APPENDIX

Details of methods, data, and assumptions used in calculating ^{131}I intakes from bioassay of urine samples

The basic calculation to estimate the average intake of ^{131}I among the Rongelap community members from whom a 24-h urine sample was collected is shown in eqn (A1):

$$\bar{Q}(^{131}\mathrm{I}) = \frac{CR \times K \times \bar{V}}{EF(t) \times \varepsilon_C}, \qquad \text{(A1)}$$

where

[Latin capital letter Q with macron above] = acute intake of ^{131}I intake (Bq, group average);

CR = background adjusted count rate of ^{131}I per mL of urine (c s^{-1} mL^{-1});

K = correction factor corresponding to the radioactive decay of ^{131}I between time of sampling and time of counting,

[Latin capital letter V with macron above] = 24-h urine volume (mL) averaged over sampled population;

EF(*t*) = urinary excretion fraction for ^{131}I on day of sampling, *t* being the time elapsed between intake and sampling; and

$[\text{varepsilon}]_C$ = gamma detector counting efficiency (count per decay).

The important parameters that are discussed here are the 24-h urine volume ([Latin capital letter V with macron above]) and the urinary excretion fraction for ^{131}I on day of sampling [*EF*(*t*)]. They will be discussed in turn.

Urine volumes.

The most difficult of the historical input data to interpret are the original volumes of urine

collected from Rongelap community members in 1954. Those data have been described by Harris (1954) and Harris et al. (2010) though here we present a more detailed discussion. Volumes of urine collected in 10 different samplings (8 from Marshallese, 2 from American military weather observers) are summarized in Table 1 in Harris et al. (2010). Note that all these samplings were only from adults.

The mean values of 24-h urine volumes within the first three weeks after exposure were 427 mL (n = 35), 448 mL (n = 31), and 385 mL (n = 15). In the fourth week, the mean values for Marshallese were 596 mL (n = 40), 523 mL (n = 43), 756 mL (n = 12), and 603 mL (n = 15). One and a half-months after exposure, the mean value was still only 573 mL (n = 21). Over many years, there has been discussion on whether the volumes of urine that were collected actually represented the total amounts excreted during 24 h, as the mean values of urine volume from each sampling of Marshallese appear much smaller than the daily water intakes associated with normal conditions. Water intake per day for adults in most familiar situations (temperate climates where fresh water is easily accessible) is usually 2 L or more and an uninformed view of urinary excretion is that urinary water losses should approximately equal water intake. However, that is often untrue in temperate climates and appears, according to much literature, as almost always untrue in tropical climates.

The volume of urine excreted daily varies with a number of factors that suggest a reasonable central estimate for the 73 kg adult reference male is 1,600 mL d^{-1} (ICRP 2002); however, that generalization is based on Western Europeans and North Americans (i.e., implying temperate climate situations with continual access to potable water). ICRP (2002) further notes that "during prolonged periods of high water loss or low water intake, urine output may decrease to as little as 6–7 mL kg^{-1} d^{-1}" and cites Johnson (1998). Such extreme conditions would lead to urine volumes

as small as 500 mL d^{-1}. Johnson explains in more detail that 500 mL d^{-1} is about the minimum water loss through urine to achieve proper glomerular filtration.

The description of reference man also indicates typical perspiration losses to be 500 and 375 mL d^{-1} and insensible losses (gaseus water losses via skin and lungs) to be 690 and 515 mL d^{-1}, for adult male and females, respectively (see Table 2.30, ICRP 2002). According to those estimates, total daily water losses via the skin (sweating or perspiration, plus insensible losses) would be 1,190 mL and 890 mL, for males and females, or a sex-averaged average value of more than 1 L water lost daily through pathways other than urine and feces (also see draft report of WHO 2004). These estimates of total perspiration plus insensible water losses agree with numerous other literature sources (see NAP 1986, 1993).

