

Neoplasms in Persons Treated With X-Rays in Infancy: Fourth Survey in 20 Years^{1, 2}

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SUMMARY—The incidence of neoplastic disease was determined by a mail survey of 2,872 young adults given X-ray treatments in infancy and of their 5,005 nonirradiated siblings. Newly diagnosed benign and malignant neoplasms appeared more frequently in the irradiated subjects than in their siblings or the age- and sex-matched general population of upstate New York. Only thyroid neoplasms occurred in sufficient numbers to permit statistical analysis for the effects on incidence of sex, age, and dose, and of being in a high-risk group (subgroup C). Thyroid cancers developed earlier in life than did benign neoplasms, especially in boys; benign goiters occurred after smaller doses, predominantly in females. Females had a greater risk of developing thyroid cancer than males—2.3 times for females of all ages and 5 times for young adults. Except for young adult females, there was no definite age effect. The risk of cancer (but not of benign goiter) was proportional to the thyroid dose, with a linear risk coefficient of 2.5/year/million people exposed to 1 rad for the entire irradiated population and 4.0 for subgroup C. The high risk of thyroid cancer in subgroup C may be the result of the high percentage of Jews, who had a 3.4-fold greater risk than non-Jews. Young adult Jewish females had a 17-fold increased risk. An incidental observation was an apparent increased incidence of asthma and rare diseases with abnormal immunologic features in the irradiated population.—*J Natl Cancer Inst* 55: 519–530, 1975.

Since the last survey, an excess number of neoplasms developed in the thyroid glands and, to a lesser extent, in the blood-forming tissues of the irradiated population. The data concerning radiation-induced thyroid neoplasms were analyzed to determine the effects on tumor induction of age, sex, dose, and of being in a high-risk group (subgroup C). Also noted in the irradiated population was an apparent increase in the incidence of asthma and rare illnesses with abnormal immunologic features (2).

METHOD OF STUDY

As in past surveys, one-page questionnaires (questions on both sides) were mailed directly to the subjects and their untreated siblings or to the subjects and siblings in care of their parents. Questions included a checklist of illnesses (e.g., cancer, tumors, thyroid trouble, and asthma). If hospitalization or surgery for these medical conditions was reported, the medical diagnoses and names of the hospitals and/or doctors were requested. The subject's consent for review of his medical records was obtained, and the diagnosis given by the subject was verified in a written request to the hospital, its pathology department, or the New York State Department of Health for clinical and pathology reports or death certificates. The cancer records of the Cancer Control Bureau, New York State Health Department, Albany, New York, were checked for the names of all nonrespondents, but no new cancer cases were found.

Usually the subjects referred only to an operation (e.g., operation on thyroid gland). When the specific histologic or medical diagnoses were given, however, they were remarkably accurate. Of the 167 tumors in the treated group, 52 histologic diagnoses were correctly reported by the patients; no incorrect specific diagnoses were reported. Of the 88 siblings with tumors, 26 gave the correct diagnosis. No incorrect histologic diagnoses were given, but 1 sibling with an ovarian cancer reported "stomach cancer" (not a specific histologic diagnosis). We concluded that if hospital records could not be located (e.g., as for some persons with military records), it was probably valid to accept a patient's word for a specific histologic diagnosis.

Unlike our past experience, the response rate for the mail survey was not good, particularly when the questionnaires were mailed directly to the subjects or sib-

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The present paper describes the current status of a 20-year follow-up of radiation-induced neoplasms in nearly 3,000 people treated with X-rays in infancy. The treatments were given to shrink the allegedly enlarged thymus glands—a procedure thought to alleviate respiratory distress or to prevent the sudden death of a previously healthy infant. For comparison, approximately 5,000 nonirradiated siblings of the treated group were also studied. As in the surveys conducted in 1954, 1959, and 1963 (1), information about the subjects' health was obtained primarily by mail questionnaires. This study, like previous ones, was designed to elicit information about surgically removed neoplasms (benign and malignant) and the cause of death.

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lings. The subjects, now mostly young adults, were more casual about our survey than their parents had been. Because of the indifference of the subjects, the response rate to the three questionnaires was only 70% in early 1971. To correct what was obviously an unrewarding approach, we resorted to telephone calls and found that most subjects and their siblings or parents were quite cooperative.

When the survey was terminated August 31, 1971, the final response rate was 85.4%. One percent refused to answer, 3.9% were located but failed to respond, and 9.7% (including the 3% adopted) were unable to be traced. All data were coded and transferred to computer tapes for analysis; all nonrespondents were assumed to be healthy and without tumors.

CASE MATERIAL

The roster of treated and sibling subjects was like that in previous surveys (1, 3), but the numbers were changed slightly (i.e., 2,872 treated subjects and 5,055 siblings). The population characteristics as well as the average air and thyroid doses and port sizes are shown in table 1. A more complete description of the characteristics of the irradiated and control populations is in (3). The uncertainties in estimating the thyroid doses were thoroughly described in (1).

One subgroup (C), treated by a radiologist using large doses and large ports (resulting in the inclusion of the thyroid gland in the primary X-ray beam), was considered separately from the total irradiated population. As determined by the last two surveys (1, 3), this subgroup had a high risk of developing neoplasms of the thyroid gland or other tissues. These individuals were informed of the risk of nodular thyroid disease in 1964-65, and 113 of the subjects still living in the Rochester area were seen at our hospital. Those with thyroid disease were closely followed (4, 5). The persons who had moved away from Rochester were advised to see a thyroid specialist of our choice and at our expense. By 1965, 148 subjects had been examined, with emphasis on thyroid pathology. Because they had been aware for several years of the potential medical problems, this subgroup had to be considered separately and with the total population. In the present survey, all irradiated subjects at low risk as well as at high risk were advised to tell their doctors of the X-ray treatments and to ask for a careful thyroid examination.

When subgroup C was considered separately, the remaining 8 subgroups, each given X-ray treatments in a different hospital or private office, were combined and designated as "others" or "all others."

RESULTS

Neoplastic Disease

All types of neoplasms

The total number of surgically removed, histologically verified neoplasms is shown by cell type in table 2 for the irradiated and control populations. The irradiated subjects had more than twice as many malignant and benign tumors (more than a threefold increase in incidence) as the larger group of nonirradiated siblings. As previously mentioned, the irradiated subjects of subgroup C had a much higher risk of developing neoplasms than did the rest of the treated population. Almost half of the tumors developed in subgroup C, which constituted one-tenth of the total irradiated population. Because of this and other reasons given in "Case Material," subgroup C was considered separately from the rest of the study group in table 2 and the subsequent text. Similarly, because approximately half of the neoplasms in the total irradiated population arose in the thyroid gland, thyroid neoplasms were also given special consideration. All extrathyroid neoplasms were pooled to provide sufficient numbers for quantitative analysis (table 6).

The observed and expected numbers of neoplasms in the treated and untreated populations are given in table 3. Whereas the expected and observed numbers of cancer cases in the siblings were nearly the same, the observed number of all malignant neoplasms in the total irradiated population was almost quadruple that expected in the age- and sex-adjusted population of upstate New York.⁵ In subgroup C, the observed number was more than five times the expectation. The ratio of observed to expected tumors in the benign category

⁵ In calculating the expected number of cancer cases, we used the annual cancer rates for upstate New York averaged over 3-year periods in the 3 decades since 1940 (1940-42, 1949-51, 1958-60) (6) and over a 3-year period in the past decade (1963, 1964, and 1969) (Greenwald P, Burnett WS: Personal communication). Since age-specific rates of benign tumors were not compiled for upstate New York, the rates in all untreated siblings were used to calculate the expected numbers of benign neoplasms in the treated population (table 3).

TABLE 1.—Population characteristics and radiation factors

| Characteristic or factor | Treated population | | Untreated siblings | |
|----------------------------|---------------------------|------------|--------------------|------------|
| | All | Subgroup C | All | Subgroup C |
| Population | | | | |
| Number | 2,872 | 261 | 5,055 | 349 |
| Average age, yr (1971) | 24.9 | 33 | 24.1 | 28.8 |
| Age spread, yr | 14-45 | 25-43 | 8-55 | 11-51 |
| Total PYR ^a | 69,402 | 8,088 | 115,921 | 9,597 |
| Males/females, % | 58/42 | 64/36 | 51/49 | 51/49 |
| Jewish/non-Jewish, % | 8/92 | 48/52 | 5/95 | 38/62 |
| Radiation factors | | | | |
| Average air dose, R | 225 | 461 | | |
| Average thyroid dose, rads | 119 | 399 | | |
| Kilovolt peak | 75-250 | 130 | | |
| Port arrangement | A, P, or AP ^b | AP | | |
| Port size | 15 cm ² -large | Large | | |

^a PYR = person-years at risk; since 90% of the subjects were treated in the first 6 months of life, birth to age on August 31, 1971 or to age at death was used for PYR.

