THE INCIDENCE OF THYROID CANCER IN ENGLAND AND WALES

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During the autumn of 1961 test explosions of nuclear bombs released into the atmosphere a measurable amount of radioactive iodine, some of which found its way into food. Vennart (1962) measured the concentration of ^{131}I in the thyroids of 20 adult subjects and estimated that the glands received approximately 7 m.rads from this source during the three months in which atmospheric activity could be detected. The dose received by children must have been greater, because of the greater consumption of cow's milk, but children under 1 year old fed entirely on cow's milk would not have received an average of more than 170 m.rads—that is, 17% of the dose that the Medical Research Council recommended could be regarded as acceptable in any one year (Agricultural Research Council Radiobiological Laboratory, 1961, 1962). Whether doses of this order can produce cancer of the thyroid is unknown; even if they can, it is unlikely that the increase in the number of cases produced could be detected. Nevertheless, it is clearly desirable to have some measure of the incidence of the disease in the absence of fall-out, and the available data have been brought together with this in mind.

Sources of Data

Mortality data for cancer of the thyroid have been published by the Registrar General since the adoption of the Fifth Revision of the *International Classification of Diseases* in 1940. Since that time there has not been any change in the policy of classification or coding which could have affected them. The validity of the figures is, however, difficult to establish. As with other vital statistics, they are dependent on the accuracy of death certification. In most cases the diagnosis is relatively straightforward. In some, however, the disease may present as enlarged cervical nodes without a palpable tumour, or the tumour may be retrosternal, and in these the true cause of death may be overlooked; in others, death may be attributed to thyroid cancer when the thyroid tumour is secondary to an undetected primary elsewhere (particularly in a bronchus). It is impossible to estimate the size of these two errors, which will partially cancel each other out—but it seems unlikely that, in this country, they should be large in comparison with the total number of diagnosed cases.

The value of morbidity statistics is more difficult to assess. Two sources are available on a national scale: the Hospital In-Patient Enquiry and the Cancer Register. The In-Patient Enquiry is based upon the number of discharges or deaths in hospital, and the results are entirely dependent on the varying policies of admission and readmission to hospital; hence it is not a suitable tool for estimating incidence. The Cancer Register is not yet complete for the whole country, although good data are available for some regions. It can be used to provide estimates of the incidence of the disease, so long as it is realized that the data are approximate. Evidence of the validity of the results can be obtained by comparing the

ratio between the mortality and the morbidity rates with that observed in other countries.

Mortality

In the 12 years 1950–61 the annual number of deaths attributed to thyroid cancer fluctuated between 316 and 385, without there being any suggestion of a systematic trend. The stability of the rates is shown in Table I, which

TABLE I.—Standardized Mortality Ratios for Thyroid Cancer
England and Wales, 1950–61*

Year	M	F	Year	M	F	Year	M	F	Year	M	F
1950	81	97	1956	119	100	1953	99	101	1959	102	98
1951	105	102	1957	93	95	1954	107	101	1960	103	94
1952	114	101	1958	95	87	1955	101	100	1961	97	95

* Base years 1950–2 taken as 100.

gives standardized mortality ratios for each sex, using 1950–2 as the base years. In view of the small numbers and the stability of the rates, a more accurate picture of the sex and age distribution of the disease can be obtained by calculating the rates from the pooled data for several years than by using data for single years. Rates are therefore given in Table II for the decades 1940–9 and 1950–9. Even with this grouping the numbers are still too small to provide useful estimates for five-year age-groups under the age of 25 years. In the whole decade 1950–9 only one death occurred at ages under 15 years and eight deaths at ages 15 to 24 years. Rates for the white population of the U.S.A. for 1950–9 are also shown in Table II for comparison.

