed hypothyroidism, but three of 146 subjects receiving 31 to 80 rads estimated thyroid dose had this condition [14]. Of 151 subjects with an estimated dose range of 81–1900 rads, five hypothyroid patients were found with an incidence of hypothyroidism of 0.23% yearly.

The present studies suggest that there is a significant risk of development of impaired thyroid function many years following estimated thyroid doses of less than 500 rads from the mixture of radioiodines present in fall-out from nuclear detonations. In the Rongelap and Ailingnae groups, the effect has apparently not been significantly severe as to result in clinically evident hypothyroidism, but by currently accepted criteria there is evidence of impaired thyroid reserve in these subjects. If left untreated, it would be expected that thyroid function would continue to decrease in such subjects to the point of clinical hypothyroidism. The data in Table VI also indicate that the frequency of an elevated serum TSH, the earliest biochemical evidence of impaired thyroid function, is also significantly more common in the exposed Rongelap population than in the control-unexposed group. There are several other exposed Rongelap individuals in whom results of basal TSH and at least one TRH test have suggested the possibility that they may also have evidence of impaired thyroid function. These individuals are currently undergoing repeated testing to determine whether or not this preliminary evidence of thyroid dysfunction can be confirmed.

In summary, these data indicate that in addition to thyroid nodularity, a well-recognized manifestation of exposure of the thyroid to radioactive iodine or external radiation, biochemical evidence of thyroid dysfunction can appear as long as 25 years after thyroid doses as low as 350 rads.

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DISCUSSION

M. DELPLA: I wonder what reliance can be placed in the doses you report, because I do not believe that 1000 rads, or even 1500, would have been enough to suppress the hormonal activity of the thyroid gland of two children contaminated when they were one year old. In fact, to obtain such a result, doctors have to administer a dose of ^{131}I giving at least 100 000 rad. It is true that this applies to adults, but all the same the dose difference appears considerable.

R.A. CONARD: There are uncertainties in the thyroid dose estimates in the Marshallese, particularly in the children. I agree it would seem likely that the two boys who developed myxoedema received higher doses than those estimated to produce atrophy of the thyroid gland.

K. SHIMAOKA: The normal human thyroid is radioresistant as far as thyroid function is concerned; patients with head and neck tumours treated by

radiation alone seldom develop hypothyroidism. However, there are two populations of patients who may develop hypothyroidism following external radiation therapy: those with head and neck tumours who received radiation therapy following surgical manipulation, and those with malignant lymphoma treated with radiation therapy after lymphoangiography. Since hypothyroidism is usually associated with high doses of radiation to the thyroid, how do you account for your findings with low doses?

R.A. CONARD: In our studies we are using very sensitive tests for thyroid function, and our findings indicate only biochemical or subclinical hypothyroidism at present. If these sensitive tests were used in other cases following external irradiation, perhaps such effects might be demonstrable.

Y. NISHIWAKI: I also conducted an analysis in Japan of the highly radioactive fall-out on the Japanese fishing boat that was engaged in fishing about 80–90 miles east of Bikini at the time of the thermonuclear test conducted early in the morning of 1 March 1954, and which returned to Japan in the middle of the same month. According to the statements of some of the crew, a few hours after the thermonuclear detonation in Bikini the whitish dust began to fall on the boat so heavily that for a period they could hardly bear to open their eyes and mouths. It continued to fall for several hours. Some of the crew apparently tasted it, to see what it was, without knowing that it was highly radioactive. Owing to the difficulty of dose estimation without more accurate information on the initial condition, the radioactive fall-out conditions on the boat were experimentally reproduced by M. Miyoshi, the chief physician in charge of treatment of the exposed crew at the Tokyo University Hospital, using pulverized coral reef. This experiment was carried out in the presence of the crew as witnesses of the actual amount of ash which had fallen on the boat. This amount was then estimated to be about 3.38–8.52 mg/cm^2. The radioactivity of the ash was estimated by extrapolation to be about 1 Ci/g at the time it fell on the boat. Taking into consideration various possible exposure conditions of the crew during the voyage, the probable gamma dose was estimated to be in the range 170–600 rad. The degree of uncertainty was far greater for the internal dose. The long-lived radionuclides detected in organs such as the liver many weeks later could not be considered the only sources of internal exposure. Depending on the assumed degree of initial incorporation of short-lived radionuclides, a wide range of estimates was possible: for the liver, a few rads to a few tens of thousands of rads, the probable dose range being 10–10^4 rads; and for bone and bone marrow, a few rads to about 60 rads. If we assume a non-uniformity factor of five for bone, the dose estimation could be five times higher. I am pleased to see that the thyroid doses you estimated in your report correspond more or less to our estimates in order of magnitude. However, I assume there would be some uncertainty in this type of dose estimation. What level of accuracy do you assign to your dose estimation? Did you also observe other radiation syndromes such as radiodermatitis, epilation, decrease of leucocytes, decrease of spermatozoa, etc. in the exposed Marshallese?

R.A. CONARD: The thyroid doses in the Marshallese were based primarily on radio-iodine measurements in urine 15 days after exposure. Uncertainties included length of time of the fall-out, relative absorption from inhalation versus ingestion, etc. Therefore the doses are subject to error. The gamma doses received should be more accurate, as they are in agreement with the values estimated from the degree of haematological changes observed.

The skin lesions, epilation and haematological effects in the Marshallese were similar to those reported by your group for the Japanese fishermen and have been described elsewhere. We were not able to do sperm counts on the Marshallese. No doubt there must have been some degree of relative sterility soon after exposure, though in subsequent years fertility does not appear to have been impaired.