^b Anterior, posterior, or anterior and posterior.

TABLE 2.—Neoplasms in irradiated and nonirradiated populations by cell type*

| Location | Treated ^b | | | | Siblings ^b | | | |
|---------------------------|----------------------|----------|------------|---------|-----------------------|---------|------------|--------|
| | All | | Subgroup C | | All | | Subgroup C | |
| | Malignant | Benign | Malignant | Benign | Malignant | Benign | Malignant | Benign |
| Thyroid tumors..... | 24 (5) | 52 (30) | 13 (4) | 20 (11) | 0 (0) | 6 (3) | 0 | 0 |
| Extrathyroid tumors..... | 22 (12) | 69 (31) | 7 (2) | 16 (6) | 25 (12) | 57 (30) | 3 (1) | 3 (2) |
| Leukemia or lymphoma..... | 8 (2) | | 2 (0) | | 7 (4) | | 0 | |
| Bone..... | 1 (0) | 18 (4) | 1 (0) | 5 (1) | 2 (0) | 4 (2) | 0 | 1 (0) |
| Nervous system..... | 4 (2) | 7 (3) | 1 (0) | 2 (1) | 4 (0) | 0 (0) | 1 (0) | 0 |
| Breast..... | 0 (0) | 13 (7) | 0 (0) | 1 (0) | 0 (0) | 17 (10) | 0 | 1 (1) |
| Salivary gland..... | 0 (0) | 4 (1) | 0 (0) | 2 (0) | 1 (1) | 2 (0) | 0 | 0 |
| Skin..... | 4 (4) | 6 (3) | 0 (0) | 0 (0) | 5 (3) | 1 (0) | 1 (1) | 0 |
| Genitourinary..... | 3 (3) | 10 (5) | 1 (1) | 3 (2) | 5 (4) | 12 (9) | 0 | 0 |
| Other..... | 2 (1) | 11 (8) | 2 (1) | 3 (2) | 1 (0) | 21 (9) | 1 (0) | 1 (1) |
| Total tumors..... | 46 (17) | 121 (61) | 20 (6) | 36 (17) | 25 (12) | 63 (33) | 3 (1) | 3 (2) |

* A few tumors were reclassified since 1967 (e.g., mixed tumors of the salivary gland changed from malignant to benign, a reticulum cell sarcoma from "other" to "bone").

^b Values in parentheses indicate new cases since the 1963 study.

TABLE 3.—Expected versus observed cases of surgically removed neoplasms*

| Location | Treated population ^b | | | | Siblings ^b | | | |
|-------------------|---------------------------------|----------|------------|----------|-----------------------|----------|------------|----------|
| | All | | Subgroup C | | All | | Subgroup C | |
| | Observed | Expected | Observed | Expected | Observed | Expected | Observed | Expected |
| | Malignant | | | | | | | |
| Thyroid..... | 24 (5) | 0.29 | 13 (4) | 0.04 | 0 (0) | 0.56 | 0 (0) | 0.06 |
| Extrathyroid..... | 22 (12) | 12.06 | 7 (2) | 1.84 | 25 (12) | 23.03 | 3 (1) | 2.29 |
| Lymphomas..... | 8 (2) | 3.97 | 2 (0) | 0.49 | 7 (4) | 6.61 | 0 (0) | 0.56 |
| Leukemia..... | 7 (1) | 2.27 | 2 (0) | 0.25 | 2 (0) | 3.80 | 0 (0) | 0.28 |
| Breast..... | 0 (0) | 0.48 | 0 (0) | 0.11 | 0 (0) | 1.56 | 0 (0) | 0.18 |
| Bone..... | 1 (0) | 0.67 | 1 (0) | 0.08 | 2 (0) | 1.03 | 0 (0) | 0.06 |
| Others..... | 13 (10) | 6.94 | 4 (2) | 1.16 | 16 (8) | 13.83 | 3 (1) | 1.49 |
| All tumors..... | 46 (17) | 12.35 | 20 (6) | 1.88 | 25 (12) | 23.59 | 3 (1) | 2.35 |
| | Benign | | | | | | | |
| Thyroid..... | 52 (30) | 3.42 | 20 (12) | 0 | 6 (3) | | 0 (0) | |
| Extrathyroid..... | 69 (31) | 32.37 | 16 (6) | 2.24 | 57 (30) | | 3 (2) | |
| Breast..... | 13 (7) | 9.65 | 1 (0) | 0.74 | 17 (10) | | 1 (1) | |
| Bone..... | 18 (4) ^c | 2.26 | 5 (1) | 0.74 | 4 (2) ^c | | 1 (0) | |
| Others..... | 38 (20) | 20.46 | 10 (5) | 0.76 | 36 (18) | | 1 (1) | |
| All tumors..... | 121 (61) | 35.79 | 36 (18) | 2.24 | 63 (33) | | 3 (2) | |

* Expected No. of malignant tumors were calculated with the use of age-specific cancer rates in upstate New York, whereas the numbers of benign tumors were based on the rates in each category observed in all siblings.

^b Values in parentheses refer to new cases since 1963.

^c One family with hereditary osteochondroma (1 treated child and 3 untreated siblings) was not included in this figure.

was less than the above figure in the total irradiated population but considerably higher in subgroup C.

Thyroid neoplasms

As seen in table 2, 24 cases of thyroid cancer occurred in the irradiated population (13 in subgroup C), whereas none developed in the nonirradiated siblings. The corresponding numbers of benign thyroid tumors in the irradiated population and their siblings were 52 and 6, respectively. However, only 5 new patients with cancer (4 in subgroup C) of the total of 24 had surgery after 1963, compared to 30 of the 52 benign tumors removed after this date. Before 1963, the excised thyroid neoplasms were almost equally divided between the malignant and benign categories, whereas after 1963 the number of benign tumors at the time of the operation greatly exceeded the malignant. This gave some hope that, with increasing time after irradiation, the risk of malignancy in radiation-induced neoplasms may decrease. (We cannot exclude a change in diagnostic criteria for an operation over the years).

The data in table 3 show that the observed number of thyroid cancer cases in the total irradiated population was almost 100 times that expected, whereas that in subgroup C was almost 300 times the expectation. By subtraction, the corresponding number of cancer cases not in subgroup C ("others") was almost 50 times the expectation. The observed number of benign thyroid tumors was also higher than that expected. In contrast to the irradiated population, the number of cases of thyroid cancer in the siblings was not elevated.

FACTORS INFLUENCING THE RISK OF DEVELOPING THYROID CANCER

We studied the possible effects of incidence of thyroid neoplasms of sex, age at diagnosis, radiation dosage, and of being in the high-risk subgroup C. Two types of analyses were done (Hall WJ: In preparation). In the first analysis, we attempted to study all factors simultaneously, as in a multifactor analysis of variance or a multidimensional contingency table analysis. We used the Poisson multifactor analysis with chi-square test, suited

to data on rare events; however, the amount of data (the number of tumors) was so small that an analysis based on so many classifications simultaneously was unreliable. Therefore, we also analyzed separately each factor (sex, age, and dose), but always treated subgroup C and "others" as individual populations. This second analysis suffered from the possible weakness that the single factor under study was confounded by the effects of other factors. The conclusions from the two kinds of analyses agreed. They were summarized in each section with the description and interpretation of the appropriate data.