For each set of data the female rates are higher than the male. At ages under 30 years the female excess is slight and irregular; at older ages the female rates are approximately double the male, but the difference is less marked

TABLE II.—Mortality from Thyroid Cancer in England and Wales and the U.S.A., by Sex and Age

Age	Annual Death Rate per Million Total Population								
	England and Wales						U.S.A. (Whites)		
	1940–9			1950–9			1950–9		
	M	F	P*	M	F	P*	M	F	P*
0–14	0.06	0.05	0.05	—	0.02	0.01	0.09	0.06	0.07
15–24	0.10	0.16	0.13	0.10	0.14	0.12	0.15	0.27	0.21
25–29	0.2	0.4	0.3	0.3	0.3	0.3	0.5	0.5	0.5
30–34	0.7	1.1	0.9	0.4	0.7	0.5	0.4	0.9	0.6
35–39	1.3	2.1	1.7	0.6	1.9	1.3	1.2	1.6	1.4
40–44	1.9	3.5	2.7	1.6	3.5	2.6	2.3	2.7	2.5
45–49	4.3	7.1	5.8	4.2	5.7	5.0	4.2	5.2	4.7
50–54	4.7	12.6	8.9	5.6	11.0	8.3	7.1	10.2	8.6
55–59	8.7	20.8	14.8	10.0	16.9	13.4	11.3	15.9	13.6
60–64	12.2	30.1	21.2	12.7	29.3	21.0	16.1	24.8	20.5
65–69	18.2	38.6	28.4	22.2	38.6	30.4	22.3	37.4	29.9
70–74	23.0	49.3	36.2	25.3	50.9	38.1	27.9	50.1	39.0
75–79	24.0	55.5	39.8	29.9	67.9	48.9	32.1	64.2	48.2
80+	25.9	61.0	43.5	26.1	75.5	50.8	33.0	76.0	54.5
All ages standardized†	4.06	11.22	7.64	4.41	11.36	7.89	5.03	10.77	7.90

* Arithmetic mean of male and female rates.

† England and Wales population 1950–9 taken as standard.

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in the U.S.A. than in England and Wales. The comparison between the rates for the two countries in 1950-9 is illustrated in the Chart. At ages under 25 years the

American rates are substantially higher than the British. The difference is less marked at ages 25-39 years and it practically disappears at older ages. At ages 35 years and older the rates for persons are almost identical in the two populations, but the mortality tends to be higher in males in the U.S.A. than in England and lower in females. Cancers of the thyroid in childhood have been attributed to irradiation of the neck in infancy (Duffy and Fitzgerald, 1950; Simpson and Hempelmann, 1957; Winship and Rosvoll, 1961), and the excess mortality at ages under 35 years in the U.S.A. may be due to a more extensive use of radiotherapy in childhood in the U.S.A.—particularly for the treatment of supposed enlargements of the thymus in infancy. The similarity of the mortality rates in adult life suggests that there is unlikely to be any great difference in the aetiology, diagnosis, or fatality from the disease in the two countries. It may be noted, however, that similar rates are not reported in all other countries. Substantially higher rates are reported in Switzerland, Austria, Denmark, and Sweden, and lower rates are reported in Japan (Segi and Kurihara, 1962).

The rates for England and Wales show little evidence of any change in incidence between 1940-9 and 1950-9. The mortality was increased at ages 75 years and over in the later period, but a similar increase has been noted at these ages in many other diseases and may reasonably be attributed to increased diagnostic precision. Comparison between the rates at ages 15 to 44 years may be biased to some extent, because many more young men and women were in the Services in the first period. The figures are, however, unlikely to be distorted to any serious extent, as few (if any) deaths from thyroid cancer can have occurred among Service men while serving abroad and the rates in Table II have been derived from all deaths occurring in England and Wales and from total populations, including men and women in the Services.

Morbidity

In 1954 the number of fresh cases of cancer registered in the National Cancer Register was 149 for every 100,000 inhabitants; four years later the registration rate had increased to 203 per 100,000 (Table II). During this period the annual mortality rate increased only from 204

to 212 per 100,000. The slight increase in mortality can be attributed to (1) the ageing of the population, and (2) an increase in lung-cancer mortality—the mortality from all other types of cancer remaining fairly constant. The increase in the registration rate, on the other hand, can be attributed principally to an increase in the efficiency of the scheme.

