A preliminary report on the frequency of thyroid surgery and particularly thyroid cancer among young people in Utah from 1948 through 1962 seems to indicate an increase primarily in the 20-29 year age group. Continued study is needed to determine whether a true excess of thyroid cancer is occurring in Utah, and if so, why.

SURGICALLY TREATED THYROID DISEASE AMONG YOUNG PEOPLE IN UTAH, 1948-1962

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IN 1963, testimony presented to the Joint Committee on Atomic Energy[1] raised a number of questions concerning the possibility of thyroid injury to Utah infants and young children as a consequence of exposure to iodine-131 derived from operations at the Nevada Test Site. Although there was general agreement that the most significant exposures (from contaminated milk) occurred in the early 1950's, no actual measurements of the concentration of iodine-131 were made at that time.

A growing body of evidence now supports the belief that several hundred roentgens of x-irradiation delivered to the neck or upper thorax of infants or young children is associated with an excess risk of thyroid carcinoma or adenoma ten to twenty years after the exposure.[2] Thyroid nodules (characterized as adenomatoid) have been observed recently in 13 of 19 Marshall Island children who were exposed to fallout in 1954.[3] The thyroid dose which the children received from ingested iodines has been estimated at about 1,000 rads in addition to an external dose of 175 rads from gamma-emitting fission products. Although there is general agreement on methods of calculating thyroid doses delivered externally from fission products or from x-rays and those internally delivered by iodine-131, equivalent rad doses, even adjusted for "relative biological effectiveness," do not imply equivalent biological damage potential.

As an average for all Utah infants for the period 1952 through 1955, Mays[4] has estimated a cumulative thyroid dose from ingested iodine-131 as 5-50 rads. Tamplin,[5] for infants and children present in the state from 1952 through 1955, estimates about 50 rads from iodine-131 ingested during that period. Estimates exceeding 100 rads have been made for selected small populations in one area of Utah 110-140 miles east of the test site.[6]

In this preliminary report we propose to record some of our observations on the incidence of surgically treated thyroid disease in Utah. These observations are intended to provide a basis for the future evaluation of the possible association of certain thyroid abnormalities with iodine-131 from fission products originating in Nevada.

Materials and Methods

A case for the purposes of this study is a resident of Utah, under the age of

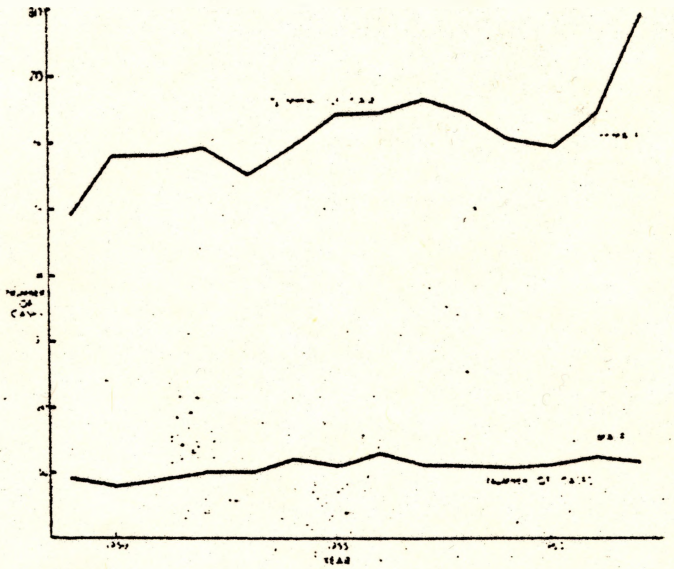


Figure 1—Number of cases of thyroid surgery under age 30, Utah, 1949-1962, by sex (three-year moving average)

30 at the time of thyroid surgery performed during the 15-year interval from January 1, 1948, through December 31, 1962. We believe that these cases provide a more reliable index of state-wide and local prevalence of thyroid disease than those treated medically. The availability of tissue blocks and slides permits expert review of diagnostic conclusions. This would not be feasible with patients seen only in private offices and clinics.