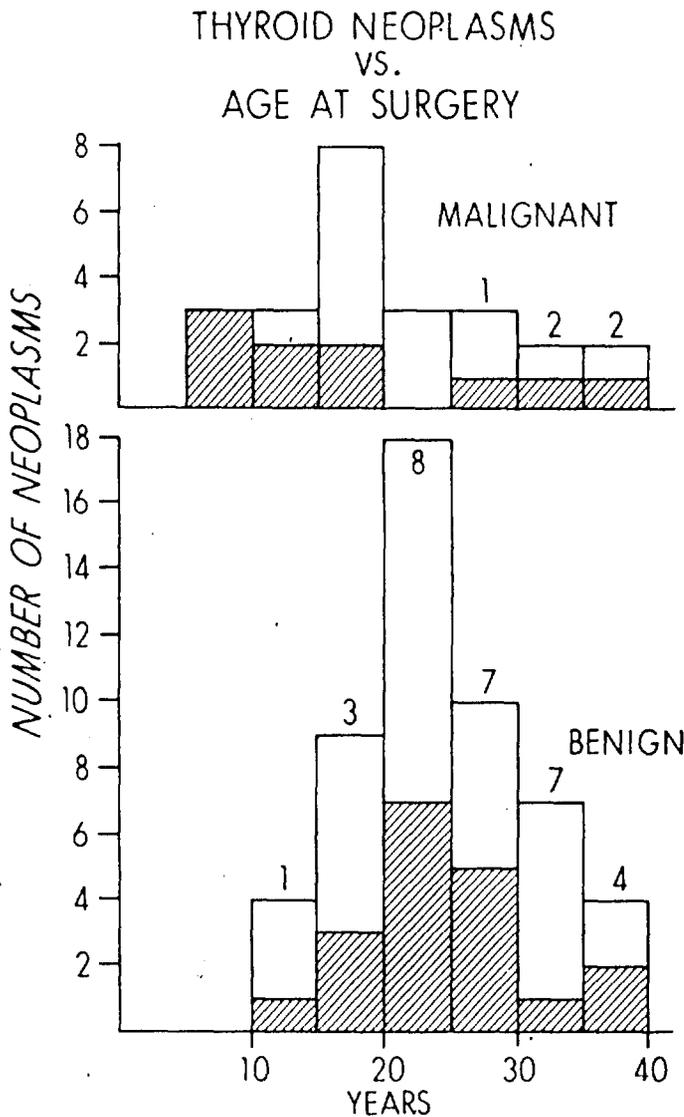
Distribution by sex (sex effect).—In the last survey (1), we reported that the ratio of females to males with thyroid neoplasms was 1.4:1. This figure was about the same as that in a retrospective study of thyroid cancer in children with a history of irradiation (7). In the present study, the ratio of females to males was 1.4:1 carcinoma and 1.7:1 for benign lesions. When these are corrected for the predominance of males in the treated population (58%), the ratios become approximately 1.9:1

and 2.3:1 for malignant and benign lesions, respectively. The increased frequency in the females (sex effect) was significant. After dose, age, and high-risk effects were considered, the incidence of cancer in all irradiated females was 2.3 times that in males, whereas in 15- to 29-year-old women the incidence was five times that of the rest of the irradiated population. In contrast, the incidence of thyroid cancer in women in the younger (< 15 yr) and older (> 30 yr) age groups was almost identical with that in males.

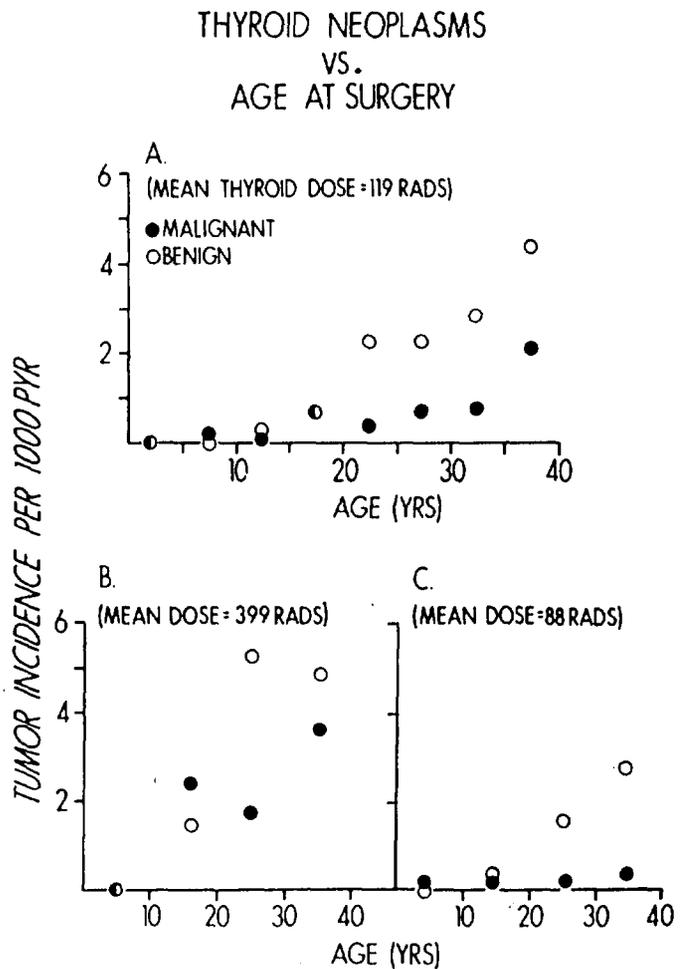
In our study, the sex ratio of females to males with thyroid neoplasms was considerably lower than those for thyroid cancer in upstate New York (6) or for goiter in the normal population (8, 9).

Age at diagnosis (age effect).—The distribution of treated subjects with thyroid neoplasms according to age at diagnosis (surgery) is shown in text-figure 1. The earliest cases were malignant and occurred in boys. The 5 new cancer cases developed in subjects over 25 years of age, whereas the new benign cases occurred in each age category over 10. Four of the 5 new cancer cases (since 1963) developed in subgroup C.

The incidence of thyroid neoplasms in the entire irradiated population per 1,000 PYR for 5-year age categories is shown in table 4 and text-figure 2. Incidence values were based on surgically removed thyroid neo-



TEXT-FIGURE 1.—Distribution of malignant and benign thyroid neoplasms by age of patient at surgery. Cross-hatched areas designate males; open areas, females. Number above each column indicates new neoplasms since 1963.



TEXT-FIGURE 2.—Incidence of benign and malignant thyroid neoplasms versus age at surgery for A) entire irradiated population, B) subgroup C, and C) all others. (●): malignant neoplasms; (○): benign goiters.

TABLE 4.—Thyroid tumors: age at surgery versus incidence/1,000 PYR

| Age (yr) | Number of subjects | PYR | Average thyroid dose (rads) | Malignant* | Benign* |
|---|--------------------|--------|-----------------------------|------------|---------|
| A. Entire irradiated population | | | | | |
| <5 | 2,872 | 13,771 | 119 | 0(0) | 0(0) |
| 5-9 | 2,796 | 13,945 | 119 | 0.2(3) | 0(0) |
| 10-14 | 2,786 | 13,888 | 119 | 0.2(3) | 0.3(4) |
| 15-19 | 2,751 | 12,221 | 118 | 0.7(8) | 0.7(9) |
| 20-24 | 1,999 | 7,893 | 152 | 0.4(3) | 2.3(18) |
| 25-29 | 1,179 | 4,366 | 224 | 0.7(3) | 2.3(10) |
| 30-34 | 654 | 2,412 | 297 | 0.8(2) | 2.9(7) |
| ≥35 | 316 | 905 | 327 | 2.2(2) | 4.4(4) |
| B. Subgroup C | | | | | |
| <5 | 261 | 1,289 | 399 | 0(0) | 0(0) |
| 5-9 | 257 | 1,282 | 397 | 0(0) | 0(0) |
| 10-14 | 256 | 1,261 | 397 | 1.6(2) | 1.6(2) |
| 15-19 | 250 | 1,249 | 396 | 3.2(4) | 1.6(2) |
| 20-24 | 249 | 1,239 | 395 | 1.6(2) | 4.8(6) |
| 25-29 | 247 | 973 | 393 | 2.1(2) | 6.2(6) |
| 30-34 | 161 | 606 | 424 | 3.3(2) | 5.0(3) |
| ≥35 | 76 | 189 | 363 | 5.3(1) | 5.3(1) |
| C. Remainder of irradiated population (others) | | | | | |
| <5 | 2,611 | 12,482 | 89 | 0(0) | 0(0) |
| 5-9 | 2,539 | 12,663 | 88 | 0.2(3) | 0(0) |
| 10-14 | 2,530 | 12,627 | 88 | 0.1(1) | 0.1(2) |
| 15-19 | 2,501 | 10,972 | 88 | 0.4(4) | 0.6(7) |
| 20-24 | 1,750 | 6,654 | 112 | 0.1(1) | 1.8(12) |
| 25-29 | 932 | 3,393 | 166 | 0.3(1) | 1.2(4) |
| 30-34 | 493 | 1,806 | 234 | 0(0) | 2.2(4) |
| ≥35 | 240 | 716 | 309 | 1.4(1) | 4.2(3) |

* Values in parentheses indicate numbers of tumors.