It is not clear from the available data whether insensible water losses result in loss of iodine from the body, but such losses do help explain the small urine volumes observed by Harris (1954). Tropical, high-humidity settings tend to favor sweating (Wright 1956; Kuno 1956; Dosios et al. 1974) over insensible losses (Comroe 1965) and sweating is known to be a loss pathway for iodine (Mao et al. 1990, 2001). All these data descriptions and data support our interpretation that the small urine volumes obtained in the Marshall Islands were a consequence of perspiration and insensible water losses. Other literature has confirmed similar losses of water through perspiration, particularly in tropical settings. For example, studies of more than 70 adult patients in Greece indicated mean evaporative water losses (via the skin) of about 1,500 to 1,750 mL d^{-1} with a range of observations of 490 to 3,600 mL d^{-1} (Dosios et al. 1974). In studies of 18 young men in the Royal Air Force transferred from the UK to Bahrain (Persian Gulf), the average daily urine volume decreased from 1,070 mL d^{-1} in the UK (before transfer to Bahrain) to 570 mL d^{-1} after transfer to Bahrain. The reductions in daily urine volume were attributed to perspiration

losses (Leithead and Pallister 1960). After transfer to a tropical environment, 48% had 24-h urine specimens smaller than 500 mL and 10% were less than 300 mL.

While the daily population-mean values of urine from the samplings of Marshallese in 1954 appear small and at first consideration, cast doubt on their validity to represent true 24-h volumes, there is not only supporting evidence that urine volumes are often small in tropical climates, there was substantial consistency among the urine volume distributions from eight different samplings, with a slight increase after 3 wk after exposure (Table 4, Harris et al. 2010).

Several other points are important with respect to understanding the volumes of collected urine. At the time of Bravo (1 March 1954), a lengthy drought was in progress in the northern Marshall Islands (Sharp and Chapman 1957; Lessard et al. 1985). According to those sources, Marshallese living on Rongelap at the time had been limited to about one pint of water (~500 mL) per day from community cisterns. Further evidence regarding the drought is from the small amounts of water in the catchments at the time of evacuation as noted by Sharp and Chapman (1957). Since 1 cup of water per day is not sufficient fluid intake for adults or children in tropical climates, it must be assumed that the additional water needed per person per day was obtained from the juice from young "drinking" coconuts. Drinking coconuts are plentiful on every atoll and island in the Marshall Islands. One medium drinking coconut can provide about 350 mL of liquid (FAO 1983).

It has been reported that at the time of fallout, the residents of Rongelap were advised by the Marshallese medical practitioner on the island, a man named Jabwe (Sharp and Chapman 1957; personal notes of P.S. Harris), not to drink the water in their open catchments because of the unknown nature of the fallout. Sharp and Chapman (1957) speculated that the native residents probably resorted to drinking more water from the catchments than advised by their medical

practitioner and supplemented their fluid intake with liquid from drinking coconuts.

The residents of Rongelap and those visiting Ailinginae Atoll were evacuated to Kwajalein around H+50 h since their exposure to unexpected high levels of fallout had been recognized by U.S. authorities. Harris was told by Jabwe that he advised the Rongelap people not to drink water on Kwajalein because of his fear of the fallout, the metallic taste of water on Rongelap Island following the detonation, and the sickness (in particular, vomiting) that some experienced after their exposure. It is not clear how much water the Rongelap people might have been consuming on a daily basis near to the time of the urine sampling (day 16 and 17 for the Rongelap group, and day 18 for the Ailinginae group). It seems to be a reasonable assumption, however, that they were consuming at least the minimum amount of water necessary for healthy sustenance in tropical climates.

Assuming that each adult was consuming more than 1 L d^{-1} as is typical in tropical locations, one explanation for the small average urine volumes is that the Marshallese did not provide complete 24-h urine samples to Harris. However, Harris has strongly disputed this (personal communication) partly based on the assurances of Jabwe that complete 24-h urine samples were collected.

If incomplete 24-h urine collections were provided, a high degree of randomness between the mean and shapes of the distributions of volumes from the eight different samplings would be expected. However, the distributions of urine volume were very similar in shape and central tendency, which suggests, by arguments of reproducibility, a degree of validity of the collected data. Our interpretation is that the volumes of urine that were sampled from adult Marshallese community members reasonably represent the true volumes excreted during 24-h periods of time.

Estimating iodine loss via perspiration.