TABLE III.—Cases of Cancer (All Sites) Registered With the National Cancer Register, England and Wales, 1948-54. Comparison Between Registration Rate and Mortality Rate

Year	Annual Rate per 100,000 Persons	
	Registration	Mortality
1954	149	204
1955	145	206
1956	163	208
1957	184	209
1958	203	212
1954-8	168	208

An estimate of the true total cancer morbidity rate can be obtained from the regions where, it is believed, registration was nearly complete. In these regions the rate was between 320 and 350 per 100,000—that is, approximately double the rate for the whole country in the same period. Estimates of the incidence of thyroid cancer can therefore be obtained by doubling the registration rate. Such estimates are shown in Table IV. It must be noted, however,

TABLE IV.—Estimated Incidence of Thyroid Cancer in England and Wales, 1954-8; by Sex and Age

Age (Years)	Annual Incidence per Million Population			Mortality as Percentage of Incidence†
	Male	Female	Persons*	
0-14	0.23	0.16	0.19	5
15-24	2.4	3.7	3.0	4
25-29	4.6	9.2	6.9	5
30-34	4.4	9.5	7.0	8
35-39	4.2	16.4	10.3	12
40-44	4.8	21.5	13.2	19
45-49	7.6	25.4	16.5	30
50-54	12	33	22	38
55-59	23	42	32	42
60-64	26	50	38	55
65-69	39	69	54	56
70-74	47	78	61	62
75-79	41	82	62	79
80+	27	95	60	85

* Arithmetic mean of male and female rates.

† Mortality for persons 1950-9 expressed as a percentage of the estimated incidence rate for 1954-8.

that the validity of these figures depends on the assumption that thyroid cancer is typical of all cancer in respect of the proportion registered, and that the proportion is the same in both sexes and at all ages—and neither assumption is necessarily true. For example, bias may be introduced by the registration of a higher proportion of cases treated by radiotherapy than of cases treated by surgery.

Survival

One means of checking the validity of the figures is by calculating the ratio between mortality and incidence and comparing it with clinical experience. More precisely, the ratios at different ages may be compared with those obtained from similar data in other countries where incidence has been determined with greater certainty.

From Table IV it appears that mortality is low compared with incidence under 25 years of age (of the order of 5%) and that subsequently it increases until at 60 years of age and over it becomes more than 50%. A result of this sort could be obtained if the fatality of the disease was low in

childhood and increased with age; or if the fatality remained fairly constant but the duration of survival was longer in younger patients. In clinical experience, the prognosis of thyroid cancer varies greatly with histological type, and both factors may well contribute to the results. Several large series of cases have recently been reported (Winship and Rosvoll, 1961; Woolner, Beahrs, Black, McCahey, and Keating, 1961; Burn and Taylor, 1962). Doniach (1963) in summarizing the literature states: "The papillary carcinoma is the commonest, occurs in all age-groups, constitutes the majority of thyroid cancers in children . . . and demonstrates a remarkably protracted course so that the effectiveness of treatment can be gauged only by 10 to 20 year survival studies." In contrast: "Anaplastic carcinomas are rapidly growing lethal tumours . . . they occur predominantly in the sixth and seventh decades, are mostly inoperable when first diagnosed and lethal within six months."

The dependence of prognosis on age is demonstrated by the follow-up results reported to the National Cancer Register. During the period 1948-54, 2,458 cases of carcinoma of the thyroid were registered and all but 48 (1.9%) have been traced until death or, if surviving, until the end of 1959. The sex and age distribution of the patients is given in Table V. The survival rates (given in Table VI) show that survival varies greatly with sex and

TABLE V.—Number of Cases of Thyroid Cancer Registered in England and Wales, 1948-54; by Sex and Age

Age (Years)	No. Traced		No. Not Traced	
	Male	Female	Male	Female
0-4	0	0	0	0
5-14	3	4	1	—
15-24	13	39	1	4
25-34	38	109	3	6
35-44	59	206	1	4
45-54	102	311	2	9
55-64	143	442	—	4
65-74	148	480	2	6
75+	71	225	1	2
Not stated	6	11	—	2
All ages	583	1,827	11	37

TABLE VI.—Five-year Survival Rate for Patients with Thyroid Cancer; by Sex and Age. Cases Registered in England and Wales, 1948-54

Age (Years)	Survival Rate per 100 Patients			
	Crude		Corrected*	
	Male	Female	Male	Female
0-24	93	93	93	93
25-34	66	88	67	89
35-44	58	72	59	74
45-54	27	56	29	59
55-64	29	36	34	42
65+	12	17	18	23
All ages	30	41	32	44

* Corrected for deaths due to other causes—that is, expressed as a percentage of the rate expected on the basis of the experience of the general population of the same age.

with age; fatality is lower in females than in males, and at young ages the prognosis is good.