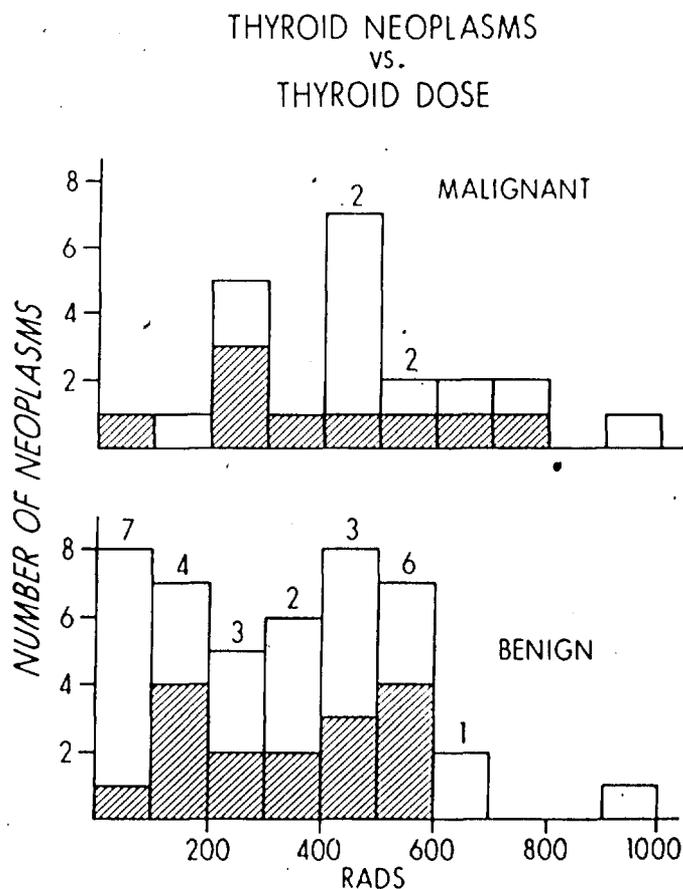
plasms only. In a study of subgroup C in 1964 (4), we reported that there were 2 unoperated nodular goiters for every 1 excised.

Unlike the curve of incidence versus age in our last publication (1), the new curves for both malignant and benign lesions in the total population did not indicate a decline after the treated subjects reached their twenties. Rather, they appeared to rise in the late twenties and thirties. The shape of the curve after age 30 is inexact, since the number of cases is small. Recently, we learned of a new case of thyroid cancer in a 37-year-old irradiated woman. The malignancy was untraced before August 31, 1971; therefore, it was not included in this study. This reinforced our impression that the incidence of thyroid cancer may actually increase in the fourth decade of life.

Although the curves for incidence versus age of both thyroid cancer and adenomas in text-figure 2 increased with age (particularly in 15- to 29-year-old females), multifactor analysis of the data failed to identify a clear proportionality between thyroid neoplasms and age. Because of the few cases, the age groupings in this analysis had to be very broad (<15 yr, 15-29 yr, and >30 yr), and perhaps this masked subtle age effects.

When the tumor incidence per 10-year age categories was plotted for subgroup C and the remaining population ("others") in text-figure 2, the plots were dissimilar, presumably due in part to the few tumors per category. Most cancer cases and about half of the benign goiters in the categories above age 20 occurred in subgroup C. According to the chi-square analyses, the data were compatible with either a "proportional age effect" hypothesis or a "no age effect" hypothesis; this indicates no clear pattern of age effect in either subgroup.

Thyroid dose (dose effect).—The distribution of malignant and benign thyroid neoplasms by thyroid-dose category is shown in text-figure 3 for the 66 subjects



TEXT-FIGURE 3.—Distribution of malignant and benign neoplasms according to estimated thyroid dose. Cross-hatched areas designate males; open areas, females. Number above each column indicates new neoplasms since 1963. One of the 5 new cancers was not included because the thyroid dose could not be calculated.

TABLE 5.—Thyroid tumors: incidence/1,000 PYR

| Thyroid dose (rads) ^a | Number of subjects | Average age (1971) | PYR | Malignant ^b | Benign ^b |
|--|--------------------|--------------------|---------|------------------------|---------------------|
| A. Entire irradiated population | | | | | |
| 0 (Controls) ^c | 5,055 | 22.9 | 115,921 | 0(0) | 0.1(6) |
| <100 (17.2) | 1,637 | 21.4 | 35,028 | 0.03(1) | 0.2(8) |
| 100-199 (137) | 211 | 25.2 | 5,310 | 0.2(1) | 1.3(7) |
| 200-299 (220) | 396 | 23.9 | 9,476 | 0.5(5) | 0.5(5) |
| 300-399 (346) | 89 | 34.0 | 3,030 | 0.3(1) | 2.0(6) |
| 400-499 (426) | 177 | 30.9 | 5,467 | 1.3(7) | 1.3(7) |
| ≥500 (648) | 94 | 31.9 | 2,997 | 2.3(7) | 3.7(11) |
| Unknown | 268 | 30.2 | 8,094 | 0.2(2) | 1.0(8) |
| B. Subgroup C | | | | | |
| 0 (Controls) ^c | 349 | 27.5 | 9,597 | 0(0) | 0(0) |
| <100 | 0 | — | — | — | — |
| 100-199 (156) | 18 | 34.4 | 617 | 1.6(1) | 3.2(2) |
| 200-299 (236) | 82 | 28.7 | 2,383 | 0.8(2) | 0.8(2) |
| 300-399 (368) | 31 | 35.9 | 1,109 | 0(0) | 3.6(4) |
| 400-499 (445) | 62 | 29.8 | 1,849 | 2.7(5) | 1.1(2) |
| ≥500 (633) | 67 | 31.4 | 2,101 | 2.4(5) | 4.7(10) |
| Unknown | 1 | 28.0 | 28 | 0(0) | 0(0) |
| C. Remainder of population (others) | | | | | |
| 0 (Controls) ^c | 4,706 | 22.6 | 106,324 | 0(0) | 0.06(6) |
| <100 (17.2) | 1,637 | 21.4 | 35,028 | 0.03(1) | 0.2(8) |
| 100-199 (135) | 193 | 24.3 | 4,693 | 0(0) | 1.1(5) |
| 200-299 (216) | 314 | 22.6 | 7,093 | 0.4(3) | 0.4(3) |
| 300-399 (334) | 58 | 33.1 | 1,921 | 0.5(1) | 1.0(2) |
| 400-499 (416) | 115 | 31.5 | 3,618 | 0.5(2) | 1.4(5) |
| ≥500 (685) | 27 | 33.2 | 896 | 2.2(2) | 1.1(1) |
| Unknown | 267 | 30.2 | 8,066 | 0.2(2) | 1.0(8) |

^a Values in parentheses indicate average dose of rads.

^b Values in parentheses indicate numbers of tumors.

^c Untreated siblings.

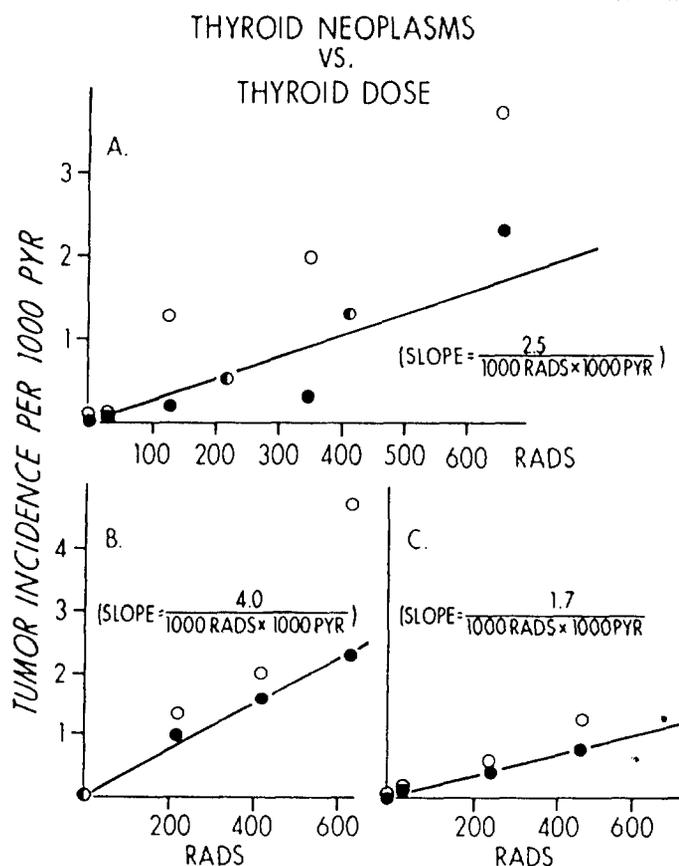
whose thyroid doses were estimated. Whereas benign and malignant neoplasms occurred at all dose levels, a greater proportion of benign tumors were in the low-dose ranges (<200 rads); the reverse was true in the high-dose ranges (>600 rads). Of the benign thyroid tumors in low-dose categories, most developed in females. Seven of 8 benign tumors in thyroid glands receiving less than 100 rads were diagnosed since the last survey, as were 11 of 15 in glands exposed to less than 200 rads.