To obtain all known cases we searched general hospital record room and pathology department diagnostic indexes in the states of Utah and Nevada and one hospital pathology department in western Colorado. There are 36 general hospitals in Utah and 20 in Nevada. Only nine of the Utah hospitals and four in Nevada have over 100 beds.[7]

The cases of thyroid surgery constitute the numerators of rates based on Utah population data derived from the 1950 and 1960 census statistics for white residents. Linear interpolation and extrapolation were used to estimate the age- and sex-specific denominators for each of the 15 years of the study period. Rates and trends for all thyroid surgery and for selected diagnostic categories were determined.

If the 15 years are divided into three equal periods, 1948-1952 spans the interval between the absence of any nuclear detonations in Nevada and the first three series of weapons tests which began in January, 1951. Among the 1951-1952 shots there were five of "nominal" yield (20 kt) or greater.[8]

From 1953 through 1957 there were 15 "nominal" or larger shots in Nevada and three (all underground) in the five years from 1958 through 1962. The moratorium on all weapons tests prevailed from November, 1958, to September, 1961, and the treaty banning atmospheric testing went into effect in October, 1963.

Results

Figure 1 shows the three-year moving average of the annual number of thyroid surgery cases for each sex. There

are about 60 cases per year among females and 10 among males, totaling 1,162 for the 15 years. The upward trend is just about proportional to the population increase in each sex from about 200,000 in 1948 to about 260,000 in 1962. The stability in the frequency of thyroid surgery in respect to population is demonstrated explicitly in Figure 2. The rate scale is logarithmic to accommodate the data for both sexes on one chart and to avoid exaggerating the effect of small changes among the low rates prevailing among the males. There are about 25 thyroid operations per 100,000 females and four or five thyroid operations per 100,000 males in each of the 15 years.

In Figure 3, again using semi-log scales, the annual rates for toxic goiter are compared with all other diagnoses of thyroid disease in each sex group. Initially, toxic goiter accounted for more than half of the diagnoses in both sexes. Since the early 1950's, it has declined both in absolute frequency and in respect to other diagnoses made after surgical intervention. This relative decrease is particularly noticeable among the females.

The changes or absence of change in incidence for each diagnostic category is shown between the earliest and most recent five-year periods in Figure 4. Because of the small number of cases among males, the data are restricted to females. In contrast to the previously noted drop in toxic goiter, again seen here, the fourfold increase in cancer from 0.6 case to 2.3 cases per 100,000 per year, and the doubling of the rate for thyroiditis from 2.0 to 4.0 are especially noteworthy. No apparent change from the first to last five-year period of observation has occurred in the incidence of nontoxic nodular goiter, adenoma, or the miscellany consisting of cases not included in one of the five designated categories.

The cancer observations are examined

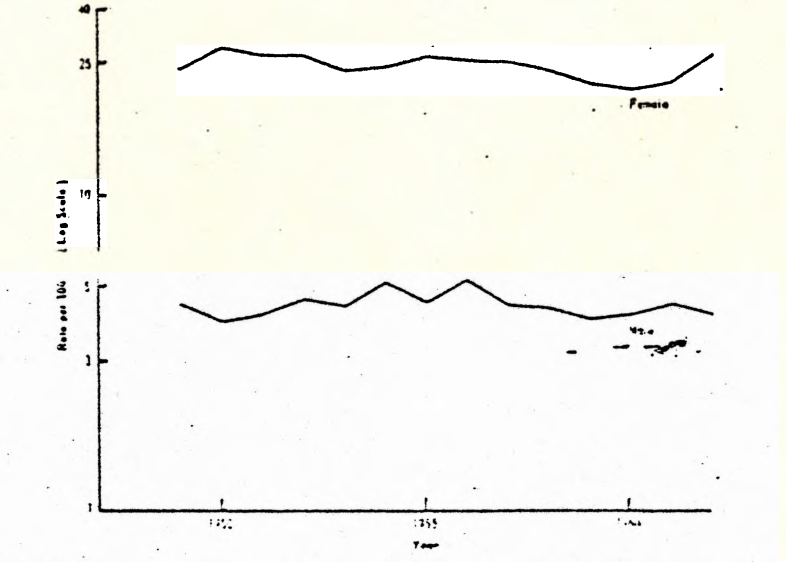


Figure 2—Rate of thyroid surgery for persons under age 30, by sex, Utah, 1949-1962

