403158

PATHOLOGICAL EFFECTS OF THYROID IRRADIATION

A Report to the Federal Radiation Council

Division of Medical Sciences
National Academy of Sciences - National Research Council
Washington, D. C.

December 1966

FOREWORD

A special Subcommittee of the National Academy of Sciences - National Research Council Advisory Committee to the Federal Radiation Council met September 19, 1966 to consider the July, 1962 Report on "Pathological Effects of Thyroid Irradiation" and to update it. The conclusions reached at this meeting and by subsequent correspondence are presented in this report and are based on information available through November, 1966. The members of the Subcommittee acted as individuals, not as representatives of their organizations.

Shields Warren, Chairman of Subcommittee on Effects of Radiation on the Thyroid Gland

Howard L. Andrews
Victor P. Bond
Leo K. Bustad
Cyril L. Comar
Louis H. Hempelmann
Albert W. Hilberg

This report was approved by the Advisory Committee to the Federal Radiation Council at its meeting on 10 December 1966.

Cyril L. Comar, Chairman

Seymour Abrahamson
Howard L. Andrews
Victor P. Bond
George W. Casarett
Louis H. Hempelmann
Samuel P. Hicks
Brian MacMahon
Joseph E. Rall
William L. Russell
Eugene L. Saenger
Shields Warren

PATHOLOGICAL EFFECTS OF THYROID IRRADIATION

INTRODUCTION

The constituent groups of the National Academy of Sciences - National Research Council Committees on the Biological Effects of Atomic Radiation, now disbanded, had met periodically since their formation in 1955 to consider various aspects of the general problem. In 1961 a report on Internal Radioactive Emitters[1] was issued, which included a discussion of the effects of iodine-131 on the human thyroid gland. A special report on the Pathological Effects of Thyroid Irradiation was issued by the Federal Radiation Council in July, 1962.[2] Enough new evidence on the effects of irradiation of the thyroid has come to hand to warrant consideration by the Advisory Committee to the Federal Radiation Council; for this purpose there was established a Subcommittee on the Effects of Radiation on the Thyroid Gland augmented by consultants with special knowledge of the field. Although parts of the available data are unpublished and incomplete, some investigations have reached a point where certain conclusions can be safely drawn.

Some of these data come from long-term studies on the effects of medically indicated irradiations involving the thyroid gland of man. Other data come from long-term animal experiments using either iodine-131 or X-rays as the source of radiation.

The human thyroid gland may be exposed to radiation from a variety of sources. Medical and dental requirements can lead to an X-ray exposure, either from a direct beam or as scatter from the irradiation of adjacent areas. Radioactive iodine may be administered for either diagnostic or therapeutic purposes. Substantial quantities of iodine-131 are produced in nuclear fission and may be released to the environment, principally during nuclear testing in the atmosphere or from some types of reactor accidents.

The most important radionuclide of iodine, iodine-131, has a very short half-life of 8 days which limits the quantities that can gain entrance into the body. Fallout from nuclear detonations or from a nuclear reactor accident may deposit iodine-131, as well as other radionuclides, including very short-lived radioiodines, on vegetation and in water supplies downwind from the point of release. The absorption of idodine-131 by inhalation will be unimportant except possibly in fallout intensities which are intolerable for other reasons or immediately following a reactor accident. Direct absorption through the skin has not been demonstrated to be an

---

[1] Publication No. 883, "Internal Emitters," 1961, of the National Academy of Sciences-National Research Council.

[2] "Pathological Effects of Thyroid Irradiation," Federal Radiation Council, Washington, D. C., July 1962.

important mode of entry of radioiodines in fallout. In sources of drinking water for major urban populations the delay between rainfall and consumption usually assures decay of iodine-131 to an insignificant level. In addition dilution and other factors are effective in reducing the fallout concentration.

Fresh food becomes, then, the main source of iodine-131 from the environment. For most foods the time delay between harvest and consumption is sufficient to reduce iodine-131 to an insignificant level. This is not generally the case with fresh milk for which the time between production and consumption averages about 3 days in the United States. There is some evidence suggesting that consumption of some locally grown vegetables and produce, even after washing and normal home preparation, could conceivably contribute to the diet amounts of the order of those from fresh milk.[3] However, there is no question but that fresh milk is by far the major contributor of iodine-131 to the United States population as a whole.