The incidence of thyroid neoplasms per 1,000 PYR as a function of thyroid dose is shown in table 5 and text-figure 4 for the total population, subgroup C, and "others." The incidence of thyroid cancer increased with almost every dose increment, whereas that for benign tumors was more erratic but had an upward trend. To test whether the incidence of cancer in the total irradiated population was proportional to the dose (after effects of age, sex, and high risk were considered), we used the chi-square test (Hall WJ; In preparation) to demonstrate a good fit for the "dose proportionality" hypothesis and a rejection of the "no-dose effect" hypothesis. The high incidence of both cancer and adenomas in the high-dose categories of the entire irradiated population was partially explained by the heavy representation of the tumor-prone subgroup C. Because the small number of cancer cases reduced the reliability of the chi-square test, we also tested the goodness of fit of the dose proportionality and no-dose effect hypotheses by the likelihood ratio test (Hall WJ; In preparation); the results were similar but not as significant. When the same statistical tests were applied to the incidence of benign tumors versus dose, we found poor fits for both hypotheses but a slightly better fit for the no-dose effect than for dose proportionality. From the multifactor analysis, we concluded that the incidence of thyroid cancer in each age, dose, and subgroup category was pro-

portional to the thyroid dose, but that of benign tumors was not necessarily so. The dose-response curve for thyroid cancer was compatible with, but not necessarily diagnostic of, a straight-line function with a slope of 2.5 ± 0.5 (estimated SE)/1,000 rads/1,000 PYR ⁶ or 2.5 cases/year/million people exposed to 1 rad.

Because of the so-called subgroup C effect (discussed later), we studied separately the dose response of subgroup C and "others." The analysis of subgroup C was made simpler because the mean ages (table 5) and sex ratios were essentially constant across dosage groups and thus nullified any age, sex, and high-risk effects. The comparisons of the observed numbers of thyroid cancers with those expected on the basis of the dose proportionality hypothesis yielded a chi-square statistic that strongly supported the hypothesis when the subjects were grouped in either the 5- or 3-dose categories. Similar analysis of the data for benign tumors in subgroup C revealed a questionable fit for the 5-dose categories, but a good linear fit for 3-dose categories. We concluded that the proportional dose hypothesis was supported by the data for malignant tumors but was questionable for benign growths. Similar analysis of the data for the remainder of the irradiated population ("others") also supported the proportionality concept in the cases of malignant tumors but clearly rejected it for benign lesions. The conclusions for "others" were not reliable because of the possibility of a confounding age effect. The slope of the dose-response curve for cancer was $4.0 (\pm 1.1)$ /1,000 rads/1,000 PYR for subgroup C, compared with 1.7

⁶ The slope of the dose-response curve differed slightly from the risk value given in the section "Risk of Developing Thyroid Neoplasms" because the calculation of slope included the PYR during the 5-year minimum latent period after exposure, whereas the risk calculation excluded the PYR during this period.



TEXT-FIGURE 4.—Incidence of benign and malignant thyroid neoplasms/1,000 PYR vs. estimated thyroid doses for A) entire irradiated population (average age, 24.9 yr), B) subgroup C (average age, 33 yr), and C) "all others" (average age, 24.1 yr). (●): malignant neoplasms; (○): benign tumors. The curve indicates the dose response of thyroid cancer cases. To eliminate extremes of variability in B) and C), we combined the dose groups of table 5 (A) to include at least 50 subjects/category. For an explanation of the difference between the slope of the dose response and the risk value, see footnote 6.

(± 0.6) for "others." The ratio of these risks was 2.4 (± 1.0); i.e., subgroup C had 2.4 times the risk of "others."

High incidence of neoplasms in subgroup C (subgroup C effect).—One reason for the excessively high incidence of thyroid neoplasms (the subgroup C effect) was the large thyroid doses used to treat subgroup C subjects. However, even after dose, age, and sex effects were considered, the increased incidence of thyroid cancer in subgroup C was almost 2.5 times that in "others." Thus factors were probably involved in addition to age, dose, and sex effects. One such factor could be the earlier examination of subgroup C subjects. More than half of this subgroup was examined specifically for nodular goiter in 1964, either by our own endocrinologists or endocrinologists of our choosing. Not until 1969 were the rest of the irradiated population informed of their increased risk of developing goiter and advised to see their family physicians (not necessarily thyroid specialists). It was possible that the earlier, and presumably more thorough, medical examination leading to earlier diagnosis was a factor in the apparent high frequency of goiter in subgroup C.

Another possible factor in the production of excess nodular goiters in subgroup C was the large proportion

of Jewish subjects⁷ ($\approx 48\%$) in contrast to the much smaller proportion ($\approx 4\%$) in the remainder of the treated population. Jews were reported to have a higher incidence of spontaneous thyroid cancer (and leukemia) than non-Jews (12, 13). Although the possibility of a Jewish factor in cancer development was considered and discarded in the 1963 study, it seemed worthwhile to study it again. A little more than half of all neoplasms in subgroup C (57%) occurred in the Jewish subjects, who comprised slightly less than half of the subgroup ($\approx 48\%$). Yet 9 of the 13 cases (69%) of thyroid cancer (and both cases of leukemia) occurred in Jews of this subgroup. The incidence of thyroid cancer in the Jews and non-Jews of subgroup C was 7.2% and 2.9%, respectively. Although the average age of the Jews in subgroup C was 1 year older and they had received a 6% larger thyroid dose (22 rads) than did the rest of the subgroup, it seemed unlikely that the slight dose and age differential would explain the greatly increased incidence of thyroid cancer, whereas the ethnic difference might do so.

The case for the importance of a Jewish background in the development of radiation-induced thyroid cancer was strengthened by consideration of "others" (excluding subgroup C) and the total irradiated population. Two of the 11 cases of thyroid cancer in subjects not in subgroup C (18%) occurred in 4% of the people who were Jews; this gave a cancer incidence of 1.9% for Jews and 0.36% for non-Jews. Admittedly, the Jewish group received almost twice the thyroid dose (153 vs. 87 rads) but did not differ in age from "others." The dose effect alone seems unlikely to explain the sixfold difference in cancer rates. Considering the total irradiated population, 11 of 24 cases of thyroid cancer (46%) occurred in the 8% of Jews. Using a triple multiplicative model and accounting for the effects of being Jewish, female, and in subgroup C (age was ignored), we discovered the risk of the Jewish factor for cancer development was 3.65 compared to 1.6 for being in subgroup C only. If dose was assumed to have a proportional effect on cancer incidence and sex was accounted for (but age ignored), multiplicative analysis showed that the large proportion of susceptible Jews in the subgroup accounted for almost all of the subgroup C effect (i.e., increased cancer incidence/rad).

Because age and sex effects were shown to be inter-related, we reanalyzed data in which young adult females were considered separately and the rest of the females combined with the males, assuming their risks were essentially identical. Considering only 4 cells— young adult females (Jews and non-Jews) and "all others" (Jews and non-Jews), analysis with the use of the multiplicative model showed that the young adult females had a fivefold increased risk of thyroid cancer, whereas Jews had a 3.3-fold increased risk (considering the proportional dose effect). Thus the increased risk of

⁷ In (10) we stated that many of the subjects of subgroup C had family names of German-Jewish derivation. This was followed up in the 1963 survey by a religious preference question. Nearly all respondents answered this question, and the 15% of families whose religion was not ascertained was largely accounted for by the non-respondents. In the present study, a judgment was made as to whether these families were Jewish by review of their surnames. Although Protestant and Catholic groups in most American communities include a variety of ethnic and cultural backgrounds, MacMahon and Pugh (11) stated that "the Jewish religion . . . does at present appear to identify a group that is more homogeneous than the population at large with respect to some characteristics," including some cultural factors and some possibly genotypic.

young adult Jewish females was almost 17 times that of the irradiated population. These results were highly significant.