Our premise that daily liquid intake was accompanied by significant perspiration and insensible water losses resolves the apparent discrepancy between a mean value of about 500 mL collected in urine samples and an average daily consumption of water of about 2,000 mL. It is well established that evaporative fluid loss in the tropics is much higher than the values usually accepted for temperate countries (Elebute 1973) and water loss through perspiration in tropical climates can equal or exceed that lost through urine (Latham 1997). Loss of stable iodine (normally obtained through dietary intake) via perspiration has been recognized as a significant loss mechanism, in particular for athletes and those living in hot or tropical climates where perspiration losses of body water can be large. Studies in Taiwan (Mao et al. 1990, 2001) of iodine loss in sweat from athletes indicate that iodine concentrations in body sweat are the same before and after strenuous exercise. Mao et al. suggested that the lack of significant differences in these various situations suggests a physiologically-based consistency to the amount of iodine lost in sweat per unit volume. In a study of 13 athletes during 8 consecutive days, Mao et al. found that 37 ± 6.6 µg iodine per L of sweat was lost and reported that average adult excretes approximately 400 to 600 mL of sweat daily through perspiration and excretes about 22 µg iodine in the sweat. The data of Mao et al. (1990) represent the best known information on iodine loss (on a concentration basis) through perspiration.

Daily stable iodine intake.

It is also of importance to make a reliable estimate of the average daily intake of stable iodine among Marshallese in order to partition the daily excretion of iodine among urine, perspiration, and feces.

Little historical data are available on dietary iodine intakes among Marshallese. While iodine intakes can, in theory, be estimated through an understanding of diet and iodine concentrations in foods consumed, it has been difficult for researchers to reconstruct anything but a semi-quantitative typical diet for Marshallese during the years of nuclear testing. Though some studies of foods and food intakes have been conducted to attempt to reconstruct typical diets, those attempts have been heavily criticized (NAP 1994) for lacking quantitative validity and for sources of possible bias.

To better understand typical daily iodine intakes among Marshallese (at least contemporarily), iodine concentration measurements have been made in recent years on fish commonly caught and consumed in the Marshall Islands (Takahashi et al. 1999, 2001). Concentrations of iodine in fresh samples were about 100 ng g^{-1} in yellow-fin tuna (Neothunus macropterus), 700 ng g^{-1} in "reef fish," 5,000 ng g^{-1} in giant clam (Tridacnidae), and 6,800 ng g-1 in mixed-type salted and dried fish. Those data are reasonably consistent with other reported iodine measurements for marine fish. For example, the Chilean Iodine Education Bureau (1952), Wenlock et al. (1982), Varo et al. (1982), Pennington et al. (1995), and Haldimann et al. (2005) reported mean fresh weight iodine concentrations in unidentified marine fish to be 832 (163–3,180), 750 (320–1,440), 460, 1,160 (±880), 486 (89–1,593) ng g^{-1}, respectively. That marine fish have average iodine concentrations in their flesh (fresh weight) of a few tens of µg g^{-1} is consistent with a equilibrium between their flesh and seawater which typically has an iodine concentration of 58 µg L^{-1} (Fuge and Johnson 1986).

For Marshallese consuming traditional diets, maintaining an adequate intake of iodine could only be achieved by eating marine foods since no other foods in their diets were significant sources of iodine (Takahashi et al. 2001). The average daily intake of iodine was a function of the frequency

of consumption of fish, the species of fish consumed, and the method of preparation. For example, drying and salting fish has been shown to increase iodine concentrations about 10-fold, while one study (Harrison et al. 1965) of iodine availability in cooked fish showed that boiling fish results in a nearly 60% loss of the iodine, and grilling and frying results in losses of 23% and 20%, respectively.

A daily consumption of 200 g of reef fish (probably the most commonly consumed fish since they are caught in nets without the use of boats) would result in a physiologically adequate daily intake of 140 µg (200 g × 700 ng g^{-1}). Despite the criticisms of reconstructed diets, we note that diets described by National Academy Press (NAP 1994) had a range of seafood intakes, varying from 69 g d^{-1} to 480 g d^{-1}, with related iodine intakes of 48 to 336 µg d^{-1} (assuming concentrations typical of reef fish).

The only known measurements of dietary intake of iodine among Marshallese in past decades can be derived from the urinary excretion measurements reported by Rall and Conard (1966). They made urinary iodine measurements in Marshallese from Rongelap in 1966. From 28 urine samples, they derived an average excretion of iodine in urine of 105 µg (range of 19.5 to 279). Their average value is in the adequate range, though not particularly high compared to some populations. While the collection and analysis of the urine samples were 12 y after exposure, the Rongelap community was then living on their home atoll, having returned in 1957 following their post-Bravo evacuation. Living conditions and diets in 1966 can be reasonably assumed not to have been greatly different from 1954 when the most important exposure took place.

Urinary excretion fraction at time of sampling.