A similar marked variation with age is shown by American data. National figures for the incidence of thyroid cancer can be derived from three large-scale studies carried out in the States of Connecticut (Griswold, Wilder, Cutler, and Pollack, 1955) and Iowa (Haenszel, Marcus, and Zimmerer, 1956) and in 10 cities selected to be representative of the whole country (Dorn and Cutler, 1955). The white population covered by the three studies was approximately 17,000,000—about 13% of the white

population of the country.* Data are available for some or all of the years 1947-51 in each study, and in view of the rarity of thyroid cancer it seems desirable to combine the material from all three sources. The combined data are shown in Table VII, and may be considered representa-

TABLE VII.—Estimated Incidence of Thyroid Cancer in the U.S.A. White Population, 1947-51; by Sex and Age

Age (Years)	Annual Incidence per Million White Population			Mortality as Percentage of Incidence†
	Male	Female	Persons*	
0-14	1.5	0.6	1.1	6
15-24	3.4	10.4	6.9	3
25-29	3.9	21.0	12.4	4
30-34	5.0	23.5	14.2	5
35-39	9.3	36.9	23.1	6
40-44	7.1	38.6	23.2	11
45-49	11	38	25	19
50-54	30	56	43	20
55-59	21	64	43	32
60-64	34	83	59	35
65-69	47	72	60	50
70-74	38	94	66	59
75-79	37	59	48	100
80+	27	88	58	94

* Arithmetic mean of male and female rates.

† Mortality for persons 1950-9 expressed as a percentage of the estimated incidence for 1947-51.

tive of the whole U.S. white population, save that residents in country areas are under-represented. This may have resulted in producing rates which are slightly higher than the true national incidence (Haenszel *et al.*, 1956).

From Table VII and Table II it is clear that the ratio between mortality and incidence varies with age in a similar way to that shown in Table IV for England and Wales. Under 15 years of age and at 65 years and over the ratios are similar in the two countries. Between these limits the ratios are somewhat lower in the U.S.A.

Unless, therefore, the proportions of the histological types are different in the two countries, these results suggest that the estimated incidence in England and Wales may be a little too low.

Summary and Conclusions

Mortality data for cancer of the thyroid in England and Wales between 1940 and 1959 are summarized. No evidence is found of a change in the death rate during this period. The death rate is slightly higher in females than in males at ages under 30 years; at other ages the female rate is approximately double the male.

Comparison between the mortality for England and Wales and that for the U.S.A. white population shows that the rates for persons are closely similar at age 35 years and over; at younger ages the American mortality is appreciably higher. The higher American mortality in youth may be attributable to the greater use of radiotherapy for benign conditions in childhood. The similarity of the adult mortality rates obscures the fact that the mortality is slightly higher among women in England and Wales and slightly higher among men in the U.S.A.

Estimates of the incidence of thyroid cancer can be obtained from data provided by the National Cancer Register, on the assumption that approximately half the cases occurring in the country during the period 1954-8 were registered. On this basis the annual incidence under 15 years of age is estimated to have been approximately 2 cases per year (0.2 per million persons).

*Almost all the populations of Connecticut and Iowa are white and these data can be regarded as applying to whites; the data for the 10-city survey are given separately for whites and non-whites.

The ratio between the mortality and the incidence rates shows marked variation with age. Mortality is low compared with incidence at ages under 15 years (5%) and at ages 15 to 24 years (4%), but subsequently it increases with age. This corresponds with the pathological finding that papillary carcinoma is the predominant type in childhood and anaplastic carcinoma the predominant type in old age. Follow-up of patients reported under the national cancer registration scheme confirms that the early prognosis is good in youth and becomes progressively worse in adult life.