Benign thyroid tumors did not occur predominantly in Jewish subjects in subgroup C; only 10 of 20 cases were in the Jewish population. In the total population, however, 14 of 52 neoplasms (27%) occurred in the Jewish (8%) population. This suggested that despite the negative analytic finding mentioned above, the Jewish factor had an important function in the development of benign and malignant thyroid neoplasms.

LATENT PERIOD BETWEEN IRRADIATION AND DIAGNOSIS

The minimum latent period was 5 years for thyroid cancer and 10 years for benign lesions (text-fig. 1). A scatter diagram of thyroid dose versus latent period between exposure and tumor diagnosis (not shown) indicated no obvious relationship between these two factors. However, the development of so many benign tumors since 1963 in the low-dose categories (text-fig. 3) suggested that with the smaller doses there was a longer latent period before benign nodular thyroid lesions developed.

CLINICAL COURSE

The answers on the mail questionnaires indicated that all subjects with nodular thyroid glands did well after surgery. Even persons with metastatic cancer to regional lymph nodes and 2 with pulmonary metastases were in good health in 1969-71.⁸

One young man with pulmonary metastases (1) treated with a massive dose of ¹³¹I in 1950 was without evidence of disease at age 34. Another man of 21, who had surgery at 8 years of age for a thyroid carcinoma with metastases to the regional lymph nodes, now has infiltrative lesions in the lungs. The roentgenographic appearance of the pulmonary lesions in 1969 suggested metastases, but the lesions did not take up ¹³¹I. The infiltration has not progressed in the past 2 years and, although untreated, the patient was well and at work.

In the rest of the patients with surgically excised goiters, 5 of the nodular lesions recurred. In the 2 cases with primary malignant tumors, the recurrent nodules were benign. In the 3 others with primary benign tumors, 1 recurrence was malignant and 2 benign.

PATHOLOGY

The histologic sections of all but 6 of the cases were reviewed by one of the present or past authors. The criteria used for histologic classification were those given in (14).

Except for the recently discovered spindle cell cancer reported on a death certificate, the histopathology of the new cases of surgically removed thyroid nodules was consonant with the observations reported in (1, 15). The microscopic appearance of the nodules ranged from benign hyperplastic involutory to adenomatous or frank carcinomatous lesions (some of the latter with distant and regional metastases). In both hyperplastic involutory glands and adenomas, the histopathology varied and included admixtures of hyperactive and atrophic epithelium with focal oxyphilic (Hürthle) cells and slight-to-abundant intra-acinar colloid.

Lymphocytic infiltration was noted in both the neoplastic and normal-appearing regions of some glands. A

diagnosis of focal thyroiditis with reactive lymphoid follicle formation was made in 7 irradiated glands and 1 nonirradiated gland with the use of the criteria of Williams and Doniach (16). The severity of the inflammatory reaction varied from slight to moderate in 5 irradiated specimens. In 2 irradiated glands, severe thyroiditis was observed. However, these 2 cases were not diagnosed clinically as thyroiditis. They were distinct from the 3 clinical cases of thyroiditis reported by the subjects (2). In the nonirradiated gland, moderate lymphocytic thyroiditis was present. Only 1 instance of thyroiditis was recorded in the surgical specimens obtained before 1963. This may reflect the increasing age of the population under study.

PATHOGENESIS

In (1) we speculated that the pathogenesis of radiation-induced thyroid neoplasms followed the multistage theory of carcinogenesis clearly demonstrated for thyroid neoplasms in rodents (17). Since then, we have observed chromosome aberrations in approximately one-third of the thyroid cells cultured from 4 glands irradiated with 468-728 rads of X-rays 30-37 years ago (18). The aberrations were frequent in the nonneoplastic cells cultured from the grossly normal thyroid tissue and in the neoplastic cells from the nodular lesions. Such chromosome damage may be related to the primary event in carcinogenesis. The multiple chromosome lesions in cells of the nonneoplastic tissue undoubtedly accounted for the multicentric nature of the disease.

In (1) we indicated that the abrupt rise in incidence of thyroid neoplasms during thyroid stress in adolescence suggested that thyroid-stimulating hormone (TSH) was a promoting or secondary factor. Although the present data indicated a more gradual increase in incidence of thyroid neoplasms during adolescence, the regression of early clinical nodular lesions resulting from suppressive therapy with thyroid hormones (5) indicated the importance of TSH in the pathogenesis of these neoplasms.

RISK OF DEVELOPING THYROID NEOPLASMS

The risk of developing thyroid cancer after irradiation (assuming a linear dose response) can be calculated for the total irradiated population, subgroup C, and "others" by the conventional formula:

$$\text{Risk} = (\text{observed No. of cases} - \text{expected No. of cases}) \\ \times \frac{10^6}{\text{Number of subjects}} \times \frac{1}{\text{Mean dose}} \times \frac{1}{\text{Mean No. of years at risk}}$$

The average risk/year/million people, each with a thyroid dose of 1 rad, was 2.7 (i.e., 2.7 cases/year/1,000,000 people, each with a thyroid dose of 1 rad) for the entire irradiated population, 4.6 for subgroup C, and 1.8 for all "others" (data from tables 1 and 3). In these calculations, we assumed a latent period of 5 years before the development of neoplasms; the adjustment for expected numbers had no noticeable effect.

⁸ After the deadline for data collection in the present study, we learned that a 37-year-old nonrespondent died after a short illness of spindle cell carcinoma of the thyroid. She had received an unusually large cumulative dose of X-rays to the chest—531 R at 1 to 3 months of age for alleged thymic enlargement and 2,400 R 1 year later for a mediastinal mass suspected of being Hodgkin's disease. Since the diagnosis was not confirmed histologically, the chest neoplasm was not included in our past and present studies.

TABLE 6.—*Extrathyroid tumors: incidence/1,000 PYR for the entire population*

| Air dose (R) | Number of subjects | PYR | Malignant ^a | Benign ^a | Inside beam ^{a,b} | Outside beam ^{a,b} |
|----------------|--------------------|---------|------------------------|---------------------|----------------------------|-----------------------------|
| Controls | 5,055 | 115,921 | 0.21 (25) | 0.49 (57) | 0.28 (33) | 0.49 (46) |
| 1-199 (78.4) c | 1,231 | 25,264 | 0.20 (5) | 0.51 (13) | 0.24 (6) | 0.47 (12) |
| 200-299 | 661 | 15,420 | 0.39 (6) | 1.10 (17) | 1.36 (21) | 0.13 (2) |
| 300-399 | 399 | 11,088 | 0.45 (5) | 0.54 (6) | 0.45 (5) ^d | 0.45 (5) ^d |
| 400-499 | 227 | 7,028 | — (0) | 1.84 (13) | 1.00 (7) | 0.85 (6) |
| 500-599 | 108 | 3,256 | 0.61 (2) | 1.53 (5) | 1.53 (5) | 0.61 (2) |
| 600 (794.0) c | 112 | 3,513 | 0.85 (3) | 2.85 (10) | 1.71 (6) | 1.99 (7) |
| Unknown | 134 | | (1) | (5) | (2) | (4) |

^a Values in parentheses indicate actual number of neoplasms.

^b In the case of tumors of the nonirradiated siblings, there was no beam. Assuming that the sibling was treated with the port used for his treated sibling, a decision was made as to whether the tumor would have been inside or outside the beam.

^c Values in parentheses are the average of the air dose.

^d In this dose category, some neoplasms cannot be classified as inside or outside the beam.

We preferred to replace the factors, mean dose times, and mean years in the denominator of the above formula by the weighted mean of the PYR, weighted by the individual doses. This gave more reliable risk values of 3.0 (± 0.06)/1,000 rads/1,000 PYR for the entire population, 4.8 (± 1.3) for subgroup C, and 1.8 (± 0.7) for "others." Without the latent period adjustment noted above, these last three figures would be 2.5, 4.0, and 1.7.

