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Follow-up of Marshall Islands Residents Accidentally Exposed to Ionizing Radiation in 1954: Quality Assurance Project

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FOLLOW UP OF MARSHALL ISLANDS RESIDENTS ACCIDENTALLY EXPOSED TO IONIZING RADIATION IN 1954: QUALITY ASSURANCE PROJECT

Prepared for U.S. Department of Energy
Environment, Safety and Health, Office of Health

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Given the constraints described, the ORISE team decided to proceed with the assessment from the perspectives of 1) current knowledge of the nature of the early and late health risks associated with exposure to radiation; 2) the radiological hazards of the accident and their potential to impact the health of the inhabitants of the affected islands; 3) the medical programs established to manage the medical care of the exposed inhabitants in the aftermath of the accident, and to monitor their long-term health with respect to the health effects of their exposure; 4) the nature and scope of the radiological health response to a similar accident occurring today; and 5) recommendations for the nature and scope of the surveillance appropriate for the Marshall Island population through the year 2000.

The team met several times early in the project to develop the scope of the assessment and outline the organization of the report. Members' concurrent review of the literature molded the report's final draft which they agreed would be submitted for external peer review before finalizing it for presentation to DOE's Office of Health. Members then developed material in their areas of expertise within the proposed framework of the report. The first draft document was compiled for members' input, edited, and circulated for internal review. Members' comments and suggestions were incorporated as appropriate to the extent reasonable, and the final draft document was prepared for concurrent administrative and peer review.

1.3 Summary and Conclusions

The clinical effects of acute whole-body, local and internal exposure to ionizing radiation above threshold doses for specific cell systems observed among the Marshallese were consistent with similarly exposed populations. This correlation was predictable given the average doses of the Marshallese population; however these doses were estimated a posteriori, and based on the observed clinical effects.

Current knowledge of the random late effects of radiation suggested the tumorigenic effect of the Marshallese exposures would be the most significant adverse health outcome in the years following initial recovery. Based on the small population originally identified for follow-up (N=239), the total population dose (101.14 Gy), and the large uncertainties in individual doses, the paucity of good data on spontaneous cancer and other disease rates among this genetically complex and socio-economically impaired population, it was considered that detection of a statistically significant increase in fatal cancers attributable to the radiation exposure would be unlikely. Based on the experience of the Marshallese Islanders, hypothyroidism and thyroid tumors would have been predicted, particularly among the children under 15 years who comprised > 40% of the population exposed in 1954.

The early medical management and subsequent monitoring and care provided the inhabitants of Rongelap, Ailingnae and Utirik were entirely appropriate in nature and scope even by today's standards, especially when considering the remoteness of the accident from basic medical facilities and personnel. While some of the clinical laboratory investigations now might be considered esoteric given the levels of exposure and the limited clinical facilities, events of this magnitude were rare during the early days of the nuclear era. Also, the medical teams were charged with evaluating the relationships between the inhabitants' health and their prior exposure to radiation.

In hindsight, attempts to identify a comparison population for the purpose of epidemiologic analyses might be considered unnecessary, given the heterogenicity of the available populations, the potential for systematic error, bias and other limitations and uncertainties in the data retrieved. Nevertheless, epidemiologists are noted for making the best of the data available, and this was an opportunity to be seized rather than justified.

If an accident of similar type and magnitude happened today, many improved approaches and methods would be available for detailed and extensive clinical and radiation dose assessments for individuals, and to manage and analyze data. Whether full scale epidemiologic studies would be justified, is doubtful. This issue was addressed in 1990 for the Committee on Interagency Radiation Research and Policy Coordination with the conclusion that thorough evaluation and follow-up of the exposed populations are indicated both from scientific as well as the humanitarian perspective. It also was recommended that plans for collection of adequate and appropriate data be developed but implementation of major epidemiologic studies to test hypothesis should be considered on the basis of the potential (power) of such a study to yield definitive results.

1.4 Recommendations

Based on its review of the scope and nature of the Marshall Islands accident and the low potential for further development of radiogenic health outcomes, sufficient to influence current risk estimates, the ORAU team recommends a medical monitoring program aimed at early diagnosis and treatment to the benefit of individuals in the exposed population. Specific recommendations are made on the desired composition of the medical team, and the need for an evaluation program comprising standardized examinations components to which additional tests could be added to benefit the patient as indicated by the health of the patient or technical and scientific advances.

Standardized examination components of an optimal monitoring program are enumerated, and standards for data collection, maintenance, preservation and quality assurance are recommended. The use of ultrasound is not recommended for routine thyroid examinations of asymptomatic patients because of the high incidence in the general population of clinically non-significant thyroid tumors. Further attempts at biodosimetry using cytogenetic techniques currently are discouraged for this population as they are unlikely to provide useful information.

2. INTRODUCTION:

The follow-up of populations exposed to ionizing radiation may be warranted on humanitarian and scientific grounds. On March 1, 1954, the residents of several islands in the Marshall Islands' chain were exposed accidentally to fall-out from a planned test of a nuclear device at the Bikini Atoll Test Site. The populations of three islands were identified for prompt and extended medical evaluation, and treatment of any acute whole-body and local effects resulting from this exposure. Subsequently, a congressionally mandated follow-up program was implemented by the U.S. Atomic Energy Commission (AEC). By this program, the populations of the three affected islands and a comparison group selected from among the islands considered to have been unexposed, were to be surveyed at regular intervals to monitor the health of these populations, and thereby to identify and evaluate adverse long-term health effects with respect to exposures to radiation in 1954.

The general medical care of the Marshallese populations was the responsibility of the government of the Trust Territory in whose jurisdiction the Marshall Islands resided. This program has continued to the present with some interim modifications in its scope and objectives. These changes reflected redefinition of the exposed populations, and temporal changes in general health care delivery, and in the sociopolitical and cultural environments of the islands (1). In addition to the benefits of routine medical monitoring to the long-term health of the Marshallese, a major outcome of the program has been its contributions to scientific knowledge about the health effects of radiation generally and specifically about the risks of exposure of the thyroid gland to short-lived isotopes of iodine (2). The results of the immediate medical response to the accident in 1954, and of the subsequent periodic medical surveys conducted through 1989 have been reported in a series of technical reports (3-19) and in referred scientific journals (20-24). In addition, an extensive bibliography has been compiled of reports, journal articles, book chapters and other publications that concern the radiological and other technical aspects of the event and its sequelae, as well as related general and specific biological and medical topics (25).

With the transition from a trust territory government to the Republic of the Marshall Islands, this program has continued under the new government with Brookhaven National

Laboratory (BNL) continuing to provide the follow-up through support from the U.S. Department of Energy (DOE).

This report concerns an evaluation conducted by a multidisciplinary team for the DOE's Office of Health, of the appropriateness of the Marshall Islands' medical surveillance program as operated from 1955 to the present, by AEC and its successor agencies. It also concerns determination of the scope and type of medical surveillance that is indicated for this population through the year 2000 with respect to the radiological health hazards of the exposure to fall-out in 1954. Current knowledge of the nature of radiation-induced health effects and the estimates of their associated risks to health were used as the basis for addressing the following specific questions:

2.1 What type and scope of surveillance should have been implemented to effectively monitor this population for development of possible and probable radiogenic illnesses/diseases and chronic conditions, by 5-year intervals between 1955 and 2000?

2.2 What type of surveillance/tests would detect the development of such possible and probable radiogenic illnesses/diseases and chronic conditions, and how frequently should the surveillance be done?

2.3 What surveillance should be provided until the year 2000 to the exposed population of the Marshall Islands?

3. HEALTH EFFECTS OF IONIZING RADIATION

3.1 Overview

The purpose of this section is to provide a basis for enumerating possible and probable health outcomes among the exposed population of the Marshall Islands with respect both to the nature of the radiation injury (i.e., deterministic; stochastic) and the types and levels of radiation present. The clinical effects of exposure to radiation are dose-related expressions of underlying biological damage induced by radiation at cellular and molecular levels. Deoxyribonucleic acid (DNA) in cell nuclei is considered to be the primary site of radiation-induced chemical reactions that can result in clinical effects, but reactions also may occur among molecules in the membrane and other cellular structures. The resulting clinical manifestations of this biological damage may be categorized as deterministic or stochastic in nature. With few exceptions these effects are non-specific and indistinguishable by existing clinical or biological technologies from clinically similar lesions caused by other agents.

Deterministic effects, also known as threshold effects, are due to biological damage that results in immediate or early cell death or sterilization and thereby, to cell depletion. There are threshold ranges for the doses of radiation that are required to cause lethal damage to cells sufficient to produce clinical evidence of cell depletion. The severity as well as the incidence of deterministic effects is related directly to the dose of radiation received. Deterministic effects may be clinically evident as acute signs and symptoms during the early (1 - < 60 days) post-exposure period in individuals exposed to radiation above threshold dose levels. These effects include the Acute Radiation Syndrome (ARS), acute local lesions including radiation burns, and decreased fertility. Expression of other effects of acute radiation injury also may be delayed for periods ranging from about 60 days to years after exposure, depending on the cell system affected and the degree of damage. These include fibroatrophy, cataracts, temporary infertility or permanent sterility, and hypothyroidism.

Stochastic or non-threshold radiation-induced effects are associated with incomplete or misrepair of sublethal radiation-induced biological damage that can result in gene mutations. Such mutations can increase an exposed population's risk of heritable genetic effects when the affected genes are in the reproductive cells, or of neoplastic effects in the case of somatic cell genes. The disease outcomes of these lesions are not unique to radiation. Their association with radiation has been identified only by observation of increased rates of the end-points in experimental and epidemiologic studies of irradiated populations. In the absence of definitive epidemiological data for stochastic effects in the low dose range (<200 mGy)[1], it is assumed for radiation protection purposes that there is no dose below which no biological damage occurs. This type of injury may be clinically expressed at random among a population exposed to radiation, (somatic effects) or their progeny (genetic effects), with the probability of the risk of clinically detectable outcomes increasing above that of spontaneous (background) risk in the non-exposed population with increasing dose above zero. However, unlike deterministic effects, the severity of stochastic effects is independent of dose.

Exposure of the pregnant woman to radiation can induce non-specific deterministic effects in the embryo or fetus that are related to dose, dose rate and the period of gestation. However, the results of experimental and epidemiological studies show that external whole-body doses of 50 mGy or less to the embryo or fetus at any time during gestation are not associated with significantly increased risks of such effects when compared with those not so exposed. It has been suggested that the fetus may be more susceptible to radiation-induced cancer in later life but there is no strong epidemiologic evidence of this (26).