Relatively little information is available on the consumption of fresh cow's milk by people in various age groups. The most detailed study now available was completed in 1962 and presents per capita consumption by age and sex.[4,5] During the first few months of life, the intake of fresh cow's milk may be zero for infants who are breast-fed or given formulas based on processed products. From the survey study, the average for children under one year of age was about 0.5 liter per day which was maintained until late in teenage after which a gradual decline occurred. For adult males and females in the population-at-large averages were 0.35 and 0.25 liters per day respectively. The range extended from persons consuming no milk to a group comprising 1 to 10 percent who consumed more than 1 liter per day. Large individual differences were found at all ages.

The thyroid gland is unique in its relation to the metabolism of iodine in either stable or radioactive form. Weighing only about 1 to 2 grams at birth, and 15 to 20 grams in the adult, this gland has a high affinity for iodine. A normal thyroid will absorb and retain 15 to 30 percent of a small quantity of ingested iodine. The exact amount retained will depend, among other things, upon the amount of stable iodine ingested during the

---

[3] R. H. Wasserman, F. W. Lengemann, J. C. Thompson, Jr., and C. L. Comar. "The Transfer of Fallout Radionuclides from Diet to Man," Chapter 9, in Radioactive Fallout, Soils, Plants, Foods, Man edited by E. B. Fowler, Elsevier, 1965.

[4] Bureau of the Census, Department of Commerce and Division of Radiological Health, Public Health Service, "National Food Consumption Survey: Fresh Whole Milk Consumption in the United States." Radiological Health Data 4:15, No. 1, 1963.

[5] Bureau of the Census, Department of Commerce and Division of Radiological Health, Public Health Service, "Consumption of Selected Food Items in U. S. Households." Radiological Health Data 4:124, No. 3, 1963.

preceding few days or weeks. Iodine not absorbed by the thyroid will be rapidly excreted, primarily in the urine. Thus, in a short time after a single intake, the gland will contain the highest concentration of the iodine remaining in the body. Because of its great avidity for radio-iodine the thyroid will receive the largest radiation dose, particularly if the form is iodine-131.

The radiation dose delivered to other tissues will be, at most, a few percent of that received by the thyroid gland. A concentration of 1 µc of iodine-131 per gram of thyroid tissue will produce a time-integrated dose of about 113 rads,[6] ranging from 90 to 130 rads.[7] About 10 percent of this dose will be received in the first 24 hours, probably over 25 percent in the first 2 days.

When the thyroid is included in the beam from an external radiation source, such as an X-ray tube, a considerable amount of surrounding tissue will necessarily receive doses equal to or even greater than that received by the gland itself.

Differences in growth rate and histology of the thyroid from birth through early childhood have led some to believe that the infant thyroid is more vulnerable than that of the adult to injury from ionizing radiation. In addition to differences in size and proportion of proliferating cells of the thyroid in infants, children, and adults, there may be significant alterations in absorption, metabolic turnover, and cell sensitivity with advancing age. Any of these factors might affect the amount of biological damage resulting from a given radiation dose. Neither the relative importance nor the aggregate effect of these variables is known.

HUMAN EXPERIENCES

1. Direct Effects of Iodine-131

It has been pointed out that iodine-131 entering the body is promptly and selectively concentrated in the thyroid gland, or is excreted. The direct radiobiological effects are thus confined to the gland itself. The principal effects, which have been observed only after high doses of radioactive iodine, include a decrease in the metabolic activity of the gland, and at still higher doses, an atrophy of epithelial cells, and the appearance of numbers of atypical cells. These changes in function and structure are seen only after doses of thousands of rads. Thyroid cancer is an uncommon result, described with certainty to date only in animals.

---

[6]Report of the International Commission on Radiological Units and Measurements (ICRU), 1959. National Bureau of Standards Handbook 78, January 16, 1961, Washington, D. C.

[7]Silver S.: Radioactive Isotopes in Medicine and Biology. Medicine. Lea and Febiger, Philadelphia, 2nd ed., 1962, page 117.

2. Indirect Effects Mediated Through the Endocrine System

The thyroid gland is one of the several endocrine organs of the body whose activity is interdependent upon and responsive to disturbance in the functions of other members of the system. For example, when thyroid function is suppressed, there is characteristically an increased production by the pituitary gland of a hormone that stimulates the cells of the thyroid. This mechanism is the basis of an hypothesis that has been advanced to explain the production of thyroid cancer by agents whose primary effect is to impair thyroid function. The resulting over-stimulation of unimpaired or slightly damaged cells by pituitary hormone is presumed to first induce hyperplasia or other effects which may then occasionally progress to true neoplasia.