Extrathyroid neoplasms

As seen in table 3, the 91 malignant and benign neoplasms developing in the irradiated subjects in tissues other than thyroid outnumbered the 76 in the thyroid gland. Of the total number of extrathyroid tumors, approximately one-third of the malignant tumors and one-fourth of the benign neoplasms occurred in subgroup C. The total number of neoplasms in the irradiated population exceeded that in the much larger group of sibling controls. Table 3 shows the excess of malignant and benign extrathyroid neoplasms in each category. Of the 10 excess cases of malignancy, 5 were leukemias, 2 were fibrosarcomas (1 in the heart muscle),⁹ and most of the remainder arose in nerve tissue. Many of the excess cases of benign extrathyroid neoplasms arose in bone or breast tissue, but others developed in skin, nerve, and other tissues.

The 91 neoplasms in the tissues outside the thyroid gland were pooled for an analysis of incidence versus dose. Pooling tumors of different cell types (each, perhaps, with a characteristic dose-response curve) for this purpose may be criticized, but the numbers of extrathyroid tumors of specific cell types were too small for analysis. The results are given in table 6 for all extrathyroid malignant and benign tumors and for all extrathyroid tumors arising inside and outside of the tissues irradiated by the primary X-ray beam. The incidence of malignant and benign tumors in the category below 200 R was almost identical to that in the nonirradiated siblings. For the malignant and benign tumors considered individually, the response was somewhat erratic, partly due to so few cases. Clearly, however, the incidence of cancer and benign tumors was higher in dose categories above 200 R than below this dose level.

If only pooled extrathyroid tumors arising in tissues irradiated by the primary X-ray beam were considered, there was no clear-cut dose response in the sixth column in table 6. The incidence of malignant and benign neoplasms arising in irradiated tissues in persons exposed to less than 200 R was the same as that in the sibling controls. In the higher dose categories, the incidence of

TABLE 7.—*Observed versus expected deaths in treated and sibling populations*

| Study group | Number of deaths | |
|-----------------------------------|------------------|-----------------------|
| | Observed | Expected ^a |
| Treated population | | |
| <1 year | 52 | — ^b |
| ≥1 year to December 31, 1960 | 50 | 31.5 |
| January 1, 1961–August 31, 1963 | 6 | 4.6 |
| September 1, 1963–August 31, 1971 | 20 | 22.9 |
| Total | 128 | |
| Siblings | | |
| Birth–August 31, 1963 | 216 | 230 |
| September 1, 1963–August 31, 1971 | 29 | 42.1 |
| Total | 245 | 272.1 |

^a The age-specific mortality rates in upstate New York (provided by Dr. P. Greenwald and Dr. W. S. Burnett) averaged for 1964–72 were used to compute the expected number of deaths.

^b Since mortality rates in upstate New York are not available for the variable period between X-ray treatments and end of the first years of life, the expected mortality during the first year cannot be computed.

tumors was 2 to 5 times that of controls. This suggested that doses over 200 R were more effective than low doses in inducing neoplasms, presumably by the direct action of the X-rays.

The incidence of pooled tumors developing in non-irradiated tissues fluctuated with no apparent relation to dose except for the highest dose category, which had an incidence almost 5 times that of the controls. Possibly these tumors in the highest dose category were an indirect or abscopal effect of exposure to the large doses administered (mean air dose, 794 R). Except for the 3 ovarian tumors (1 teratoma and 2 dermoid cysts), the diversity of the tumors—1 case each of meningioma, osteochondroma, lipoma, and fibromyoma—argued against any common mechanism of tumor induction.

Deaths

In (1), we concluded that there was no evidence for an increased death rate during 1960–63 in either the irradiated or sibling populations. The present data on observed and expected deaths (table 7) indicated that since 1963 the observed numbers of deaths were not excessive.

DISCUSSION

The fourfold increase in cancer cases over the expectation was largely accounted for by the nearly 24 excess

⁹ A myxosarcoma of the heart was reported in one thymus-irradiated subject of the Ann Arbor, Michigan survey (19).

cancers of the thyroid and the 4 excess lymphomas. Similarly, 15 of the 18 excess cases of cancer in subgroup C occurred in the thyroid or blood-forming organs. The remaining 6 excess cases in the total irradiated population (3 in subgroup C) arose in other organs. No cancers developed in breast tissue (1 was discovered after 1971) or in the salivary glands, as reported in other irradiated populations (20-22). The number of observed cancers in the siblings was almost the same as that expected.

The incidence of benign tumors in the irradiated population also increased almost fourfold over that in the sibling controls. The increase in benign tumors in subgroup C was 16-fold. Thyroid and bone neoplasms accounted for 64 of the 85 excess neoplasms in the total population. The other 21 excess benign tumors arose in the breast, skin, nervous system, salivary glands, and genitourinary tract. Benign tumors in the category designated "others" in table 2 (mainly lipomas and fibromas) did not increase over the expectation.

Thyroid neoplasms, particularly in women, were clearly the most frequent late consequence of irradiation of the chest and neck in infancy. Fortunately, even the thyroid cancers usually had well-differentiated cells and responded favorably to treatment. An exception was the recently discovered spindle cell cancer in a woman who received a tumoricidal dose of X-rays in infancy. Benign rather than malignant thyroid neoplasms occurred primarily in women after exposure to low doses, but either could result from any dose in the range under study, including the extremes. The minimum latent period between exposure and clinical manifestation was 5 years for cancer in males, and 10 years for cancer in females and benign tumors in both sexes. It was suggested but not proven that the latent period was inversely related to the dose.

Although statistical analyses did not show a significant age effect except in the young adult females, text-figure 4 clearly indicated that the thyroid cancer incidence did not decline after age 20, as suggested in (1). The 5 cancer cases (1 not included in our data) in the over 30-year group indicated that the risk of thyroid cancer continued at least into early middle age. Further study of the irradiated population was necessary to determine the age response in middle life.

After taking age, sex, and high-risk effects into account, we used two statistical tests to show that the incidence of thyroid cancer was proportional to the thyroid dose. The dose-response curve was compatible with, but did not prove, a straight-line function with a slope of 2.5/1,000 rads/1,000 PYR. Similarly, analysis of subgroup C data showing a constant mean age across dose groups revealed a proportional dose effect on cancer

incidence with a slope of 4. We cannot definitely say how far down the dose scale the linear fit was valid, since there was only 1 case of cancer in each of our lowest two dose categories.¹⁰ There was no evidence of a decline or "turn down" in the highest dose category. If there is an optimum dose for induction of thyroid cancer in man as in animals (23), it exceeds the doses used to treat our subjects.

Why the benign goiters did not show a dose proportionality was not apparent, except that we were not dealing with the total sample of benign lesions. Except for the large goiters which were symptomatic or unsightly, in young adults only those lesions which were suspected of being malignant were treated surgically and included in our analysis. About 10 years ago, we found that for every patient in subgroup C with a surgically excised goiter, there were 2 others with unoperated, clinically palpable thyroid nodules. If we had been able to study the entire sample of unoperated and operated benign nodules, we might have shown a dose response as suggested by another study of clinically palpable radiation-induced nodular goiter (21).

The increased risk of thyroid cancer in young women and Jews was of considerable interest. The increased risk of spontaneous thyroid cancer in women who had not received radiation exposure over that seen in males was described (6). Similarly, Jews reportedly had a higher risk of dying from spontaneously developing thyroid cancer than non-Jews, although the increased risk was less than a factor of 2 (12, 13). Because of the high incidence of spontaneous thyroid cancer, it seemed reasonable to assume that women and Jews were more susceptible than the rest of the population to the action of a known carcinogenic agent on the thyroid gland. The Jewish factor alone (with correction for age, sex, and dose) may account for the increased cancer incidence in subgroup C. Although the early examination of persons in this subgroup cannot be excluded as a factor in explaining the high incidence of thyroid cancer, both Jews (48%) and non-Jews (52%) participated in the examination program. If thyroid cancer occurred with the same frequency in both ethnic groups, we would not have expected the observed difference in incidence.

¹⁰ In a recent publication, Modan and his associates reported 12 cases of thyroid cancer in 10,902 traced persons given X-ray treatment to the scalp during childhood for tinea capitis (22). By use of a phantom and simulated treatment conditions, they estimated the thyroid dose to be 6.5 rads. Using the data given in (22), we estimated the cancer incidence to be 0.06/1,000 PYR. This value, a little more than twice the incidence for subgroup C subjects extrapolated to 6.5 rads, suggested that linearity held at least to this dose level. If there was a threshold for cancer induction, it was below 6.5 rads.