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[1] mGy = milligray = .001 Gy; International System (SI) unit of radiation absorbed dose. 10 mGy = 1 rad (conventional unit); 1 Gy = 100 rad (conventional unit). SI units are used throughout the text except in citing original data that were reported in conventional units; in these instances the data are presented in SI units with the published form of the data following in parentheses.

3.2 Deterministic Effects

3.2.1 Factors Influencing the Clinical Expression of Acute Radiation Injury

Early clinical expression of radiation-induced biological damage is influenced by several physical and biological factors. These include radiation type, radiation dose and dose rate, the radiosensitivity of the irradiated tissues, the area of the body irradiated, and variations in individuals' biological response to radiation.

The type of radiation determines its penetrating power, a key factor in considering the clinical consequences of exposure. For present purposes, distinction is made between penetrating radiations (i.e., X and γ rays, and neutrons), and those having less penetrating power (i.e., α and β particles). X and γ rays are sparsely ionizing electromagnetic waves emitted, respectively when a metal target is bombarded by electrons in a vacuum, from nuclear fission process or during radioactive decay of fission products. Neutrons are uncharged particles that typically are released in the fission process but that also can be produced in cyclotrons and linear accelerators. They also occur naturally in cosmic radiation. Being uncharged, neutrons do not interact directly with biological targets. In traveling through tissue they are absorbed by interaction with the nuclei of atoms in the tissue thereby releasing high energy particles that cause ionization of molecular materials. Penetrating radiations can deliver dose to any tissue irrespective of whether the activity is internally or externally distributed. Alpha particles are densely ionizing; they have a penetrating power of only a few microns, equivalent to one or two layers of cells and thus are not a health hazard when external to the body. Beta particles are sparsely ionizing; they may penetrate up to a few centimeters of tissue depending on their energy. When near or in contact with skin, β radiation can induce acute radiation burns locally but has a limited whole-body effect. Internally deposited β particles can induce local and whole-body effects depending on their energy and distribution.

The type, incidence and severity of radiation-induced deterministic effects are directly related to the magnitude of the radiation dose and the rate at which it is delivered. A single dose of radiation delivered in a short period of time (i.e., acutely) will have greater biological and clinical effects than the same dose delivered in increments at intervals over an extended period of time (i.e., fractionation, protraction). In the latter situation, the interval between exposures allows biological repair of radiation-induced damage to occur so that the total damage is less than if the dose had been delivered acutely, and the clinical effects are correspondingly less severe.

The sensitivity of cell systems to radiation is directly related to the rates at which the cells are undergoing division, i.e., their mitotic index, and inversely to their level of differentiation. Thus in general, stem cells of rapidly proliferating cell systems are highly radiosensitive (e.g., the stem cells of the hematopoietic systems, spermatocytes). Conversely, muscle and nervous tissue cells are highly radioresistant. Cells having intermediate mitotic rates and differentiation, such as those of the gastric mucosa, fall between these extremes. An important exception to this generalization is the small lymphocyte which, despite its low mitotic index and high degree of differentiation, is highly radiosensitive and an early clinical indicator of acute whole-body irradiation at doses higher than 0.5-1.0 mGy.

As hematopoietic stem cells are highly radiosensitive, the extent to which they lie in the radiation field influences the magnitude of the acute whole-body effect of the exposure. Uniform exposure of the whole-body, or a significant portion of it, to penetrating radiation can result in an acute whole-body response that is directly related to dose. If, however, the exposure is non-uniform or limited to a small area of the body, thereby exposing only a limited variety and number of stem cells, the whole-body response will be less than if the same dose had been delivered to the whole-body. The ability of internally deposited sources of alpha or beta radiation to induce serious acute whole-body effects (e.g., clinically significant bone marrow depression) is dependent on the amount of activity and its distribution within the body, and the penetrating power of the emitted radiation.

3.2.2 Early Clinical Features of Acute Radiation Injury

Depending on the nature and type of the exposure, exposure to radiation above threshold levels can elicit acute whole-body or local responses that become clinically evident within minutes, hours or days. In some cell systems, acute radiation injury may not become clinically evident for several weeks, months or years post-exposure. The various types of radiation injury can occur alone, in combination with each other, or with physical trauma or with other medical conditions or complications of the injury. The clinical effect of such combined injuries has been shown to be synergistic so that the acute response to a given whole- or partial-body dose of radiation is apparently greater in the presence of other radiogenic or non-radiogenic injuries or in complications such as infection, than it would have been if received alone (28).

For the purposes of this report, the following topics are addressed in the context of acute (high dose, high dose-rate) exposures to radiation:

3.2.2.1 Whole-Body Exposures

Exposures in excess of threshold levels to the whole-body or substantial portions of it cause irreversible biological damage that is expressed in a group of dose-related signs and symptoms that comprise the Acute Radiation Syndrome (ARS), sometimes referred to as "acute radiation sickness." The ARS is characterized by an acute illness that follows a four-phase clinical course. The severity and duration of each phase are inversely related to radiation dose. The prodromal phase (Phase I) is characterized by symptoms that result from acute cell death and from effects on the gastrointestinal and central nervous systems mediated by direct injury to the parasympathetic nervous system. Symptoms include fatigue, lassitude, anorexia, nausea and apathy. At higher doses vomiting, diarrhea, hyperexcitability, ataxia, erythema, perspiration and fever can occur. Radiation-induced conjunctivitis has a threshold of approximately 200 mGy to the eye. During this phase the earliest detectable clinical signs are of bone marrow depression beginning at doses of 0.5-1.0 Gy with the absolute lymphocyte and granulocyte counts being the parameters of interest. The development of signs and symptoms during the prodromal phase serve as a basis for radiological triage and assessment of medically stable patients. The latent period (Phase II) is characterized by the disappearance or decreased severity of the prodromal symptoms and an apparent improvement in the patient's well-being. At lower doses the patient can proceed to recovery. At higher doses cell systems become increasingly depleted during the latent period until their viability falls below the levels required for homeostasis. The appearance of signs and symptoms of incompetence in one or more systems marks the onset of the manifest illness (Phase III). These dose-related syndromes are (1) hematopoietic, with signs and symptoms of increasing leukopenia reaching a nadir 28-30 days after an acute sublethal dose; (2) gastrointestinal, with radiogenic injury to the gastrointestinal tract resulting in vomiting, bloody diarrhea, fluid and electrolyte shifts, malabsorption and (3) cerebro- or cardiovascular (formerly known as the central nervous system syndrome), with early and increasingly severe signs and symptoms of increasing intracranial pressure due to cerebral edema associated with a generalized vasculitis. In the absence of treatment, death (Phase IV) can occur 48 hours to 60 days after acute exposure to doses in the lethal range ($LD_{50/60}$ ~3.25 Gy to bone marrow). The $LD_{50/60}$ may be increased to 8-9 Gy with modern treatment modalities. The exposure-to-death interval decreases with increasing dose. Spontaneous recovery (Phase IV) may be anticipated after day 30 among individuals exposed to radiation at sub-lethal levels (27).

3.2.2.2 Acute Local Radiation Injury

Except for doses in the range of several hundreds of grays, acute local irradiation alone is unlikely to cause a significant whole-body effect or critical illness in the immediate post-exposure period. Local radiation injury can result from exposure to a source of penetrating radiation, close proximity to or contact with a β radiation source, or contamination with β emitting radionuclides.

The earliest observable effect of local exposure above threshold levels (~6 Gy) is a transient erythema that appears within two to three hours. It possibly is associated with the release of endotoxins from necrotic cells. Except for this reaction, the effects of doses of less than several hundreds of grays to skin do not become apparent for several days or longer, depending on the dose. One or more waves of erythema will follow approximately five or more days after moderate local doses (~20 Gy). These waves are associated with radiation damage to endothelial cells and initially reflect capillary incompetence. With increasing dose, subsequent waves of erythema and increasing edema reflect expression of radiation damage affecting larger and deeper vessels. The deeper damage can affect other structures in the dermis and subcutaneous tissue such as sweat glands, hair follicles and nerve endings, as well as the vasculature. Resulting progressive endarteritis obliterans can lead to ischemic pain, ulceration, and at higher doses to irreversible tissue necrosis.

3.2.2.3 Contamination

Contamination with radioactive materials alone is unlikely to cause symptoms of ARS, although clinical signs of bone marrow depression and oligospermia are possible depending on the amount and radiological characteristics of the contaminant and its disposition on or in the body. It can result in local radiation-induced burns of the skin at the contaminated site.

3.2.3 Delayed Clinical Features

Some deterministic effects of acute radiation exposure may not become clinically evident for several months or years post-exposure; these include:

3.2.3.1 Vascular sclerosis, fibroatrophy

Endothelial cells lining blood vessels are sensitive to radiation at doses above 5 Gy. Death of these cells predisposes to vascular sclerosis with the eventual reduction or elimination of the blood supply to dependent tissues; such tissues ultimately atrophy. Evidence of these delayed changes may be observed within two or more months after irradiation of skin at doses 6 Gy and higher.

3.2.3.2 Cataracts

Radiation-induced cataracts are associated with exposure of the lens to an acute radiation dose of about 2 Gy or more, or a protracted dose totally about 1.1 Gy over a period of months. The interval between the exposure and cataract formation ranges from about 10 months up to approximately 30 years, depending on the dose and dose-rate.

3.2.3.3 Infertility

Temporary reduction in sperm counts have been reported following whole-body doses of radiation of 12 cGy. The threshold for permanent male sterility ranges from 2 to 6 Gy. With doses below this threshold, temporary sterility may persist for prolonged periods (up to 5 years has been reported) the duration of which are related to dose. Permanent sterility can be induced in women by acute doses to the ovary of 3 to 4 Gy; the effective dose varies inversely with age at exposure.

3.2.3.4 Hypothyroidism

Single doses of at least 10 Gy of external penetrating radiation are required to sufficiently injure the thyroid tissue as to result in clinically evident hypothyroidism. Internal emitters, specifically radioactive iodines, deposited in the thyroid gland can cause clinically detectable hypothyroidism in adults at internal doses to the gland of approximately 3-3.5 Gy. These dose data are derived primarily from the experience of the Marshall Islands' population. The thyroid becomes active at approximately eleven weeks post-conception. It and the child's thyroid having smaller mass than the adult gland, concentrate iodine to a greater extent, and thus are more sensitive to injury from internally deposited radioiodines. Thyroid hypofunction in the fetus and children up to about 10 years of age can result in growth retardation, or cretinism at higher doses.