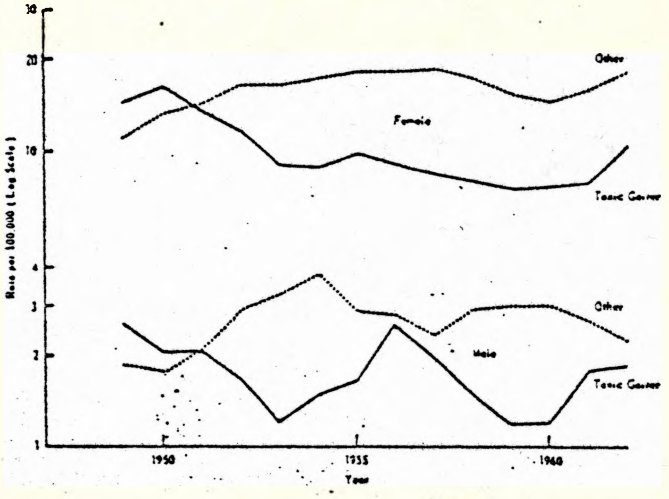


Figure 3—Rate of toxic goiter and of all other surgically treated thyroid disease for persons under age 30, by sex, Utah, 1949-1962

in greater detail than that given to the other diagnoses beginning with Figure 5. First, the fluctuations due to the small numbers are not greatly dampened by the use of the three-year moving average. There is an increase among the females and little or none among the males over the 15-year period. However, the early peak in males may be noteworthy. Of the six cases in this first five-year interval, four were veterans between the ages of 23 and 29, diagnosed at the Veterans Administration Hospital which provided no further cancer cases. Assuming the possibility of earlier medical detection of thyroid cancer during or at the termination of military service, if these cases are excluded from the analysis then there is also a suggestion of an increasing trend in males.

Table 1 shows the 70 cancer cases in young people in Utah by age and sex compared with expected frequencies derived from three independent sources. The first is the Public Health Service "Ten Cities" cancer survey of 1917-1918.[9] Applying the age and sex specific annual incidence rates of that study to the estimated Utah population at risk yields a sum of 36 cases for the 15-year period. This is approximately half of the total observed and, when the sexes are examined separately, this twofold difference applies to both. When the *age groups* are examined, there is *no* difference between observed and expected frequencies[1] in persons under 20 years of age and more than a 2.5-fold difference in persons 20 to 29 years of age. However, the other comparisons with figures derived from the New York[10] and the Connecticut State Tumor Registers[11] do show differences of the order of 2:1 in three of the four sex and age groups.

Although these comparison data appear consistent among themselves there are important differences in the methods used for case reporting which will not be considered at this time. Nevertheless, it should be mentioned that the "Ten Cities" survey showed a twofold excess of thyroid cancers in "western" cities versus other regions of the United States. Further, the decade following the time of that survey (1918-1919) was a pe-

riod in which there was an 80 per cent increase in the number of thyroid cancer cases reported among persons under 30 years of age to the New York State Department of Health.[10]

Since they are the only relevant data available covering almost all the 15 years, the New York rates have been used to determine expected numbers of cases in Utah during each of the three five-year periods under observation. Table 2 shows the results for each sex in two age groups and summations within each time period.