An important parameter of eqn (A1) is the urinary excretion fraction, $EF(t)$. However, there are

few empirical data available on the excretion of ^{131}I as a fraction of intake at more than one week after intake. In the case of the urine sampled by Harris in 1954, the lengthy time from intake to when urine samples were collected (>=16 d) adds substantial uncertainty to knowing the true excretion fraction for any individual or the true average for the group of people that contributed to the pooled sample. Hence, prediction of the urinary excretion fraction is necessary through calculations of an iodine biokinetic model.

Models of the time-dependent behavior of iodine in the body have been evolving since the landmark analysis of Riggs (1952). The solution of these models requires quantitative estimates of the rate of iodine transfer among compartments, though, fortunately, iodine kinetics is relatively well understood.

Iodine is essential in the body as it is accumulated by the thyroid gland in the production of the hormones thyroxine and triiodothyronine, which are essential for regulating the metabolic rate of the body. Several publications have shown that 70 µg is the daily intake requirement to maintain adequate stores of iodine in the thyroid; this value has been assumed as the normal thyroid secretion of hormonal iodine. Intakes of iodine below 70 µg d^{-1} may cause symptoms of deficiency. The fraction of iodine ingested that is taken up by thyroid at 24 h after intake and the thyroid size vary according to long-term average dietary iodine intake (Stather and Greenhalgh 1983; Zvonova 1989). Zvonova (1989) derived a relationship between thyroid uptake and dietary iodine intake, which shows that the thyroid uptake increases with any deficiency of daily iodine dietary intake. This relationship is based upon the numerous human experimental data on ^{131}I uptake and thyroid secretion. It has also been shown that larger than typical values of thyroid mass tend to be associated with iodine intake deficiency and with larger than typical values of thyroid uptake.

The fractional urinary excretions of iodine on the days of urine sampling were predicted using the ICRP compartmental recycling model (ICRP 1993) with a modification to include the perspiration loss pathway. A schematic diagram of the iodine biokinetic model assumed in this work is shown in Fig. A1. The assumptions used to derive the parameters of the iodine model were based on literature data. We assumed, for example, that the normal thyroid gland (adult) contains about 8,000 µg of stable iodine and that the organic iodine pool (protein-bound iodine, or PBI) is about 800 µg (Stather and Greenhalgh 1983; Zvonova 1989; ICRP 1993). The transfer rates from the inorganic iodide pool to the thyroid gland and from the thyroid gland to PBI are assumed to be 76 µg d^{-1}. From the PBI compartment, 80% returns to plasma with a transfer rate of 61 µg d-1 and 20% is excreted by feces with a transfer rate of 15 µg d^{-1}.

The parameters of our model are slightly different from the standard ICRP assumptions. Our assumption of 76 µg d^{-1} for the transfer rate from thyroid gland to PBI is based on the data reported by Rall and Conard (1966) for Marshallese. Those authors measured the thyroid uptake of iodine for the Rongelap inhabitants. Their estimate of 42%, based on measurements, was somewhat higher than might be expected for a population with good access to seafood. For most populations today, 30% uptake is typically assumed (ICRP 1990, 1993). Rall and Conard (1966) also reported an average urinary loss of 105 µg d^{-1}, which was assumed to be equivalent to the daily intake of iodine. An amount of iodine secreted by the thyroid of 76 µg d^{-1} is inferred from a thyroid uptake of 42% and a urinary excretion rate of 105 µg d^{-1} if both the perspiration and the fecal excretion losses are ignored.

Applying the relationship developed by Zvonova (1989), the data reported by Rall and Conard (1966), constraining fecal losses to be 15 µg d^{-1}, and using our assumption of perspiration as an additional pathway of excretion, we could not find complete concordance between a urinary

excretion of 105 μg d^{-1} and a fractional thyroid uptake of 0.42. We found that a fractional thyroid uptake of 0.42 is exactly consistent only with urinary losses of 32 to 69 μg d^{-1}, and that the value 105 μg d^{-1} for urinary losses of iodine is precisely consistent only with fractional thyroid uptakes between 0.30 and 0.35. Based on these constraints, we proposed six plausible sets of physiological parameters (Table A1) by attempting to merge somewhat disparate historical information on various measurements made on Marshallese with physiologically reasonable values for other parameters. In particular, we proposed reasonable rates of daily water intake for tropic locations, ranging from 1.5 to 2.5 L d^{-1}. To simulate the group-average urine observed by Harris, we maintained 500 mL d-1 urine excretion implying perspiration losses from 1 L d^{-1} to 2 L d^{-1}. We based the urine losses on the concept that water lost via perspiration (sweat) is the difference between water intake and daily urine volume. Those assumptions are supported by experimental studies in tropical climates (e.g., in Tanzania, see Dore et al. 1975), which showed a strong correlation (r = 0.87) between the sweat loss and the difference of water consumed and urine volume (Dore et al. 1975).