3.2.4 In Utero Effects

Exposure of the pregnant woman to radiation can cause effects in the embryo or fetus that are related to dose, dose rate and the period of gestation. Radiation doses high enough to induce ARS in the mother will have a similar and possibly greater acute effect per unit dose on her fetus and can result in acute fetal death although she may survive. The effect of exposure to lower doses during the embryonic or pre-implantation period is described as "all or nothing," indicating that if the embryo survives -- and in the absence of other risk factors -- it will continue to grow and develop normally. Deterministic effects of fetal exposure include non-specific congenital malformations, growth retardation including microcephaly and mental impairment or retardation. Depending on the dose, dose rate and period of gestation, the severity of these effects may range from clinically undetectable, or insignificant, some degree of disability, to incompatibility with intrauterine or neonatal life. Although the threshold for specific end points may be greater, the overall risk to the embryo or fetus of exposure at any time during gestation does not appear to be increased below a threshold of 50 mGy (29).

3.3 Stochastic Effects

Experimental and epidemiological studies have contributed an extensive body of knowledge about radiogenic stochastic effects. The clinical outcomes are not unique to radiation. Their association with radiation has been established only by observation among a number of irradiated populations of disease rates that increase significantly with increasing dose. It currently is not possible to unequivocally attribute specific outcomes in individuals to their exposure to radiation. Relationships between specific outcomes and prior radiation exposure are necessarily expressed in terms of probability using estimates of risk derived from epidemiologic studies of irradiated populations, and taking into account known risk factors such as age at exposure and gender.

3.3.1 Heritable Genetic Effects

There is no genetic disease that is uniquely radiogenic. Increased rates of conditions associated with inherited genetic mutations have been observed among the progeny of experimentally irradiated organisms. However, to date there is no evidence of statistically significant increases in the rates of genetic diseases or conditions among the progeny of irradiated populations (30).

3.3.2 Somatic Effects

Epidemiologic studies of such populations have clearly identified the major stochastic effect of ionizing radiation to be a dose-related increase in the risk of tumors, primarily malignant tumors. This association has been demonstrated statistically for all cancers combined at radiation dose levels greater than about 200 mSv (31).

3.3.2.1 Radiogenic Tumors

Although all tissues are considered to be susceptible to radiogenic tumorigenesis, some tumors have been shown to be more strongly associated with prior radiation exposure than others. Based on current epidemiologic data, tumor types most strongly associated with exposure to radiation are benign thyroid nodules, all types of leukemia, except the chronic lymphocytic type, and cancers of the lung, female breast and thyroid. Exposure to radiation from certain internally deposited radionuclides also has been associated unequivocally with malignancies of target organ tissues, significantly thyroid (radioactive iodines), lung (radon) and bone (radium), and leukemia and lung in the case of injected Thorotrast. The radiogenicity of malignancies of the head and neck (other than thyroid), digestive and genito-urinary systems, brain and the central nervous system, and skin appears to be weaker than is the case for the malignancies listed above; and it is equivocal or unidentified for certain site-specific malignancies within these organ systems, such as Hodgkins lymphoma and cancers of the uterus and prostate (2).

Although there have been some suggestions to the contrary, there is to date no strong evidence of increased cancer rates among children or adults who were exposed to radiation in utero (26).

3.3.2.2 Latent Periods and Duration of Increased Risks

Based on the epidemiologic data, the minimum latent periods (interval between exposure and diagnosis) for radiation-induced leukemia and solid cancers are generally accepted to be 2-5 years, and 10 years, respectively. The increased risk of radiogenic leukemia appears to decrease almost to the natural baseline rate for the control population 25-30 years post-exposure. However, the risk for most solid cancers remains substantially elevated for at least 40 years post-exposure (2).

3.3.3 Risk Estimates

The total life time excess risk to a population (all gender/age groups) for all types of stochastic effects combined, i.e., fatal and non-fatal malignancies, and severe genetic effects, associated with high dose and high-dose rate exposures to radiation, currently is estimated to be approximately 15 x 10^{-2} Sv^{-1} [2](26). The overall risk is estimated to be decreased by a factor of 2 or greater for low dose and low-dose rate exposures (26). The overall estimate of the excess life-time risk of radiogenic cancer is approximately 10 x 10^{-2} Sv^{-1} based on the natural rate in the control population (26). Estimates have been calculated for the risks of radiation-inducted site and type-specific cancers. Overall, the radiogenic cancer risk estimate is greater among persons exposed at younger ages, and among females, primarily because their baseline rates for cancers of the breast and thyroid are higher than those of males. The overall risk also is higher among populations with certain genetic defects, e.g., xeroderma pigmentosum, (2).

As in the case of estimate of the risk for all stochastic effects combined (v.s.), the risk estimates for radiogenic cancers associated with exposures to radiation at low doses and low dose rates, are estimated to be lower by a factor of 2 or greater than those for high levels of radiation (26).

3.4 Psychological Effects

The psychological impact of radiation accidents on persons directly and indirectly involved in them has received greater attention in recent years than heretofore among the medical and scientific communities. Some experimental and clinical studies suggest that exposure to radiation may induce neurophysiological changes that are manifested clinically as altered psychological states among the exposed population. While this issue continues to be debated, there is evidence to suggest that radiophobia and the socioeconomic repercussions associated with serious radiation accidents may induce psychosomatic effects, even among minimally or non-exposed populations (30).

[2] Sv = sievert = 1000 mSv; International System (SI) unit of dose equivalent in man. 1 Sv = 100 rem (conventional unit).

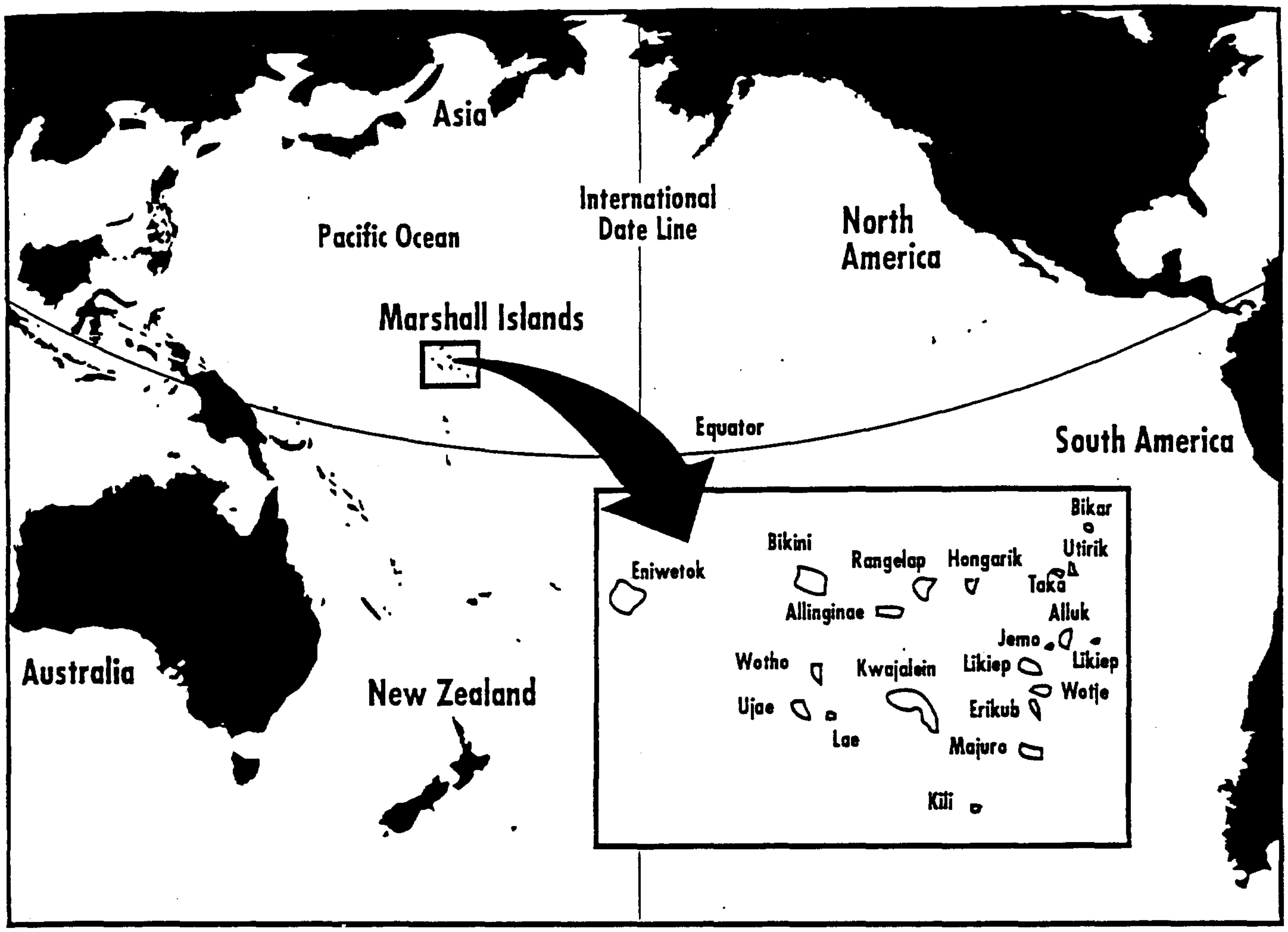

Figure 1 Location of the Marshall Islands

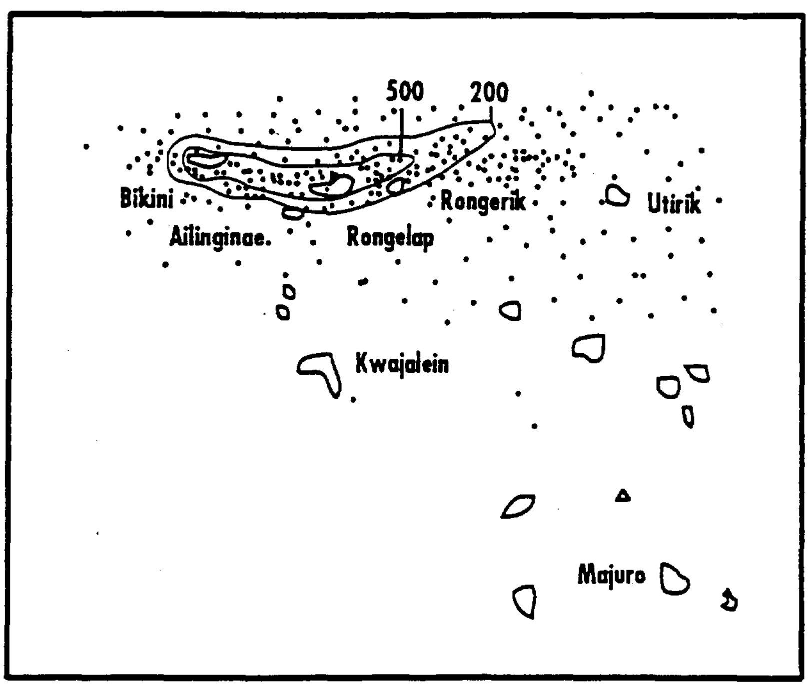

Figure 2 Fallout area in the Marshall Islands

4. THE INCIDENT AND ITS IMPLICATIONS FOR RADIOLOGICAL HEALTH

4.1 The Incident

On March 1, 1954, at 0645 hours, at Bikini Atoll (Bikini) in the Marshall Islands (Figure I), a thermonuclear device was detonated in a test referred to as "Bravo." The device was detonated from a barge floating in shallow water, thus resulting in considerable fall-out material described as largely consisting of calcium oxide from the coral with adherent radionuclides. The yield of the detonation was approximately 15 megatons which considerably exceeded that anticipated. Because of an unexpected change in wind direction, the radioactive cloud or plume traveled in a generally easterly direction depositing fall-out over the inhabited atolls of Rongelap, Ailingnae, Rongerik and Utirik (Figure 2). As a result of this incident, more than 250 people were exposed externally and internally to significant amounts of radiation. Those exposed were inhabitants of various islands of the atolls and some U.S. military personnel. These individuals were evacuated to minimize their exposure and to provide for examinations and care. Fall-out from Bravo was also deposited on U.S. naval vessels thirty miles east of Bikini and on a Japanese fishing vessel, the Lucky Dragon, and her crew of 23 Japanese fishermen.