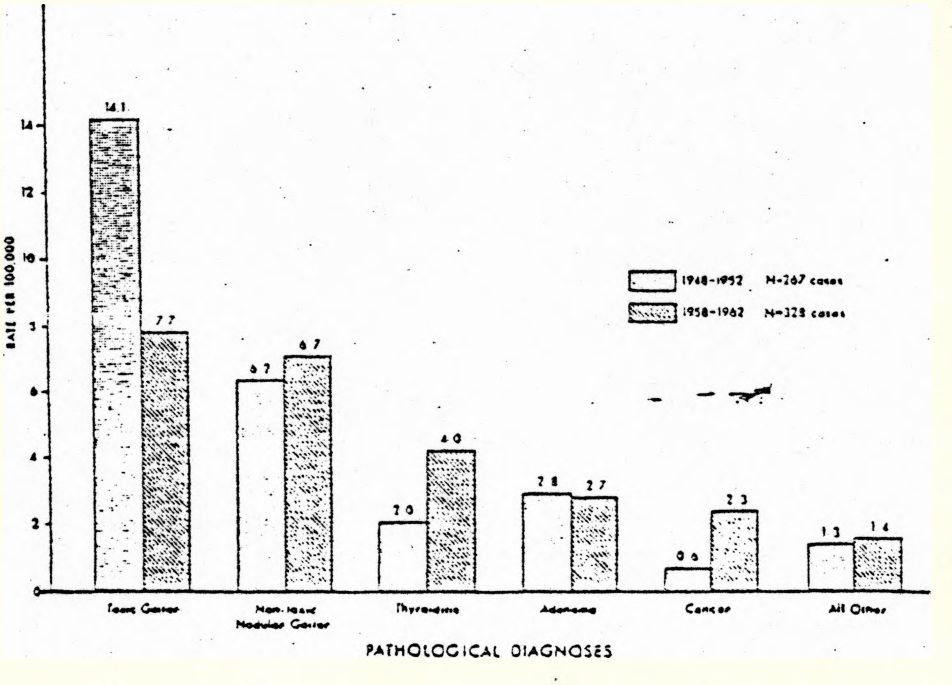
In the earliest period, twelve cases were observed in Utah, three more than the nine expected. However, the excess was observed only in males of the 20-29-year age group. The veterans mentioned previously are four of the six cases in this group.

In the middle period, 19 cases were observed versus 14 expected. The excess was again restricted to the age group 20-29 years and mainly among the females. In the last period, however, a more than twofold difference is noted; 39 observed versus 17 expected. The difference is seen for each age group within both sexes.

Discussion

At least since the draft examinations of the first World War, Utah has been identified as an area having a high prevalence of endemic goiter.[12] There are two consequences of this situation. One is that neoplasms may arise more frequently in hyperplastic glands than in the normal and the other is that physicians may look for thyroid abnormalities more often than they would in an area of low endemicity.

Figure 4—Thyroid surgical cases among Utah females under age 30 (average annual rate per 100,000) 1948-1952 vs. 1953-1962



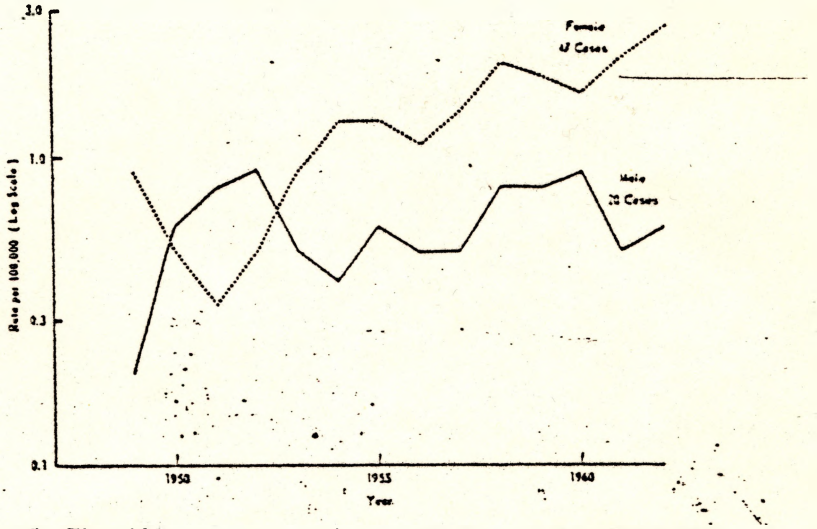


Figure 5—Thyroid cancer rates under age 30, by sex, Utah, 1949-1962

In respect to the first point, Pendergrast[13] has shown no relationship between the state-to-state prevalence of goiter in World War II selective service candidates and thyroid cancer mortality. He also reported that inspection of unpublished data from the "Ten Cities" survey indicated that one western city (San Francisco) had more than twice the median incidence of thyroid cancer compared to the other nine.