The iodine biokinetic model and its transfer rates, presented in Fig. A1, were applied to derive the daily urinary excretion fractions for iodine for the six data sets using available computer codes.[§§] Solving the biokinetic model as a function of time, *t*, gave the urinary excretion on each day following intake. The ratio of the calculated daily excretion on each day to the acute intake, specified as input, produced the values of EF on each day following intake (Fig. A2). The estimates of EF(t), i.e., the ^{131}I excretion fractions, were found to be only moderately affected by the differences in the six sets of physiological parameters. In the three sets of parameters where the urinary excretion of stable iodine was constrained to be 105 μg d^{-1} (sets 1a, 1b, 1c), the ^{131}I excretion fraction on day 16 varied at most by 37%. In contrast, among the three sets of

parameters which constrained the fractional thyroid uptake to be 42% (sets 2a, 2b, 2c), the ^{131}I excretion fraction on day 16 varied by up to a factor of two.

In this work, two of the six sets of physiological parameters with a daily water intake of 2 L d^{-1} (sets assigned as 1b and 2b on Table A1) were considered as preferred. Set 1b assumes a daily intake of iodine of 176 µg, 0.32 for the fractional thyroid uptake, 76 µg d^{-1} of iodine secreted by the gland, and 105 µg d= of urinary excretion of stable iodine. Set 2b (Table A1) assumes a daily intake of iodine of 121 µg, 0.42 for the fractional thyroid uptake, 76 µg d^{-1} of iodine secreted by the gland, and 51 µg d^{-1} of urinary excretion of stable iodine. The ^{131}I excretion fractions on day 16 from those two scenarios were similar, differing by less than 35%. Hence, we used an average of the excretion fractions from sets 1b and 2b for all intake and dose estimates. The values obtained for the ^{131}I excretion fraction are presented in Table A1; they are 1.76×10^{-4}, 1.65×10^{-4}, and 1.43×10^{-4}, for days 16, 17, and 19 after intake, respectively.

For Air Force and Army military personnel (weather observers) stationed on Rongerik, we also assumed a daily water intake of 2.0 L d^{-1} with body water losses of 1.1 L d^{-1} via urine as reported by Harris (1954) and 0.9 L d^{-1} via perspiration. The parameters of the iodine model were derived assuming a daily intake of iodine of 194 µg, 0.30 for the fractional thyroid uptake, 76 µg d^{-1} of iodine secreted by the gland, 146 µg d^{-1} of urinary excretion of stable iodine, and 33 µg d^{-1} eliminated by perspiration. Using these parameter values, the ^{131}I excretion fraction for the weather observers is found to be 1.85×10^{-4} for day 19 after intake. [Context Link]

§ Donaldson LR. Evaluation of radioactivity in the marine environment of the Pacific Proving Ground. Conference on Nuclear Detonations and Marine Radioactivity, Kjeller, Norway, 16–21 September 1963. [Context Link]

** This means that the ^{65}Zn to ^{137}Cs activity ratio at the time of fallout from Bravo was 4.07 times greater at Rongelap than at distant atolls. [Context Link]

†† The logarithms of the point estimates of ^{137}Cs intake per unit ^{137}Cs deposition had associated multiplicative uncertainties (similar in form to geometric standard deviations). These estimates were used in a conventional inverse variance weighting method (see Bevington 1969) as follows: [Context Link]

‡‡ Note to reader: A distinction is made in this paper between "residents" of either Majuro and Kwajalein and "community members" of Rongelap Island or Utrik Atoll. In the former case, we are referring to anyone living permanently on those atolls during the testing period. In the latter case, we are referring to the entire group of persons exposed on either Rongelap Island or Utrik Atoll and who were members of the group relocated from each of those atolls. [Context Link]

§§ AIDE (Bertelli et al. 2008) and STELLA (ISEE Sytems, Inc.) [Context Link]