4.2 Radiological Exposures

4.2.1 Chronology of the Acute Exposures

Radioactive fall-out from the device was recorded at around 1400 hours (7.75 hours after detonation) by low-level gamma detectors on the nearby Rongerik Atoll (Rongerik), where 28 U.S. servicemen were operating a weather station. These personnel were evacuated to Kwajalein Atoll (Kwajalein) in two groups between 1245 and 1800 hours on March 2. They had protected themselves by wearing long-sleeve shirts, long pants, hats, etc. and by remaining indoors as much as possible since about 1530 hours on March 1, under instructions from the Joint Task Force Headquarters, who had been notified of the detected fall-out radiation.

The Marshallese who were exposed have been categorized into three groups by atoll. The majority was located on Utirik Atoll (Utirik) and was evacuated to Kwajalein between 55 and 78 hours after detonation. The next largest group was located on Rongelap Atoll (Rongelap), this group was evacuated to Kwajalein at about 50 hours post-detonation. The third largest group was on Ailingnae Atoll (Ailingnae), and was evacuated to Kwajalein at about 58 hours post-detonation. The majority of the Marshallese was mostly outdoors and unprotected by clothing or shoes during the passage of the fall-out plume over other atolls; thus their skin was exposed to substantial quantities of fall-out materials.

4.2.2 Types of Acute Exposures

The radiation exposures of these individuals comprised combinations of (1) external exposure to the whole-body and skin from materials in the cloud and fall-out, (2) external exposure to the skin from fall-out materials deposited on exposed surfaces of the body, and (3) internal exposure of the body organs to radiation from inhaled or ingested fall-out materials. All these individuals were exposed externally to the external radiation from activity in the plume. According to survey meter measurements (with varying degrees of certainty), the populations of the four atolls (Rongerik, Rongelap, Ailingnae, and Utirik) were exposed to levels of radiation that varied according to their proximity to the path of the plume, their activities and evacuation time. The quantitative estimates of these exposures are discussed later in this section. Radiation doses to skin from external contamination, and probably also internally from inhaled or ingested radionuclides, were considerably greater among the Marshallese on Rongelap, Ailingnae, and Utirik than the among the U.S. servicemen on Rongerik. Unlike the servicemen, the Marshallese were unaware of the potential hazards of the fall-out materials. While the servicemen were covered by clothing and shoes, took shelter and were careful to consume uncontaminated food and water, the Marshallese were not so protected. Several individuals who spent time in the ocean managed to wash off some of the contamination from their feet and other parts of their bodies. When indoors, these people were typically inside houses constructed of palms and other natural materials that offered very little shielding. The clinical symptoms and signs reported for the exposed groups were generally consistent with the estimates of the whole-body doses of radiation received from both external and internal sources.

In summary, it is clear that the Marshallese initially were exposed to radiation from the detonation via all three of the major exposure routes, i.e., externally from sources of penetrating radiation and contamination, and from internally deposited radionuclides.

4.2.3 Potential for Protracted Exposures

The populations evacuated from Utirik and Rongerik were returned to their homes in 1954 and 1957, respectively. These groups may have received additional doses of radiation from exposure to residual activity on the atolls, and ingestion of contaminated food and water. The evacuees from Rongelap also were repatriated in 1957. However, in 1985 they were re-evacuated to Kwajalein where they are still living. This re-evacuation was prompted in part by the Marshallese' concern about residual activity on Rongelap.

4.3 The Exposed Population

According to early reports of the incident, the four groups considered to have been exposed comprised a total of 267 people. Of these, 28 were U.S. servicemen stationed on Rongerik, the remainder (239) were inhabitants of the Marshall Islands who were located as shown on Table 1.

TABLE 1. Distribution by Atoll of the Marshall Islands Population Exposed to Radiation Following the 1954 Bravo Test Showing Initial and Revised Estimates of the average external gamma doses to these populations

				External Gamma Dose Estimates			
				Initial		Revised	
Atoll	Number of People	Approximate time Fall-out Began	Time of Evacuation	C kg^{-1}	(R)	Gy	(rad)
Rongelap	64	4 to 6	50 to 51	0.045	(175)	1.20	(120)
Ailingnae	18	4 to 6	58	0.018	(69)	0.48	(48)
Rongerik	28	6.8	28.5 to 34	0.020	(78)	0.37	(37)
Utirik	157	22	55	0.0036	(14)	0.10	(10)
Total	267						

Adapted from Conard and Hicking, 1965; Goetz et al., 1987.

A more recent report (35) listed a total of 249 Marshallese who were exposed at Rongelap (n = 67), Ailingnae (n = 19), and Utirik (n = 163). This total included 12 individuals who were in-utero at the time of the incident (3, 1, and 8 at Rongelap, Ailingnae, and Utirik, respectively) . The exposed population comprised individuals of different ages ranging from those in-utero to the elderly as shown in Table 2.

Table 2. Distribution of Marshall Islands' Residents by Atoll and Age-at Exposure

	Age (years) at exposure, 1954										
Atoll/Gender	In utero	0-4	5-9	10-14	15-19	20-39	40-59	60-80	>80	Total	%
Rongelap/ Ailingnae											
Males	3	9	5	2	2	11	6	4	0	42	16.9
Females	1	8	6	6	3	7	9	3	1	44	17.7
Utirik											
Males	7	16	8	11	3	11	14	7	1	78	31.3
Females	1	20	13	2	5	22	15	7	0	85	34.1
Total	12	53	32	21	13	51	44	21	2	249	100
%	4.8	21.3	12.9	8.4	5.2	20.5	17.7	8.4	0.8	100	

Adapted from Lessard et al., 1985.

Subsequently, some environmental samples from atolls other than Rongelap, Ailingnae, and Utirik indicated that radioactive fall-out may have been transported to other islands. An instrument reading on Utirik (classified as non-exposed) was 0.01 Gy/hr (1 rad/hr) one hour after detonation. Furthermore, a statistically significant increase in the incidence of thyroid tumors over background rates was observed in residents of atolls thought to be non-exposed (33). Collectively, these findings suggest that the geographic area representing the "exposed" population may have been much broader than originally thought, and therefore, the exposed population may be much larger than initially reported. In addition, some inhabitants of nearby atolls chosen as part of the "non-exposed" group may have received cumulative radiation doses similar to, or even higher than, those exposed on Utirik (33).

4.4 Radiation Dose Estimates

The estimates of radiation dose calculated by various groups are discussed with respect to these three sources of radiation to which the Marshallese were exposed.

4.4.1 External Whole-Body Doses from the Plume

Current knowledge and practice indicates that two approaches may be taken to estimate the residents' external whole-body doses from sources in the passing plume of fall-out materials. One would be a theoretical approach, in which the known device yield and characteristics are used to calculate a source term, and other plume transport and radiation production; attenuation and scattering models are used to estimate typical absorbed doses near ground. Another approach would be to use observed survey meter readings, integrating dosimeter readings, etc, at the various locations over time to estimate residents' absorbed doses.

The early attempts to characterize the external whole-body radiation doses used recorded survey meter and dosimeter readings. These initial estimates are shown in Table 1. The Rongelap inhabitants were thought to have received the highest doses, because of their proximity to the blast and the approximately two-day delay before evacuation. Although Ailingnae is physically closer to Bikini than either Rongelap or Utirik (see Figure 1), it is farther to the south, and was less under the center of the plume than was Rongelap. The largest group of inhabitants was on Utirik, which is the farthest of these atolls from Bikini; and this group apparently received the lowest doses. These estimates were based primarily on average readings of radiation survey instruments, taken at about 1 meter above ground, several days after evacuation of the residents. An approximate energy spectrum was derived from spectroscopic measurements on the fall-out material, and adjustment of the assumed (ground plane) geometry and air attenuation. The chronology of the exposure was inferred from survey meter and film badge readings on Rongerik, visual identification of the arrival of the plume over Ailingnae and Rongelap, and other considerations.

Re-estimation of the absorbed dose to the servicemen on Rongerik, taking into account the chronology of the exposure, personnel activities and assumed protection factors (when inside buildings), rate of decay of fall-out radiation intensity, and other data, suggested a population average total body dose equivalent of 0.37 Gy (37 rad). The revised estimates are shown in Table 1; they are based on free air ionization estimates. The authors of the detailed study suggested a conversion factor for average dose equivalent from exposure in air to be 27.1 Gy C^{-1} kg (0.7 rad/R) (34). They also assumed that the servicemen spent more time indoors than did the authors of the original dosimetry. When these factors are taken into account, the two estimates are in agreement, and a value of 0.3-0.4 Gy (30-40 rem) is established. The protection factors for the Marshallese, however, are not as great. As noted above, the houses of the island residents were made of light, natural materials and offered little shielding. Also, the residents, being unaware of the radiologic hazard, spent most of their time outdoors. Therefore, the adjustment of their whole-body exposures to dose equivalent by the 27.1 Gy C^{-1} Kg (0.7 rad/R) factor probably is reasonable, but further reduction by a factor of about 2.0 for shielding is not warranted. This would suggest whole-body external dose equivalents from early exposure to be 1.2 Gy (120 rad), 0.48 Gy (48 rad), and 0.10 Gy (10 rad) for the Rongelap, Ailingnae, and Utirik residents, respectively.