APPENDIX

Since we cannot describe the methodology at this time, we present the raw data which, with tables 4 and 5, can

be used for statistical analysis of the tumor incidence in the section "Factors Influencing the Risk of Developing Thyroid Cancer."

| Group and measurement | Thyroid dose (rads) | | | | | | | | | | | |
|---|---------------------|--------|-------|----------------------|--------|--------|----------------------|--------|--------|-------------------|--------|--------|
| | <100 at ages (yr) | | | 100-299 at ages (yr) | | | 300-499 at ages (yr) | | | ≥500 at ages (yr) | | |
| | 0-14 | 15-29 | 30+ | 0-14 | 15-29 | 30+ | 0-14 | 15-29 | 30+ | 0-14 | 15-29 | 30+ |
| Subgroup C: Jewish males | | | | | | | | | | | | |
| Number of cases | 0 | 0 | 0 | 22 | 21 | 9 | 26 | 25 | 15 | 27 | 25 | 23 |
| PYR | | | | 306 | 585 | 314 | 360 | 704 | 533 | 365 | 719 | 781 |
| Number malignant | | | | 1 | — | — | — | — | 1 | 1 | — | 1 |
| Number benign | | | | — | — | 1 | — | 1 | — | — | 1 | — |
| Average age (yr) | | | | 13.90 | 27.85 | 34.88 | 13.85 | 28.16 | 35.53 | 13.52 | 28.76 | 33.96 |
| Average dose (rads) | | | | 226.50 | 225.09 | 208.00 | 421.19 | 420.40 | 394.86 | 611.89 | 612.44 | 612.83 |
| Subgroup C: Jewish females | | | | | | | | | | | | |
| Number of cases | 0 | 0 | 0 | 17 | 17 | 9 | 19 | 19 | 17 | 11 | 10 | 9 |
| PYR | | | | 238 | 478 | 321 | 266 | 546 | 617 | 143 | 290 | 290 |
| Number malignant | | | | — | — | — | — | 2 | 1 | — | 2 | — |
| Number benign | | | | — | 1 | — | — | 2 | 1 | 1 | 2 | — |
| Average age (yr) | | | | 14.00 | 28.11 | 35.66 | 14.00 | 28.74 | 36.29 | 13.00 | 29.00 | 33.22 |
| Average dose (rads) | | | | 212.94 | 212.94 | 210.11 | 408.79 | 408.79 | 404.18 | 696.91 | 678.40 | 685.22 |
| Subgroup C: Non-Jewish males | | | | | | | | | | | | |
| Number of cases | 0 | 0 | 0 | 40 | 39 | 18 | 37 | 35 | 22 | 15 | 14 | 13 |
| PYR | | | | 546 | 1,083 | 632 | 510 | 977 | 805 | 207 | 405 | 431 |
| Number malignant | | | | 2 | — | — | — | — | — | — | 1 | — |
| Number benign | | | | 1 | 1 | — | — | 1 | — | — | 3 | — |
| Average age (yr) | | | | 13.65 | 27.77 | 35.11 | 13.78 | 27.91 | 36.59 | 13.80 | 28.93 | 33.15 |
| Average dose (rads) | | | | 229.10 | 229.66 | 220.25 | 419.27 | 418.00 | 396.00 | 626.06 | 617.86 | 613.69 |
| Subgroup C: Non-Jewish females* | | | | | | | | | | | | |
| Number of cases | 0 | 0 | 0 | 21 | 20 | 11 | 11 | 10 | 5 | 14 | 14 | 13 |
| PYR | | | | 291 | 558 | 372 | 141 | 280 | 178 | 216 | 398 | 435 |
| Number malignant | | | | — | 2 | — | — | 1 | — | — | — | — |
| Number benign | | | | — | — | — | — | 1 | — | — | 1 | 2 |
| Average age (yr) | | | | 13.86 | 27.90 | 33.82 | 12.82 | 28.00 | 35.60 | 15.43 | 28.43 | 33.46 |
| Average dose (rads) | | | | 223.76 | 234.40 | 219.91 | 432.64 | 427.50 | 409.40 | 630.53 | 630.43 | 621.46 |
| "Others": Jewish males (49)^b | | | | | | | | | | | | |
| Number of cases | 26 | 26 | 1 | 9 | 9 | 3 | 11 | 11 | 6 | 3 | 3 | 3 |
| PYR | 364 | 617 | 30 | 126 | 228 | 96 | 154 | 309 | 218 | 42 | 87 | 78 |
| Number malignant | — | — | — | — | — | — | — | 1 | — | — | — | — |
| Number benign | — | 1 | — | — | — | — | — | — | — | — | — | — |
| Average age (yr) | 14.00 | 23.73 | 30.00 | 14.00 | 25.33 | 32.00 | 14.00 | 28.09 | 36.33 | 14.00 | 29.00 | 32.66 |
| Average dose (rads) | 26.65 | 26.65 | 32.00 | 167.44 | 161.74 | 183.66 | 396.55 | 396.55 | 398.00 | 569.66 | 596.66 | 596.66 |
| "Others": Jewish females (41)^c | | | | | | | | | | | | |
| Number of cases | 21 | 20 | 4 | 14 | 13 | 5 | 4 | 3 | 3 | 2 | 2 | 1 |
| PYR | 286 | 462 | 128 | 189 | 334 | 165 | 45 | 87 | 101 | 28 | 57 | 37 |
| Number malignant | — | — | — | — | — | — | — | — | — | — | 1 | — |
| Number benign | 1 | 1 | — | — | — | — | — | — | — | — | — | — |
| Average age (yr) | 13.61 | 23.10 | 32.00 | 13.50 | 25.69 | 33.00 | 11.25 | 29.00 | 33.66 | 14.00 | 28.50 | 37.00 |
| Average dose (rads) | 24.71 | 24.09 | 31.25 | 163.21 | 165.76 | 183.60 | 412.00 | 410.66 | 410.66 | 790.00 | 790.00 | 756.00 |
| "Others": Non-Jewish males (1,292)^d | | | | | | | | | | | | |
| Number of cases | 894 | 865 | 44 | 296 | 275 | 43 | 90 | 89 | 54 | 12 | 11 | 8 |
| PYR | 12,188 | 18,677 | 1,430 | 3,943 | 6,147 | 1,572 | 1,260 | 2,484 | 1,935 | 156 | 312 | 293 |
| Number malignant | — | 1 | — | 2 | — | — | — | — | — | — | — | — |
| Number benign | — | — | — | — | 1 | 2 | — | 3 | — | — | — | — |
| Average age (yr) | 13.63 | 21.59 | 32.50 | 13.32 | 22.35 | 36.55 | 14.00 | 27.91 | 35.83 | 13.00 | 28.36 | 36.62 |
| Average dose (rads) | 16.98 | 16.86 | 30.39 | 184.07 | 183.63 | 190.06 | 393.33 | 393.66 | 432.39 | 698.08 | 715.18 | 751.25 |
| "Others": Non-Jewish females (962)^e | | | | | | | | | | | | |
| Number of cases | 696 | 687 | 44 | 188 | 180 | 43 | 68 | 64 | 50 | 10 | 10 | 8 |
| PYR | 9,656 | 14,948 | 1,402 | 2,559 | 4,216 | 1,609 | 914 | 1,834 | 1,777 | 140 | 287 | 302 |
| Number malignant | — | — | — | 1 | — | — | — | 2 | — | — | 1 | — |
| Number benign | 1 | 4 | — | — | 3 | 2 | — | 2 | — | — | 1 | — |
| Average age (yr) | 13.87 | 21.75 | 31.86 | 13.61 | 23.42 | 37.41 | 13.44 | 28.65 | 35.54 | 14.00 | 28.70 | 37.75 |
| Average dose (rads) | 16.93 | 16.94 | 33.27 | 187.42 | 186.89 | 189.28 | 402.06 | 381.27 | 374.46 | 680.70 | 680.70 | 706.13 |

* One woman's thyroid dose is unknown.

^b This does not include 17 Jewish males for which the dose is unknown; in 1 of these, a benign tumor occurred.

^c Dose is unknown for 10 females; 1 had a benign tumor.

^d Dose is unknown for 144 males; 1 had a malignant thyroid tumor and 2 had benign tumors.

^e Dose is unknown for 96 females; 1 had a malignant thyroid tumor, and 4 had benign thyroid tumors.

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