These specified considerations and others implicit in the technics of collecting and presenting our data impose serious restrictions on interpreting the significance of the reported differences between observed and expected numbers of thyroid cancers in Utah.

Further complications arise from changes in pathologists' nomenclature and classification schemes. In the early 1950's there began a trend to give preference to the term "papillary adenocarcinoma" to some specimens which would previously have been called "papillary adenoma."[14] In the same period, the concept of "aberrant thyroid" was being discarded in favor of considering most manifestations as a consequence of metastatic thyroid carcinoma.[15] Thus a comparison of records from before 1950 with those prepared ten or more years later may not be completely valid.

From a collection of 328 cases of thyroid cancer in which a history of previous x-irradiation had been established, Raventos and Winship[16] calculated a

Table 1—Number of cancer cases observed and expected, by age and sex, Utah 1948-1962

	Observed	Expected		
	Utah 1948–1962	10 cities 1947–1948	N. Y. 1949–1960	Conn. 1948–1962
Female				
under 20	11	10	9	4
20–29	38	15	20	21
Male				
under 20	5	6	3	2
20–29	16	5	8	4
Grand total	70	36	40	31

median latent interval of 11 years. The authors recognize that since almost half of their cases are from a series of childhood cancers, the 11-year figure is likely to underestimate the latent period. Since the interval measured is that between the date of radiation exposure and the time of surgery rather than the recognition of the neoplasm, sometimes a year or two earlier, there may be some inherent self-correction in the data. Nevertheless, if about ten years is required to observe about half of the neoplastic effects of massive x-ray exposure of the thyroid, many more years of observation are likely to be needed to secure the data necessary to evaluate the possible consequences of the iodine-131 exposure we have postulated.

We may anticipate, however, some changes in the nature of selection of young people for thyroid surgery because of more awareness of the possibility of cancer. The data presented here were obtained for a period prior to public and professional concern about thyroid cancer in Utah. Future analyses should, therefore, consider this possibility which may be adjusted for in part by comparing the relative frequency of cancer in nontoxic thyroid surgical procedures as well as by comparing population frequencies. Further analyses should also consider geographic differences in incidence in relation to improved exposure estimates being developed by other investigators.

Summary

This initial and preliminary report of thyroid surgery incidence and in particular thyroid cancer in the young people of Utah from 1948 through 1962 may be summarized as follows.

1. The annual rate of thyroid surgery

Table 2—Comparison of numbers of thyroid cancer cases observed in Utah with expected numbers derived from reported frequencies in New York State, 1948-1962

Age and sex groups	Time periods					
	1948–1952		1953–1957		1958–1962	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
Female						
0–19	1	2	0	3	10	4
20–29	5	5	13	6	20	9
	—	—	—	—	—	—
0–30	6	7	13	9	30	13
Male						
0–19	0	1	1	1	4	1
20–29	6	1	5	3	5	2
	—	—	—	—	—	—
0–30	6	2	6	4 (5)	9	4
Both sexes						
0–19	1	3	1	4	14	5
20–29	11	6	18	9	25	12
	—	—	—	—	—	—
0–30	12	9	19	13 (11)	39	17

( ) Rounding and adjustment.

has been constant at 25 per 100,000 females under age 30 and four to five for males.

2. Surgery for toxic goiter has decreased approximately 50 per cent over the study period.

3. Thyroiditis increased twofold and thyroid cancer increased almost fourfold.

4. The cancer increase was observed for both sexes but primarily in the 20-29-year age group.

5. Observed frequencies of thyroid cancer were compared with expected numbers derived from other incidence studies. These numbers suggest an excess in Utah most marked in the most recent five-year period.

6. Continued study is needed to determine whether a true excess of thyroid cancer is occurring in Utah and, if so, what genetic or environmental factors may be associated with it.

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