One estimate of external doses has been attempted through purely theoretical treatment of the device yield, meteorologic dispersion (35), etc. The calculated results are not in agreement with measurements and analyses carried out for the atolls. A lack of available "wind rose" data may have contributed to the weakness of this analysis.

4.4.2 External Radiation Doses to the Skin From External Fall-out Contamination

Theoretical estimation of the external doses to the skin from electrons is not feasible, and must be inferred from the observed clinical signs based on current knowledge. When the radionuclides and their distribution and concentration on the skin are well-known, calculations may provide some estimates of the radiation dose to sensitive layers of the skin. In this case, the fall-out contained complicated mixtures of radionuclides that were not uniformly distributed, and the distribution over the skin and the duration of exposure are not known. Doses to skin from photon sources deposited on Rongelap, were estimated to range from 3-20 Gy (300-2000 rad). This rough estimate was based on the assumption that the sources were distributed over a large, flat area of ground. Observations of skin erythema, ulceration and epilation on the scalp gave clear indication of high radiation doses of up to 35 Gy (3500 rad) to local areas of skin. Of course radiation dose to the skin was not uniformly deposited. A lack of correlation between skin effects and hematologic effects led early researchers to believe that skin contamination did not significantly contribute to total-body radiation dose.

4.4.3 Internal Radiation Doses

As in the case of external skin contamination, an estimation of radionuclide intake is impossible, due to a lack of knowledge of the radionuclide concentration in the air, water, and food, particle sizes, chemical compositions, etc. A retrospective analysis of probable radionuclide intake was performed based on observed excretion of radionuclides in the urine. Pooled and individual urine samples were collected at various times starting at 15 days post-detonation, and the samples were analyzed for gross beta activity as well as radionuclide-specific activity. In addition, analyses of tissue samples from animals present at the contaminated sites (mostly pigs, chickens, and fish) were used to confirm the internal distributions of radionuclides when considered with the human urine excretion data. Estimated early body burdens of various radionuclides in the Rongelap population are shown in Table 3. Analysis of radioactivity in tissue samples of the animals showed the highest concentration of radionuclides in the skeleton (over 90% of the body burden of the pigs), with the liver and colon containing the second highest levels of activity, and all other tissues having some measurable contamination. The iodine-131 content of human urine and the observation of bone-seeking fall-out nuclides in the human urine samples and the animal skeletal tissue samples focus the concern for internal radiation doses on the thyroid, skeleton, and bone marrow.

TABLE 3. Estimated Early Body Burdens of Radionuclides in the Rongelap Population in Kbq (μCi)

Radionuclide	Estimated Activity,
Sr-89	59-81 (1.6-2.2)
Ba-140	13-100 (0.34-2.7)
"Rare Earths"	00-44 (0-1.2)
I-131 (in thyroid)	240-410 (6.4-11.2)
Ru-103	0-0.48 (0-0.013)
Ca-45	0-0.70 (0-0.019)
"Fissile Material"	0-0.016 μg

Source: Conard et al., 1980.

Most radioiodine absorbed into the body is excreted within two days, therefore, urine samples, especially pooled urine samples, are an ineffective means for estimating the initial iodine intake. From the one pooled sample collected on day 15 after the Bravo detonation, it was apparent that there was some intake of iodine-131, but, a sample at this date cannot account directly for short-lived nuclides that might have contributed to thyroid dose. Although good anatomical models did not exist in 1954 for the thyroids of the children exposed, the early estimates of the thyroid doses probably were fairly accurate. We base this conclusion on the fact that the electron dose to the gland typically is the dominant component, and that it can be calculated with good precision given a good estimate of gland mass. The masses of the thyroids of individual Marshallese residents were not well-known, but estimates were available for children elsewhere who were of similar ages to those exposed on the islands. The earliest estimates of thyroid doses were 1.5 Gy (150 rad) for the Rongelap population and 0.5 Gy (50 rad) for the servicemen exposed on Rongerik. It was reported that the gross beta activity in urine obtained from the Ailingnae group was about 50% of that of the Rongelap group. Thus, it can be surmised that a rough estimate of thyroid dose to the Ailingnae people was about 0.75 Gy (75 rad). The radiation dose received from external exposures must be added to these numbers to estimate the total thyroid dose. However, when observations of thyroid abnormalities began, a more careful evaluation of the dosimetry was made, including the contributions from iodine-131, 132, and 135. Revised estimates of the thyroid doses in the Marshallese by James (36) and Lessard et al. (37) are shown on Table 4. The dose reassessment by Lessard et al. suggested higher absorbed doses than those estimated by James because of differences in assumed isotopic ratios.

TABLE 4. Estimates of Thyroid Dose [Gy, (rad)] in the Exposed Populations By Age (Years) at Exposure

Atoll	Early Estimates*	<10 yr	10-18 yr	James (1964) >18 yr		<10 yr	10-18 yr	Lessard et al. (1985) >18 yr	
Rongelap	150								
Gy			8.1-18	3.4-8.1	3.35		18-50	12-17	10-11
(rad)			(810-1800)	(334-810)	(335)		(1800-5000)	(1200-1700)	(1000-1100)
Ailingnae	75								
Gy			2.75-4.50	1.9	1.35		7.40-13.0	N/D	2-3
(rad)			(275-450)	(190)	(135)		(740-1300)		(280-290)
Rongerik	50		—	—	—		—	—	—
Utirik	—								
Gy			0.60-0.95	3.0-6.0	2.7-6.7		1.5-2.5	2.7-6.7	1.5-1.6
(rad)			(60-95)	(30-60)	(270-670)		(150-250)	(270-670)	(150-160)

* Original dose estimate (rad), adult population only.

N/D = No Data

The doses to skeleton and marrow initially were assumed to be small compared to the external doses received. Actually, before the thyroid abnormalities became apparent, it was assumed that "the internal hazard to the contaminated inhabitants of the Marshall Islands is minimal both from the acute and the long range point of view" (5). However, the long-term doses to the skeleton and marrow might be important in assessing of stochastic effects (see 4.4.4). Also, doses to the gastrointestinal tract may have been significant if these nuclides were inhaled in an insoluble form. (Approximately 61% of inhaled insoluble aerosols >1 micron in diameter will be returned into the pharynx and swallowed). Indeed, high amounts of activity were detected in the gastrointestinal tracts of some of the animals whose tissues were sampled after the exposure. It is difficult to separate oral intakes from inhalation intakes in which material was later swallowed. Table 5 gives worst case dose estimates for marrow, skeleton and gastrointestinal tract based on the initial body burdens in Table 3.

TABLE 5. Worst Case* Dose Estimates for Skeleton, Marrow, and GI Tract for the Marshallese Islanders Based on Estimates of Initial Radionuclide Body Burdens

Estimated Radiation Dose (mGy)

Radionuclide	Bone Surfaces	Red Marrow	Intestines**
Sr-89	0.38	0.72	2.3
Ba-140	0.24	0.13	2.6
Ru-103	0.0003	0.0003	0.008
Ca-45	0.004	0.002	0.002

* Highest dose assuming all inhalation or all ingestion, inhalation class and solubility category chosen by worst case. For inhalation cases, intake assumed to be (Body Burden ÷ 0.63), where 0.63 is the fraction of a 1μm aerosol inhaled which is deposited in the lung. Dose estimates taken from ICRP Publication 30.

** Small intestine, upper large intestine, or lower large intestine - highest estimate.

4.4.4 Additional Absorbed Doses During Rehabilitation

In an analysis of the exposures to internal and external radiation sources that may have occurred during rehabilitation of Rongelap and Utirik, Lessard et al. studied the dietary intakes of cesium-137, zinc-65, cobalt-60, strontium-90 and iron-55. Based on their analyses of excreta and on in-vivo measurements, and interpretation of biological retention functions, the authors concluded that from 1954 to 2004 the inhabitants returned to Utirik will receive an additional 0.044 Gy and that from 1957 to 2007 inhabitants on Rongelap will receive an additional 0.025 Gy from these nuclides. These dose equivalents are committed effective whole-body dose equivalents integrated over the 50 years following repatriation. The values have large uncertainties associated with them because f the uncertainties in the analyses. Standard deviations associated with the estimates of committed effective dose equivalent from individual nuclides vary from 52% to over 600%. Data on the intake of plutonium-239 were limited, and no attempt was made to reach any conclusions about the dose equivalent received from this nuclide. From external radiation readings, Lessard et al. concluded that the residents of Utirik will receive an additional 0.041 Sv from external sources over the 50 years following rehabilitation and that the residents on Rongelap residents will receive an additional 0.017 Gy. They also project that the external exposure rate will decline to natural background levels by about 2072. These additional doses average 0.34 mGy (34 mrad)/year and 0.82 mGy (82 mrad)/yr respectively, which are comparable to rates from natural background. The cumulative absorbed doses are lower than the prompt external whole-body doses received by the Rongelap inhabitants by about a factor of 30, but are comparable to those received on Utirik. These doses, however, will be delivered over 50 years at low-dose rates.

4.5 Early Medical Findings

4.5.1 Acute Systemic Effects

About two-thirds of the individuals exposed in 1954 to fall-out on Rongelap are reported to have experienced anorexia and nausea during the first two days after exposure. In a few cases, vomiting and diarrhea were reported. Only about 5% of the Ailingnae group was so affected.

Depression of certain blood elements, especially lymphocytes and platelets, was observed over the first few weeks reaching levels of about one-half to one-fourth normal values. The change was greatest among children. Relative to the Rongelap group, this depression was much less among the Ailingnae group and the U.S. servicemen, and only slight for the Utirik group. At six weeks post-exposure, recovery of the blood elements had progressed to near but below normal values.

4.5.2 Acute Local Lesions

Itching and burning of exposed skin were reported by most of the Rongelap individuals. These symptoms were not noted by the people on Utirik or U.S. Military Personnel on Rongerik. Following subsidence of initial skin symptoms, there were no further symptoms referable to the skin until about 14 days post-exposure when lesions appeared on areas of skin that had been contaminated by fall-out and epilation of the scalp and exposed skin surfaces began.

The skin lesions and epilation were extensive among the Rongelap exposure group, less extensive among those exposed at Ailingnae, slight among the Americans at Rongerik, and absent among those exposed at Utirik. Ninety percent of Rongelap and Ailingnae people are reported to have developed lesions.

The time of onset for neck lesions, and epilation as well as the percentage of the group with such changes is included from an early report. In the early stages, the lesions were hyperpigmented in the form of macules, papules or plaques which coalesced into larger lesions. Those that were superficial underwent dry desquamation and subsequently repigmentation. Deeper lesions were characterized by transdermal necrosis and wet desquamation leaving weeping crusting ulcerations. After six months to a year, skin appeared normal. Some of the deeper lesions showed some residual damage.