In the case of human beings irradiated as infants or children, the incidence of thyroid neoplasms rises sharply during puberty and adolescence. The high requirement for thyroid function during this period of life presumably plays a powerful secondary role in inducing neoplastic transformation of the irradiated gland. The incidence of radiation-induced thyroid disease in this group appears to fall off after age 20 to 25 years.

3. Other Indirect Effects in Cancer Induction

In the last report of this group, it was stated that the probability of developing thyroid cancer after irradiation is influenced by factors other than endocrine effects or the direct action of radiation absorbed in the thyroid gland itself. The reasons for this statement were twofold: first, the apparent absence of a dose response in thyroid cancer in persons treated with a wide range of dosage; and, second, the remarkable variation in thyroid cancer incidence in selected groups of children who received comparable doses of X-rays to the thyroid but different doses to tissues other than thyroid.

In the past four years, the data on which these conclusions were based have been reconsidered in the light of new estimates of thyroid doses in these cases under study. The radiation dose to the thyroid depends strongly upon the exact location of the gland with respect to the primary beam, as well as upon the air dose. By estimating thyroid dose using reasonable assumptions as to beam port placement, it is possible to show a strong dose response for radiation-induced thyroid neoplasms. Furthermore, the remarkable variation in incidence of thyroid cancer in selected groups of persons who received comparable air doses of X-rays can be explained by the variation in thyroid dose resulting from variations of the geometrical relations to the primary beam. Although the possibility that irradiation of other tissues may have influenced thyroid tumor induction cannot be excluded, it is not necessary to invoke this hypothesis to explain the observations.

4. Diagnostic and Therapeutic Exposure to X-rays

a. Diagnostic X-ray

In various diagnostic procedures such as radiography of the teeth, cervical spine, or larynx and fluoroscopy of the larynx or esophagus, the thyroid gland may be exposed to a fraction of a roentgen up to several roentgens. These are frequent procedures, and to date no examples of cancer of the thyroid have been attributed to such exposures. However, systematic effort to determine such a relationship has not been made to our knowledge.

b. Therapeutic X-ray

In radiation treatment of hyperthyroidism, the thyroid gland may be exposed to doses of several thousand roentgens. This procedure has been carried out on thousands of patients, and carcinoma of the thyroid is an extremely rare complication.

Another practice, no longer in common use, is to treat supposedly enlarged thymus glands in infants and children by exposing the upper chest and neck to doses of 100 r to 600 r or more of X-ray. When large treatment ports, particularly those placed posteriorly, were used, the thyroid gland often received the full depth dose from the primary X-ray beam. Similar exposures of the thyroid may result from X-ray treatment of enlarged cervical lymph nodes or skin diseases. Subsequent studies of these patients, both retrospective and prospective, by several authors, have disclosed a small but significant incidence of thyroid cancer in excess of the expected rate as determined by comparison with control groups of siblings. This indicates that the thyroid gland in children is susceptible to cancer induction by radiation at relatively high doses. Evidence at low doses is incomplete.

5. Exposure to Iodine-131

a. Diagnostic Procedures

The use of iodine-131 was introduced into clinical medicine about 25 years ago, and for 15 years it has been widely used in a variety of diagnostic procedures. Most of these diagnostic procedures utilize between 5 to 100 microcuries of iodine-131, and most of the retained dose concentrates in the thyroid. No cases of thyroid cancer induction have been reported in the patients who have undergone these procedures.

b. Therapeutic Procedures

The principal uses of iodine-131 are in the treatment of hyperthyroidism and in the management of some cases of thyroid cancer. The latter cases must be ~~exluded~~ excluded from present consideration since the radiations were acting on tissues already cancerous. There is little evidence[8] at hand that any of the treatments for hyperthyroidism has produced a thyroid cancer, although doses have ranged from a few thousand rads upward. Ablative doses would in effect rule out the possibility of tumor induction.

[8] Staffurth, J. S.: Thyroid Cancer After 131-I Therapy for Thyrotoxicosis. Brit. J. Radiol.39:471-473, 1966

From this and other evidence, it appears that iodine-131 is considerably less effective than comparable doses of externally applied X-rays in producing thyroid cancer. The magnitude of this difference cannot be stated since not a single confirmed case ascribable to iodine-131 is known. In making a comparison it must be kept in mind that X-rays are ordinarily delivered at a high dose rate in a single sitting or in a few divided doses; and the thyroid as well as the blood vessels supplying it and the adjoining tissues are uniformly exposed. In addition the age of the patients treated and their clinical conditions are rarely the same in the two types of treatment. If the radiation were administered at the same low dose rate for both iodine-131 and X-ray, the ostensible difference might not be as great.