Data obtained from three studies in the U.S.A. show a similar change with age in the ratio between mortality and incidence. The ratio is somewhat lower at ages 20 to 69 years in the U.S.A., suggesting that the incidence in England and Wales may be slightly underestimated.

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POST-CRICOID CARCINOMA: REGIONAL INCIDENCE IN ENGLAND AND WALES

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This report on the regional incidence of post-cricoid carcinoma in England and Wales was stimulated by the observation of Scott (1960) and Payne (1961) that the incidence of pernicious anaemia varies in different parts of the country, and the occurrence, in a few patients, of both post-cricoid carcinoma and pernicious anaemia (Jacobs, 1962). It was made possible by the fact that since 1957 the Registrar-General has placed deaths from post-cricoid carcinoma in a class of their own (I.S.C. No. 147.2) instead of including them under the general class of "malignant neoplasms of the hypopharynx" (I.S.C. No. 147).

Material.—The numbers of deaths due to post-cricoid carcinoma occurring in England and Wales during the five years 1957-61 were obtained from the Registrar-General. These were subdivided into the standard regions of England and the two subregions of Wales (Registrar-General, 1963). Separate figures were given for the two sexes. For the years 1959-61 details of age and social class were also obtained. An assessment was made of regional differences for each sex separately and of possible differences due to age or social class.

Results

Post-cricoid carcinoma is not a common disease. The total number of deaths due to this cause in the whole of England and Wales did not exceed 250 in any of the years under review. Deaths occurring during the whole period 1957-61 in each region, together with the average crude death rate for those years, are shown in Table I. Death rate in this disease probably reflects the true incidence fairly accurately, and the greater mortality in females agrees with clinical impressions. In both sexes the death rate is higher in Wales than elsewhere, and highest in North and West Wales (Wales II). The χ^2 test was applied to these mortality figures, and the results are highly significant in females. Comparing all the regions, $\chi^2=117.9$, $P<0.001$. When Wales II is excluded the other regions compared give $\chi^2=48.1$, $P<0.001$, and for England alone $\chi^2=31.8$,

$P<0.001$, indicating that the regional variations in England are also significant. When applied to male deaths in the whole of England and Wales $\chi^2=25.7$, $P<0.01$; but when Wales II, the area of high mortality, is excluded the other regions compared show no significant difference.

TABLE I.—Deaths and Average Crude Death Rate Due to Post-cricoid Carcinoma in England and Wales, 1957-61

Region	Male		Female	
	No. of Deaths	Average Death Rate (per Million Population)	No. of Deaths	Average Death Rate (per Million Population)
Wales I	12	2.6	51	10.7
" II	12	6.7	41	21.4
North-Western ..	35	2.6	137	8.0
South-Western ..	17	2.1	67	7.9
Northern	21	2.6	44	5.4
East and West Ridings	16	1.6	74	6.9
North Midlands ..	22	2.5	60	6.6
Midlands	29	2.6	63	5.3
Eastern	12	1.4	49	5.4
London and South-Eastern	41	1.6	140	4.8
Southern	13	1.9	26	3.6

Death rates were calculated for both sexes in 10-year age-groups from 35 years upwards in the two Welsh regions and in England. The increased mortality in Wales was apparent in all groups except men of 75 years and older (Table II). Social class could be established in only 329 cases, but so far as could be seen from these limited data deaths were distributed proportionately between classes (Table III).

TABLE II.—Total Death Rate from Post-cricoid Carcinoma in Different Age-groups, 1959-61 (Per Thousand Population)

Sex	Region	35-44	45-54	55-64	65-74	75+
Male	Wales II	0.022	—	0.019	0.111	0.071
	" I	—	0.030	0.018	0.050	—
	England	0.001	0.002	0.039	0.029	0.074
Female	Wales II	0.062	0.037	0.104	0.270	0.250
	" I	0.016	0.030	0.035	0.093	0.095
	England	0.008	0.027	0.042	0.056	0.049