Epilation is reported to have been first observed on the 14th post-exposure day. The severity was variable and occurred to the greatest extent in children. Regrowth began during the third month post-exposure and was complete at six months with hair of normal texture, color and abundance.

Discoloration of nails (i.e., radiation onyx) occurred in a large proportion of those exposed at Rongelap and Ailingnae. It was first documented on the 23rd day post-exposure. A bluish-brown pigment appeared first in the semilunar area of the fingernails and grew out as a band. At six months it was gone from nearly all individuals.

4.5.3 Other Early Health Effects

There were essentially no other significant medical findings in the early period of a few weeks and months post-exposure. However, none was anticipated (probable) based on the doses estimated.

4.5.4 Association Between the Early Medical Findings and the Radiation Exposure

The early findings summarized above were reported in detail in the clinical reports (5). Their incidence and severity are consistent with current knowledge and experience of the acute effects of radiation doses in the ranges estimated for the Marshallese. The systemic effects are attributable to external whole-body exposure to penetrating (gamma) radiation. The lesions of the integumentum are consistent with exposure to beta radiation from fall-out deposited non-uniformly over exposed body surfaces. However, attribution of the reported early medical findings to the doses of radiation received is circuitous, because the dose were estimated primarily on the basis of the acute clinical effects. Nevertheless, it is highly probable, even definite, that the observed early effects were caused by exposure to radiation, associated with the Bravo detonation. Thus the observed early effects are probable, both in terms of radiation exposure and estimated doses.

4.5.5 Association Between Subsequent Health Experience of the Marshallese and Their Radiation Exposure in 1954

4.5.5.1 Medical conditions probably related to the radiological exposure

Based on current scientific knowledge of the health effects of the types and levels of radiation to which the Marshall Islanders were exposed, the following medical conditions probably are related to radiation exposure to internally deposited radionuclides incorporated by the Marshall Islanders from the fall-out in 1954. Each condition is discussed in terms of the period of time during which each is expected to appear among individuals who received sufficient exposure.

Thyroid nodules probably resulted from these exposures. New cases would be expected to appear for the first twenty-five to thirty years following the exposure, that is during the 1981 to 1985 five-year period.

Decreased thyroid function and thyroid cancer most probably resulted and (can be expected to appear up until the year 2000 years) and the population can be considered at risk of developing these conditions through the year 2000.

Inheritable, genetic, effects may have resulted and would be expected to be expressed most frequently until 1980. Expression could continue throughout the entire period until the year 2000 and beyond, but probably not in sufficient numbers to be detected in this small population.

Leukemias, other than chronic lymphocytic leukemia, would be expected to have resulted up until 1980, and possibly beyond. To date only one case has been observed in the population.

Bone marrow depression, aplastic anemia, and male infertility would be expected to be diagnosed, if present within the first five or ten years, that is until 1965.

4.5.5.2 Medical Conditions Possibly Related to the Radiological Exposure

Medical conditions possibly related to exposure to the types and levels of radiation experienced in the Marshall Islands include:

Benign breast tumors, cancers of the brain or lung, immune system deficiencies, all of which could possibly appear, as far as is known, throughout the entire surveillance period.

Cancer of the breast, vascular sclerosis (fibroatrophy), leukemias in the second generation, if caused, would be expected to be seen beginning in the 1961 to 1965 five-year period and continuing through the year 2000.

5. THE RESPONSE 1954-1992

Following the initial medical evaluation and period of care in 1954, medical teams reexamined the exposed population at intervals of 6, 12 and 24 months post exposure. In 1956 the Atomic Energy Commission (AEC), with the concurrence of the government of the Trust Territory of the Pacific Islands requested BNL to establish a regular, continuing medical examination and treatment program for the exposed Marshallese population.

The purpose of the medical surveillance was to document the health status of the exposed population, to identify radiologically-related illnesses, and to help provide specialized medical care to this remote, underserved population. Primary care remained the responsibility of the Trust Territory medical department for all Marshallese.

5.1 Follow-Up 1954-1992

5.1.1 Actions

In 1954 a program of at least annual medical team visits to the Marshall Islands was established by BNL. The program involved physicians from many medical institutions in the United States. These physicians provided expertise in several medical specialties to ensure a complete evaluation of the exposed population. Over the years these specialties included internal medicine, radiology, ophthalmology, pediatrics, gastroenterology, cardiology, endocrinology, and others. Medical technologists, nurses, and dentists also participated. A Trust Territory medical officer also participated, when available.

In 1972, BNL assigned a physician from its Medical Division to provide greater continuity of medical care. This was discontinued in 1981.

Members of the original comparison group were selected randomly in 1957 from residents of Majuro Atoll (Majuro). They were individually matched by age and gender with the combined Rongelap and Ailingnae groups.

Somewhat later, an additional 200 persons thought at the time to be unexposed, and who had moved to Rongelap from neighboring atolls, were added to the group and followed medically at yearly intervals. Over the years the composition of the control group has varied due to non-participation, mortality, and loss to follow-up. As of the 1989 survey, approximately 135 persons were still participating, including 60 remaining from the original unexposed group of 86. Follow-up by BNL at that time identified 26 of the original unexposed group as deceased.

5.1.2 Findings

The medical findings of the visiting teams have been described in the literature. The early effects are described in Section 4.5. The most frequently observed late effects in the exposed Marshallese were thyroid abnormalities. Growth retardation though to be related to hypothyroidism was observed and its relationship with radiation was established. Benign and malignant thyroid nodules developed beginning nine years following the event. One case of acute myelogenous leukemia, probably related to radiation exposure, was diagnosed in 1972. In addition, the general health of the population has been documented. Other malignancies have been seen and therapy provided. The relationship of these latter malignancies to the exposure is not known and cannot be firmly established due to the conditions discussed in Section 5.5. Without individual thyroid dose estimates, radiation exposure cannot be established to be causal. However, other risk factors (dietary iodine deficiency, head and neck irradiation for medical purposes, dietary or environmental goitrogens) did not appear to be prominent in this population.

5.2 What Should Have Been Done

The medical surveillance of the Marshall Islanders from 1954 through 1992 cannot be faulted considering the geographic, transportation, social and political considerations of the area, and due to the lack of dose information on specific individuals. These services included detailed medical examinations that comprise all feasible medical history, clinical examinations, and laboratory, and hematological testing, that were possible under the field conditions. The activities even included such exceptional measures as the construction, transport and use of whole-body counting, and x-ray including mammography examinations. These are well-documented (7). In addition, state of the art medical surveillance and care was modified when applicable to incorporate newer procedures as they became available.

The efforts to collect, study and publish information describing what occurred were complete and admirable. Efforts to perform epidemiological research using these data were very aggressive, considering the lack of accurate background incidence data and other factors discussed in Section 5.5.

5.3 Primary Purposes of Medical Surveillance

The medical surveillance that began in 1955 in response to the contamination of the Marshall Islanders from the Bravo test should have been planned for the following primary purposes:

- To assess the need for additional medical services to treat conditions caused by deterministic doses of radiation, or by secondary infection of the primary radiation skin damage,

- To detect and ensure early treatment for the medical conditions that were known or assumed to be associated with radiation,

- To augment the local medical care resources in order to make the diagnosis and treatment of radiation-induced medical conditions possible,

- To determine, describe and document all medical conditions which resulted in the exposed population over time, including the recording of mortality data including the causes of death, when known, and

- To record and identify any unexpected health outcomes that possibly were related to the exposure, (if they became evident).

These medical activities did, in fact, uncover and document an unexpected incidence of both benign thyroid nodules and thyroid cancer.

5.4 Factors Limiting Epidemiological Studies of Exposed Marshall Islands Population

The medical activities provided the Marshall Island population would not be expected to be of value for effectively evaluating (measuring) the dose-response relationships between exposure and disease or to test hypotheses in this regard. The problems detailed in this section preclude (prevent) effective application of the information for this purpose. Briefly these problems include:

- the lack of individualized exposure measurement or estimation,
- unknown rates of naturally occurring disease in this population,
- the small number of individuals exposed,
- lack of preexisting formal birth, death and other vital records, and
- the inability to define a comparable unexposed control population.

In addition, the victims of the radiation incident did not, and are not likely to continue to appreciate being perceived as experimental subjects. Specific problems are discussed below:

5.4.1 Incomplete population identification

The total exposed population may not have been completely identified and the control population selected may have included individuals with some exposure. Rongelap, Ailingnae, Utirik and Rongerik (U.S. servicemen) were exposed atolls. In early studies these were selected as exposed because they were "nearby" and inhabited, and thought to be downwind of Bikini, the test site. However, several other islands also may have received fall-out. The following are data (several justifications for) that support this supposition:

5.4.3 Possible Exposure Misclassification

Radiation doses received by residents on the other atolls may have been as high or higher than the residents of Utirik. The residents of other atolls were not evacuated as were those on Rongelap and Utirik and may have had continued exposure.

5.4.4 Pooled Exposure Data

The use of pooled urine samples and population dose estimates resulted in the inability to assign dose estimates to individual Marshallese Islanders.

5.4.5 Uncertainties in Instrument Calibration

Instruments used for measuring exposure were uncalibrated in some instances. Variations and errors in the collection and analysis of urine samples used in the radiation dose estimates also were reported.

5.4.6 Possible Case Ascertainment Bias

- Diagnostic differences may exist between the exposed and unexposed control populations because medical services have been provided by different systems. The unexposed control group has been referred to the Marshallese health care system if further work-up was indicated. Further referrals are made on the basis of priorities established by a medical committee in Majuro. The exposed group has been referred to tertiary care centers in the U.S. by a medical screening team.

- Regular participation in a medical screening program may reduce all-cause death rates among Marshall Islanders. If so, the result may be underestimation of the effects of radiation.

- Vital record information was obtained from informal sources. Because medical visits were periodic, interim cause of death information was obtained largely from verbal accounts from family members, and some records kept by local health aides. In addition, health records and death certificates are available from Ebeye and Majuro hospitals, but the accuracy and validity of these records are unknown. Autopsies are rarely performed in the Marshall Islands.

- Not all causes of death were confirmed by pathological diagnosis. Of eight possible cancer-related deaths in the follow-up population, only four have been confirmed by pathological diagnosis. In the Rongelap population, only three of five deaths attributed to cancer have been confirmed by pathologic examination.

5.4.7 Lack of detailed Environmental/Lifestyle Data

- Sparse data existed on contamination of fish, coconuts, other edible vegetation, animals (pigs, chickens) and other foods in local diets

- Specific dietary histories of each atoll/cultural group were not available

- There was a lack of information on individual consumption rates from locally grown food vs imported food supplied by the U.S.