6. Reactor Accident

In a reactor accident, radioactive iodine was released to the environment[1], and control measures were instituted to prevent human thyroid doses from exceeding 20 rads. No increase in the incidence of thyroid neoplasia in this area has been reported, but it must be remembered that the complete effects of this episode will not be known for many years.

7. Total Radiation Doses in Childhood Cancer of the Thyroid

Although thyroid cancer occurs in children who are not known to have been exposed to artificially produced radiation, some history of X-ray exposure has been obtained by several workers in well over half the cases in which careful inquiry has been made. The X-ray doses received by most of these subjects are difficult to determine, but by tracing the records of radiologists it appears that the smallest doses associated with subsequent cancer range from about 100 r measured in air upwards. Only a very small number at these low levels have been reported.

8. Thyroid Abnormalities in a Marshallese Population Exposed to Radioactive Fallout

The development of thyroid nodules and hypothyroidism has been noted in a number of Marshallese people of Rongelap Island in the Pacific who had been exposed to radioactive fallout in 1954.[9] This development is believed to be a late effect of irradiation of the thyroid gland from internal absorption of radioiodines and from external gamma radiation at the time of the fallout. A total of 64 Rongelap people (54 living in 1966) received a whole body dose of gamma radiation of 175 rads, extensive direct irradiation of the skin from deposition of fallout thereon and internal absorption of radionuclides in the fallout. Eighteen other Rongelap people (14 living in 1966) received a lesser exposure of about 70 rads of gamma radiation along with a smaller dose to the skin and internal absorption of less amounts of radioelements. A total of 157 individuals on the island of Utirik received a whole body gamma dose of approximately 14 rads.

---

[9]Conard, R. A., Rall, J. E., and Sutow, W. W.: Thyroid Nodules as a Late Sequela of Radioactive Fallout. New England J. Med. 274:1392-1399, 6/23/66.

During the two-day period following the accident before the evacuation of the people occurred, the inhabitants absorbed radionuclides in the fallout by inhalation and ingestion of contaminated food and drinking water. Based on radiochemical analyses of pooled urine samples taken several weeks after the accident it was estimated that the adult thyroid gland in the main Rongelap group received about 160 rads from the radioiodine plus another 175 rads from the external gamma radiation. Taken into consideration in those calculations were the time and length of the fallout period, the isotope energies and half-lives of the various iodine nuclides, and the yield of the isotopes. Similar estimates for the smaller thyroid glands of the young children ranged from 700 to 1400 rads in the more heavily exposed group. Though "beta burns" were prevalent in the neck region, it is believed the beta energies were too weak to have contributed significantly to the thyroid dose. The thyroids of the Utirik children received an estimated 55 to 125 rads from iodine, plus the 14 rads from external gamma radiation.

In 1963, 9 years after exposure to fallout, the first thyroid nodule was detected in a 12-year-old girl in the more heavily exposed group, and 2 further nodules were detected in 1964. In March, 1965, 5 other cases were noted and in addition hypothyroidism was diagnosed in two boys who had shown growth retardation. Five further cases were detected in September of 1965 and 5 more in March, 1966, making a total now of 16 cases with nodules plus two cases of hypothyroidism.[10] Only one nodule was found to be malignant. These cases are described in Table I (page 11). Table II (page 13) summarizes the incidences of thyroid abnormalities in the various populations examined. Note that 79 percent of children less than 10 years of age at time of exposure in the more heavily exposed group developed thyroid abnormalities, in comparison with no thyroid pathology noted in children of the same age range of the non-exposed population or in the lesser exposed populations. The incidence in those exposed at a greater age is considerably lower, and only slightly above that seen for the unexposed or less exposed populations. It should be noted that the only nodules noted in the unexposed population were in the older age group, that is, greater than 50 years of age.