- Sparse meteorological data such as wind directions

- Sparse data on air, soil, water, and other local media such as "coral gravel" contamination

5.4.8 Lack of Statistical Power

The extremely small numbers of exposed and non-exposed participants, rarity of disease outcomes, low mortality from target outcomes (ex., thyroid cancer), and natural fluctuations in disease occurrence all serve to make statistical interpretation of outcome events extremely difficult. Even if the exposed group were re-defined to include residents of islands originally though to be unexposed, if a truly non-exposed population could be identified, and if the exposed to non-exposed ratio were increased (ex., four non-exposed participants for every exposed participant), it is doubtful if the statistical power would be sufficient to enable statistical conclusions to be drawn for any outcome except possibly thyroid nodules or thyroid deficiency.

5.4.9 Possible Selection Bias

- Self-selection bias is possible due to voluntary participation in the medical surveillance program

- Some persons moved to the larger populated areas (exposed and non-exposed) and could not be located. To the extent that these persons differ from those not relocating, (i.e., are healthier, better educated, etc) selection bias may be introduced.

5.4.10 Pre-existing Health Status of the Marshallese

The general health status of both exposed and non-exposed inhabitants could have confounded interpretation of epidemiological data. Early surveys of the island community demonstrated unsanitary conditions with regards to flies, garbage disposal, and excretory habits, which made for multiple parasitic infestations and diseases in the population prior to their exposure. After the Bravo detonation, there were numerous serious epidemic diseases, such as poliomyelitis, influenza, chicken pox, and pertussis. The extent to which such diverse clinical conditions could have modified the health impact of radiation exposure, or affected interpretation of radiobiological data is unknown.

6. ADVANCES IN RADIATION DOSIMETRY

Significant improvements and advances have occurred in the methods and technologies available for personnel and environmental radiation monitoring and dosimetry, metabolic modeling and internal dosimetry since the Marshall Islands accident in 1954. This section addresses the use of such technologies in evaluating persons involved in a comparable accident today.

6.1 Radiation Dosimetry: Physical Methods

If an accident of similar character and magnitude occurred today, the approach to radiation dosimetry would involve the use of considerably more detailed and precise methods than were available and applied in the 1954 accident.

Current radiation accident response would include immediate deployment of the equipment necessary to conduct a fairly extensive evaluation of the dose from various sources of radioactive material. These surveys would yield information about external radiation fields, environmental radioactive contaminants, and individuals' radionuclide body burdens and excretion rates. Newer technologies would enable more detailed characterizations of the types of radiation involved and their energies than were possible at that time. Also, various predictive models, often in the form of computer software, are now available that may enable more thorough evaluation of plume behavior, transport of contaminants, and internal doses. These assessments would improve the reliability of the data needed for estimating radiation doses to individuals from these sources.

6.1.1 External Whole-Body Dosimetry

The various types of integrating dosimeters with filters of different thicknesses and composition that are now available can distinguish between hard and soft electrons, hard and soft photon doses, and various neutron components. Survey meters also have been refined to provide more accurate measures of the contributions of the different types of radiations, and in some cases to provide information on the energy spectrum and directionality of incoming radiations. Use of this equipment would allow reasonably good description of the integrated doses received from the plume, and possibly knowledge of the time history of how the doses were received as well. In addition, *in-situ* measurements of ground, air, and water contamination may provide input to various published results or computer models which predict doses to the skin and internal organs of the body from such sources external to the body.

6.1.2 Skin Dosimetry

Uncertainties in the radionuclide mixtures, matrix densities, and exact distribution on the skin limit the precision of the estimates of the expected radiation doses to the sensitive layers of skin. In cases in which a well-defined monoenergetic beam or perhaps a single nuclide contributes to skin dose over a well-defined time-frame, and in a known geometry, calculations yield reasonably accurate prediction of the magnitude of radiation doses expected. In a case involving an unknown mixture of fall-out nuclides in an unknown distribution over the skin within an ash of undetermined constitution, the best estimates of the actual doses received are obtained after the fact through observation of the severity of actual effects suffered.

6.1.3 Internal Radiation Dosimetry

Substantial progress has been made over the last ten years in the development of anatomical models for adults and children, as well as in understanding of the physiology of certain elements. The important issue in the evaluation of the internal radiation doses is accurate quantitation of the nuclides taken in and their pathways. The best input to these models is measured data on the retention and excretion of the radionuclides. This requires the availability of some equipment, including *in vivo* detectors, and *in vitro* sampling and analysis equipment. Characterization of the radionuclide content of the body and associated excretion rates can be assessed with germanium-based detector systems, some of which can give fairly accurate assessments of activity in the skeleton and lungs by direct measurements over these areas. Sampling of excreta also is a well-developed science, and extremely sensitive analyses exist for all forms of internal contamination. The knowledge of retention and excretion functions is fairly well-accepted, and is certainly much better established than at the time of this incident. However, if poor or limited data exist, the use of these models will produce results with large uncertainties. For instance, the use of a single sample of pooled urines obtained 15 days after the initial intakes, will have a very poor predictive potential. If periodic sampling is conducted for individuals beginning shortly after exposure to catch short lived radionuclides and characterize early clearance, analyses of internal doses can be made with good confidence. Long term follow-up, by continued in-vivo counting can also result in characterization of retention patterns and dosimetry of radionuclides sequestered in the thyroid or skeleton that are reasonably accurate.

6.2 Radiation Dosimetry: Biomarkers

Several biomarkers are currently in use or under investigation as tools for estimating biological dose in populations exposed to ionizing radiation (38). Among these are assays that detect chromosome damage and somatic mutations at the hprt or HLA-A locus in peripheral blood lymphocytes and two assays that detect mutations induced in erythroid stem-cells that are subsequently expressed as variants or mutations in erythrocytes (i.e., hemoglobin variants or mutations at the glycophorin-A [GPA] locus). Each of the assays for mutations has advantages and disadvantages. For example, GPA analyses are automated and can be rapidly accomplished on large numbers of blood samples. However, mutations are only detected in heterozygotes, the assay requires several weeks post-exposure for expression of stem-cell mutations, and it is not possible to produce in vitro dose response curves as calibration standards.

By far the most sensitive biological method that is currently available for estimating whole-body radiation dose soon after exposure is cytogenetic dosimetry using radiation-induced chromosome aberrations in cultured lymphocytes as the biomarker of exposure. The Bravo accident occurred some six years before techniques for the culture of lymphocytes were first published and a full decade before the first suggestion that radiation-induced chromosome aberrations could be used as a biological dosimeter to estimate absorbed dose in irradiated persons. Although it was not possible to employ this technique in studies of the Marshallese in 1954, evaluations of chromosome aberrations or micronuclei in cultured lymphocytes would be the biological method of choice for estimating dose in individuals if such an accident occurred today.

During the last three decades, cytogenetic methods have been widely and effectively applied for estimating dose among exposed persons in radiation accidents that have occurred world-wide including the Chernobyl; Goiania and El Salvador accidents. In-vitro dose-response curves have been generated for chromosome aberration induction in lymphocytes exposed to a variety of radiation qualities, and such curves are readily available to serve as calibration standards for comparing with findings in recently exposed persons. When blood samples are obtained promptly after exposure and delivered to laboratories with a minimum of delay, cytogenetic evaluations using classical staining for radiation-induced dicentric chromosomes can detect average whole-body doses of about 100 mGy and above in the exposed individual. As newer techniques are being developed, for example, the use of fluorescence in situ hybridization techniques to "paint" chromosomes, combined with automated systems for metaphase location and possibly metaphase analysis, it is possible that the sensitivity of as low as 50 mGy may be achieved in the future.

In instances when several dozen to several hundred persons are exposed, single laboratories could not be expected to have the capability for providing timely dose estimates for each individual; however, collaborative efforts between several laboratories in the international community have been successful in the past, as has been demonstrated in several biological dosimetry evaluations in persons exposed during the Chernobyl accident. Similar approaches could be used should a major radiation accident involving large numbers of persons occur in the future. When cytogenetic analyses are employed as biomarkers of dose, consideration should be given to the following issues:

6.2.1 The Limitations of the Technique

Evaluations of radiation-induced chromosome aberrations in cultured lymphocytes serve as useful "integrating dosimeters" that would provide information relative to whole-body exposures in the range of 100 or more mGy. Such evaluations would not provide relevant information regarding localized dose to the thyroid or to other organs resulting from internal deposition of radionuclides.

6.2.2 The Need for Baseline Data

Information should be collected on baseline or background frequencies of various types of chromosome aberrations and micronuclei in cultured lymphocytes in the particular population having suspected exposures. Careful, unbiased, selection of age-and sex-matched control individuals would be imperative if biomarkers were to be used to estimate levels of whole-body exposure to penetrating external radiations. Such data would be particularly important in a group such as the Marshallese since the inhabitants of the islands are genetically isolated and consanguinity is common, and as discussed in Section 5.5.11, the general health status of the population could be a potential confounder in interpretation of cytogenetic findings.

6.2.3 Preservation of Tissue

If such an accident occurred today, it would be prudent to establish a repository of cryopreserved tissue samples from both exposed and non-exposed persons that would provide material for detailed study at some time in the future. Purified preparations of peripheral blood lymphocytes could be preserved for viability and maintained in liquid nitrogen, whereas other nucleated blood cells could simply be frozen to provide DNA for analysis.

7. RECOMMENDATIONS FOR FUTURE FOLLOW-UP

In this section, general and specific recommendations are made for the follow-up from the present through the year 2000, of the inhabitants of the Marshallese Islands who were involved in the nuclear test accident in 1954. The basis for the recommendation also is provided.

7.1 General Recommendations

Follow-up by medical surveillance should continue and build on the past efforts, focusing on describing the health status of the exposed population, early diagnosis of disease, and assuring proper treatment and referral. Clinically appropriate new tests suitable for use on site should be introduced as they become available. Quality assurance procedures should be strengthened and future observations carefully documented.

7.2 The Basis for the Recommendations

The basis for the recommendations include:

- The humanitarian and ethical need to monitor the health of this population to assure early detection of disease and appropriate treatment.
- The Marshall Island population has been extensively studied (clinically well-studied) since the exposure in 1954.
- A dose-related increase in the risk of neoplastic disease has been established as the major late health effect of exposure to ionizing radiation (see Section 3).
- Apparent increases have been reported in other populations exposed to radiation in the risk of some non-neoplastic diseases e.g., cardiovascular disease, and of non-specific life-shortening (see Section 3).
- Deterministic effects, such as cataracts, and vascular sclerosis and associated tissue atrophy, can become clinically detectable only months or years following exposure to relatively high levels of radiation (see Section 3).

- Contamination outside the defined area: Environmental assessment samples (soil, vegetation) suggested that fall-out contamination was not confined to Rongelap and Utirik.

- Radioactivity measured on "unexposed" atoll: An instrument measured dose at Ailuk, previously classified as "unexposed" was 0.01 Gy/h (1.0 rad/h) one hour after detonation.

- Plume reconstruction probably was inaccurate: A computer simulation using all available meteorologic data indicated that the initial path of the fall-out cloud followed was in an easterly direction, but then it shifted to a south/southwesterly direction. This computer simulation was criticized later as being based on wind data that was too sparse to provide sufficient support for conclusions as to the trajectory of the radioactive cloud.

- The prevalence of thyroid nodules among populations classified as "unexposed": Thyroid nodules ranged from 1-10.6% among residents of atolls previously thought to be "unexposed" compared to 2.4% background prevalence in two southern islands farthermost from Bikini, a statistically significant increase. A well-designed retrospective cohort study of thyroid neoplasia in 7,266 Marshall Islanders from 14 atolls of which 2,273 were alive in 1954 and were potentially exposed to Bravo fall-out was published in 1987.

5.4.2 Duration of Follow-Up

Follow-up of the exposed cohort differed from that of the unexposed group.
Follow-up of the exposed group began in 1954, whereas it did not begin until 1957 for the unexposed group, and some deaths among the unexposed group already had already occurred during the intervening three years.

- The lack of the necessary data to conduct valid analytic epidemiologic studies (see Sections 4 and 5).

7.3 Medical Surveillance

7.3.1 End-points of Interest

7.3.1.1 Neoplastic disease

Additional neoplasms are expected to occur as this population ages, therefore a major focus of follow up should be on their detection. However, because of the lack of data to conduct valid analytic epidemiological studies it will not be possible to estimate the magnitude of the risk of neoplasms that is attributable to the radiation exposure relative to the baseline intake of neoplasms in this population unknown. For certain malignancies, such as leukemia, should they occur, some indication of the relationship may be possible through the use of the NIH Radioepidemiological Tables (National Institutes of Health; 1985). Unfortunately these tables are based on observed health effects and mortality rates in other exposed populations and so may not be applicable to the Marshall Islanders.

Follow-up of this and other radiation-exposed populations suggests that thyroid tumors have been and will remain the major risk of radiogenic neoplasms among the Marshall Islanders.

7.3.1.2 Non-neoplastic and Non-specific Aging Conditions

Cardiovascular and other non-specific aging conditions are also expected in this aging population, but they are likely to be related to factors other than radiation exposure.

7.3.1.3 Late Deterministic Effects

Because of the long interval (39 years) since the exposure, and because the estimated radiation doses were below accepted threshold levels for such deterministic effects, radiogenic cataracts and fibroatrophy of tissues other than skin and permanent infertility were and are unlikely to occur. Radiation-induced thyroid hypofunction has been observed in the population and warrants continued surveillance. Individuals who experienced beta-burns should continue to be monitored for atrophic skin changes.

7.4 Specific Recommendations

Continued periodic medical evaluations are recommended for the individual members of the exposed populations through the year 2000. The value of the comparison group as originally established is questionable because of its small size, the different referral practices, and other factors that could differentially influence population's responses to radiation. However, since all residents are offered the yearly medical examination, they may contribute to the establishment of background rates for various disorders.

7.4.1 The Medical Surveillance Team

The team should continue as a U.S. visiting medical team with representation from the Marshall Islands' Trust medical care system. Team members should include physicians, nurses, and laboratory and x-ray technologists. Also, assisting logistics and technical personnel with the appropriate skills and training will be needed to collect medical data and to operate the laboratory and x-ray equipment in the field.

The team should visit the islands at least annually. In addition to the medical department of the Marshall Islands' government, a medical aide also should be available on-site to provide or request medical assistance and to monitor and immediately report health events including deaths that occur in the interim between medical team visits.

7.4.2 The Scope of the Periodic Medical Evaluations

The periodic medical evaluations performed by the team throughout the period should include standardized examination components. Elements may be added when indicated by changes in medical knowledge or in response to changes in observed health status of the population. For planning purposes there is no apparent basis to anticipate a need for changes in the standardized examination at five year intervals. Each standardized examination should include:

7.4.2.1 Interval History

The medical history should include name, place of residence, birth date, gender, education completed, occupation if employed, smoking history, alcohol consumption, medical history, family history of medical conditions, and descriptions of illnesses, injuries and pregnancies since last examination. It is assumed that information concerning, location during fall-out, evacuation, and return to resident island has already been recorded.

7.4.2.2 Physical Examination

The standardized examination data should be recorded on a standard form, and include height, weight, pulse, blood pressure, skin examination, eye examination, (including fundus photography and slit lamp examination as clinically indicated), general examination to include head and neck, chest, abdomen, skin, and extremities, and a prostate (males) or pelvic examination with PAP smear (females).

7.4.2.3 Clinical Laboratory Tests and Measurements

The periodic standardized laboratory testing should include urinalysis to evaluate renal function and glucose metabolism; microscopic examination is recommended if blood, protein or other abnormalities are found. A hematologic profile that includes a complete blood count (CBC) with differential white cell counts, and a hematocrit, should be performed if logistical feasible. A thyroid profile that includes the TSH and T_4 assays, should be conducted routinely because of the increased incidence of thyroid function in this population (see Section 3). Additional tests of endocrine function, and blood chemistry determinations should be performed as clinically indicated in the judgement if the physician.

7.4.2.4 X-ray Examinations

If clinically indicated, radiographic procedures should include a chest x-ray and other radiographic procedures. Women should be offered mammograms at the ages and the intervals recommended in the American Cancer Society protocol.

7.4.2.5 Referrals for Special Procedures/Consultations

Team physicians should continue to be authorized to refer individuals for further evaluation and treatment as necessary.

7.4.3 Vital Records

A history of mortality and morbidity in the population should be obtained by recording medical information about each examinee's relatives and acquaintances. This information should include questions about causes of any deaths and illnesses occurring since the last examination to augment existing vital records systems. This is necessary because deaths may occur without medical attention and autopsies are rarely performed. This and other information obtained from examinees about their relatives and acquaintances also can assist on tracking individuals for future follow-up.

7.4.4 Medical Records

Medical record data should be recorded in a standardized format, and the records retained by the visiting team with copies made available to the medical department of the Republic of the Marshall Islands. The Department of Energy's contractor responsible for the medical follow-up of the population should maintain these records. These should be treated as confidential. The records should be microfilmed or copied and a duplicate set kept separately from the original records and retained indefinitely. The records should include illness diagnoses, coded according to the International Classification of Disease, Clinical Medicine, Ninth Revision (ICD-CM-9). Causes of death should be coded according to the International Classification of Disease, Adapted for use in the U.S., Ninth Revision (ICDA-9).

All information obtained from interviews, laboratory tests, other diagnostic procedures and examinations should be computerized either on-site or in the U.S., to facilitate subsequent summarization and description of the data.

7.4.5 Quality Assurance

Data collection forms should be standardized and designed so that interviewers will require minimal instruction to obtain and record data in a consistent manner. Completed records should be reviewed for clarity, and consistency. Any missing information should be obtained if possible. Additional services will be required to validate the quality of medical data collected, (e.g., referral to original records to verify pertinent items of self-reported data). These data should be preserved and retained indefinitely.

7.4.6 Other Procedures Considered but not Recommended

7.4.6.1 Screening by High Resolution Ultrasonic Imaging

Although most experts agree that high resolution ultrasonography is useful at referral centers to evaluate palpable thyroid nodules, opinions differ about its usefulness as a screening tool in the field because of its high sensitivity and lack of specificity in identifying non-palpable lesions. For example, in the adult U.S. population the prevalence of palpable thyroid nodules is estimated to be about four percent; however, the true prevalence of nodules as indicated by autopsy studies or by high-resolution ultrasonography is estimated to be about 40 to 50 percent. The clinical significance of such non-palpable lesions is considered to be negligible. Should U.S. DOE decide to include its use in future medical evaluations of the Marshall Islands' population, only palpable nodules should be biopsied; non-palpable nodules should remain under medical surveillance pending observation of any significant changes in their clinical status (39-41).

7.4.6.2 Chromosome studies of cultured lymphocytes

Chromosome studies of cultured lymphocytes for radiation dose estimation are not recommended for this population.

Long-term follow-up evaluations have been conducted in several populations having previous radiation exposures, including survivors of the atomic bomb at Hiroshima and Nagasaki. The frequencies of "persistent" stable chromosome aberrations in cultured lymphocytes, and mutations at the glycophorin A locus show some correlation with radiation dose among groups of persons who were exposed up to 40 years ago. However, such long-term follow-up studies show considerable variability among persons thought to have received similar doses. Thus, such evaluations provide information that may be useful in comparing radiation dose between groups of persons having low, medium, or high exposures, but do not provide information regarding levels of exposures of specific individuals within groups. Because it has been almost 40 years since the residents of Rongelap, Utirik, and Ailingnae were exposed, and the population has since experienced numerous incidental secondary diseases and/or exposures, and no baseline data on similar genetic isolate groups are available, evaluations of chromosome aberrations in cultured lymphocytes or other types of somatic cell mutations are not likely to yield any relevant scientific information regarding radiation levels received at the time of the Bravo detonation.

8. CONCLUSIONS

The scientific and technical literature relating to the exposure of the inhabitants of the Marshall Islands to ionizing radiation in 1954 was reviewed to evaluate the appropriateness of the follow-up of the population from 1954 to the present, and as a basis for recommendations for its follow-up from the present through the year 2000. The following conclusions were drawn:

1. The scope and nature of the early medical management and subsequent monitoring and care of the exposed Marshall Islands' inhabitants, are judged appropriate by current standards.

2. Medical follow-up since 1954 has been sufficient.

3. There are humanitarian and ethical needs to monitor the exposed population to assure early detection of diseases, particularly cancer, that may occur as the population ages and that are possibly (though unlikely), associated with the exposure to radiation in 1954.

4. Continued follow-up by a comprehensive medical surveillance program using established medical practices and procedures on an annual basis, is recommended to meet the needs identified above.

5. Quality control of all aspects of the medical surveillance program should be assured by the use of standardized and peer-reviewed procedures of professional organizations, such as the American Cancer Society and the College of American Pathologists.

6. The value to this population of high resolution ultrasonography to screen for thyroid tumors is debatable. If it is so used, it is recommended that only palpable nodules be biopsied.

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