In most cases the thyroid glands contained multiple nodules ranging in diameter from a few millimeters to a few centimeters. All were nontender, some firm, others cystic, and sometimes even hemorrhagic. No lymphadenopathy was noted. The microscopic sections of the benign lesions showed quite bizarre appearance with a wide variety of different sized follicles, some small and atrophic, others large with hyperplasia or cystic formation. The hyperplastic changes were characterized in some cases by infolding of the epithelium giving an arboreal appearance. These changes resemble those seen in iodine deficiency goiter (adenomatoid goiter). The one case of cancer of the thyroid occurred in a 42-year-old woman and was of the mixed papillary and follicular type.

A hypothyroid etiology for growth retardation noted in children in the exposed group is strongly suggested by the findings of definite hypo-

---

[10] Conard, R. A.: Personal Communication.

thyroidism in two of the most retarded boys who had atrophic glands but no nodules, and a positive growth response to thyroid hormone therapy. Their protein bound iodine levels were below 2 μg percent. Two other children with thyroid nodules showed low values also.

The radiation etiology of these thyroid lesions appears to be reasonably certain in view of the following facts. (1) The thyroid glands received a substantial dose of radiation from radioiodines and external gamma radiation. (2) Only a few older people in the unexposed or low exposure groups have shown any nodules of the thyroid gland. (3) The diet is not lacking in iodine and there are no known goitrogenic foods.

9. Atomic Bomb Casualty Commission -- Adults

The Atomic Bomb Casualty Commission has reported 14 cases of thyroid cancer among survivors less than 1400 meters from the hypocenter; 12 were found in the Hiroshima group, 2 in the Nagasaki group. These survivors had received external radiation; radioactive iodine probably was not a contributory factor. The frequency of thyroid cancer appears greater in the Japanese population than in the United States. The estimates of thyroid cancer range from 4.7 percent among all cases of thyroid disease in Japanese hospitals,[11] 3.1 percent in a study made at the Kyoto University Medical School,[12] to 13 percent at the University of Hiroshima.[13] Socolow[14] points out that although the over-all incidence of thyroid cancer may not differ greatly among the atomic bomb survivors the age incidence does differ. Eight of his 21 cases were under 35 years of age whereas at Kyoto[12] 85 percent of the cases were diagnosed after the age of 40. Three of Socolow's cases at Hiroshima were between 3000 and 3500 meters from the hypocenter. These probably received little or no radiation on the basis of the most recent recalculations of dose.[15] The estimates of doses given by Socolow for his cases range from 33 rads to 2620 rads.[14] Seven of the thyroid cancers found in the two cities developed in persons under 20 years of age at the time of the atomic bombing. The estimated thyroid dose received by them ranged from 256 to 2620 rads.

---

[11]Sano, S., Konoe, K., and Iokawa, N.: Statistics on thyroid diseases in Japan. Nihon Naibunpi Gakkai Zasshi 34 (3):230, 1958.

[12]Miyake, T., Torizuka, K., and Kusakabe, T.: Epidemiology of thyroid disease in Japan. Shindan to Tiryo 50:783-796, 1962.

[13]Kusunoki, N., Aoki, M., Nakagawa, S., and Masuda, T.: Diseases of thyroid gland. Hiroshima Igaku Gencho 7 (6):1461-1467, June 1959.

[14]Socolow, E. L., Hashizume, A., Neriishi, S., and Niitani, R.: Thyroid carcinoma in man after exposure to ionizing radiation. A summary of the findings in Hiroshima and Nagasaki. New England J. Med. 268:406-410, February 21, 1963

[15]Auxier, J. A., Cheka, J. S., Haywood, F. F., Jones, T. D., Thorngate, J. H.: Free-field radiation-dose distributions from the Hiroshima and Nagasaki bombings. Health Physics 12:425-429, March 1966.

10. Fallout in Utah

In May 1953, Washington County, Utah, was thought to have received an unusual amount of radioactive fallout from a nuclear test at the Nevada test site. The exact dosage of iodine-131 from this fallout is not known but estimates for the dose from iodine-131 to the thyroid gland range from less than 10 rad to above 400 rad. Examination conducted in 1965 of school children in Washington County, Utah, revealed several thyroid abnormalities but nothing which can be specifically ascribed to radiation as an etiological agent. Because of the fact that Washington County residents seem, historically, to have had a relatively high prevalence of thyroid disease and because children in Utah outside Washington County and in Northern Arizona at the time of fallout showed the same frequency of the more severe thyroid abnormalities as did the children who were in residence within the County, it is not possible, from this particular study, to ascribe any degree of significance to radiation exposure. If indeed the exposures to iodine-131 from fallout through the past several years were of significance throughout the State of Utah rather than confined to Washington County, the question of residence in Washington County, in May 1953, may be of little or no importance.

ANIMAL DATA

Data from animal experiments indicate that thyroid tumors originate spontaneously less frequently and may be less easily induced by radiation than tumors of some other organs. Thus leukemia is frequent in numerous strains of mice, breast tumors common in rats, squamous cell carcinoma in white-faced cattle and mast cell tumor in dogs, whereas thyroid tumors were infrequent in all except in regions where goiter is endemic. The two general types of thyroid tumors are: (1) rounded, circumscribed, benign nodules: adenomas; and (2) invasive, destructive growths: carcinomas. Adenomas do not necessarily develop into cancers but may precede them. Ionizing radiation, as well as a number of chemical agents, may induce either.

Most animal experiments with radiation have been done when the animals were young, though not in infancy. However, a limited number of sheep at Battelle-Northwest (formerly Hanford Laboratories) have been continuously exposed to various levels of iodine-131 from conception to death (up to 10 to 12 years of age). These animals have shown no thyroid tumors at dose levels giving 150 rads per year, but have shown adenomas after several years, with accumulated thyroid doses of 5000 to 40,000 rads.

Two cancers involving the thyroid gland were seen at cumulative doses of 10,000 and 30,000 rads. Thyroid exposures of 30,000 to 40,000 rads as a result of single doses of iodine-131 to young adult sheep also resulted in many adenomas after 4 to 5 years.

When rats were subjected to radiation combined with substances producing goiter (which act by reducing thyroid hormonal production and stimulating the pituitary), a few thyroid cancers were produced by 1100 rads of X-ray. About 15,000 rads were required to produce a comparable tumor incidence when iodine-131 was used as the source of radiation.

When the head and neck are exposed to X-rays, up to 5 percent of exposed rats may develop thyroid cancer. Parabiont rats develop cancer of many organs readily when one of the pair is given 1000 rads of X-ray, but cancer of the thyroid is rare.

Whole-body doses of X-rays that readily induce leukemia in most strains of mice very rarely produce thyroid cancer. Iodine-131 given to mice in large doses (delivering thousands of rads to the thyroid) will heavily damage the thyroid without causing cancer there, perhaps because of the many thyroid cells destroyed. However, this may produce adenomas or cancers of the pituitary gland, which is not itself significantly irradiated but is assumed to be stimulated to abnormal activity and hyperplasia by the absence of normal feedback from a functionally impaired thyroid.

The animal data are inadequate to permit firm conclusions, but available information suggests that cancers of the thyroid are not easily induced by radiation and that radiation from iodine-131, largely restricted to the thyroid, is an even less efficient carcinogen in laboratory animals than are X-rays.

CONCLUSIONS

1. Therapeutic doses of X-rays to the thyroid region of children have been followed after some years by the development of thyroid neoplasms. Whereas the percent of cases of malignant neoplasms is small, the proportion of persons irradiated who develop nodular thyroid disease can be extremely high. The incidence of radiation-induced thyroid disease is strongly dose dependent above 100 rads (thyroid dose). The shape of the response curve below 100 rads is unknown.

2. X-rays are probably as effective if not more so than iodine-131 in producing thyroid lesions for equal, average absorbed doses delivered to the gland at similar rates. An apparent greater effectiveness ot X-ray irradiation may be due to the higher dose rate used.

3. Whereas it was formerly believed that the induction of thyroid tumors was enhanced by irradiation of tissues other than the thyroid itself, it now seems possible to explain variability in tumor induction in children on the basis of whether or not the gland was in the primary X-ray beam.

4. Radioactive iodine in amounts sufficient to deliver several hundred rads to the thyroid of the infant or young child has been shown to produce a high incidence of thyroid nodules. Radioactive iodine has been shown to be carcinogenic in some animals. No case of thyroid cancer clearly ascribable to it has been reported in man.

TABLE I

THYROID ABNORMALITIES IN EXPOSED RONGELAP PEOPLE, 1966

			Abnormality Noted		
Case No. and Sex	Present Age	Age at Exposure	Years	Age	Findings
3, M	13	1	1965	12	Hypothyroid, PBI less than 2 µg% March 1965; retardation of growth preceded these findings by a number of years. 3/66 growth spurt and improved appearance on hormone.
5, M	13	1	1965	12	Hypothyroid, PBI less than 2 µg% March 1965; retardation of growth preceded these findings by a number of years. 3/66 growth spurt and improved appearance on hormone.
17, F	15	3	1963	12	Adenomatous goiter, complete thyroidectomy, 1964. No recurrence.
21, F	15	3	1964	13	Adenomatous goiter, complete para- and thyroidectomy, 1964. No recurrence.
69, F	16	4	1964	14	Adenomatous goiter, partial thyroidectomy, 1964. No recurrence.
2, M	13	1	1965	12	Adenomatous goiter, partial thyroidectomy, 1965. No recurrence.
20, M	19	7	1965	18	Adenomatous goiter, partial thyroidectomy, 1965. No recurrence.
64, F	42	30	1965	41	Mixed papillary and follicular carcinoma, thyroidectomy -- surgical and with radioiodine, 1965. No recurrence noted.
72, F	18	6	1965	17	3 mm. nodule left lobe. No exam 3/66.

TABLE I (Continued)

THYROID ABNORMALITIES IN EXPOSED RONGELAP PEOPLE, 1966

Case No. and Sex	Present Age	Age at Exposure	Abnormality Noted: Years	Abnormality Noted: Age	Findings
42, F	15	3	1965	14	2 mm. nodule right lower lobe; 3/66 - nodular enlargement entire gland; firm 5 mm. nodule right lobe. 7/66 subtotal thyroidectomy. Adenomatous goiter.
61, F	20	8	1965	19	6-8 mm. smooth nodule left lower pole; 3/66 1 cm. nodule left lobe. Subtotal thyroidectomy 7/66. Adenomatous goiter.
40, M	41	29	1965	40	2 mm. nodule right lower pole; 3/66 no nodules detected.
59,* F	46	34	1965	45	5 mm. nodule midline; 3/66 same. Subtotal thyroidectomy 7/66. Adenomatous goiter.
54, M	13	1	1966	13	Nodular enlargement left lobe and isthmus with 2 mm. firm nodule.
19, M	17	5	1966	17	Multinodular soft goiter-- gland 1½ normal size; 1 cm. nodule right lower pole.
36, M	19	7	1966	19	About 1 cm. nodule--not clearly demarked--right lower pole. Many tiny nodules surface of gland.
33, F	13	1	1966	13	In 9/65 questionable irregular gland. 3/66 definite 5 mm. nodule left lobe. Subtotal thyroidectomy 7/66. Adenomatous goiter, Hürthle cell adenoma.
65, F	13	1	1966	13	In 9/65 questionable small nodule; 3/66 a 5 mm. nodule right lobe. 7/66 right subtotal thyroidectomy. Adenomatous goiter.

*Exposed to only 69 rads whole body radiation and presumably proportionately less thyroid dose.

TABLE II

THYROID ABNORMALITIES (NODULES AND HYPOTHYROIDISM)--

	Age (1954) < 10 yrs.			Age (1954) 10-19 yrs.		
Island Group	No. in Group	Estimated Thyroid Dose in Rads*	% Abnormalities	No. in Group	Estimated Thyroid Dose in Rads*	% Abnormalities
Rongelap	19	I 700-1400	78.9	12	I 350-600	0.0
		γ 175			γ 175	
Ailingnae***	6	I 275-550	0.0	1	I 175-300	0.0
		γ 69			γ 69	
Utirik***	40	I 55-110	0.0	16	I 25- 55	0.0
		γ 14		-	γ 14	
Unexposed (Rongelap Utirik)	61	-	0.0	36	-	0.0

* I = Dose from β and γ radionuclides; γ = dose from external γ radiation.

** Dosage in this group was the same as in the 20-40 year group.

*** In estimating the thyroid doses to the Ailingnae and Utirik exposed group it was assumed that these doses were proportional to the corresponding thyroid doses of the Rongelap exposed group, based on relative whole body gamma dose received.

TABLE II (Continued)

--MARSHALLESE POPULATIONS EXAMINED 1964-1966

Age (1954) 20-40 yrs.			Age (1954) > 40** yrs.		All Ages	
No. in Group	Estimated Thyroid Dose in Rads*	% Abnormalities	No. in Group	% Abnormalities	No.	% Abnormalities
14	I 160 γ 175	14.3	10	0.0	55	30.9
4	I 54 γ 69	25.0	3	0.0	14	7.1
22	I 16 γ 14	4.5	21	4.8	99	2.0
48	-	0.0	49	6.1	194	1.5