

	1940-1949		1950-1959		1960-1964		1965-1969	
	Male	Female	Male	Female	Male	Female	Male	Female
No. of patients	197	500	574	1803	416	989	392	1053
Percent at 3 years	54	72	73	84	80	87	80	88
Percent at 5 years	51	69	73	83	78	87	—	—
Percent at 10 years	48	68	73	83				
Percent at 15 years	48	68						

Source: End Results in Cancer, Report No. 4, End Results Section, Biometry Branch, National Cancer Institute, 1972, p. 162.

and carcinoma of the colon, osteomas and sebaceous cysts.⁴³ The multiple hamartoma syndrome (Cowden's disease) is an analogous disorder first described by Lloyd and Dennis in 1963.^{44,45} Patients with this autosomal dominant disorder exhibit some form of thyroid neoplasia, most often as goiter or multicentric adenomas, but in some cases as carcinoma. Other prominent familial features of this syndrome include mucocutaneous papillomas, lichenoid keratoses of the face, neck, hands and forearms, angiomas, subcutaneous and retroperitoneal lipomas, ovarian cysts, fibrocystic disease and carcinoma of the breast. Adenomatous, metaplastic or inflammatory polyps and ganglioneuromas of the gastrointestinal tract have been described.

Iodine Deficiency as a Co-factor in Thyroid Carcinogenesis

In experimental animals such as rats, mice, and Syrian hamsters, chronic iodine deficiency may eventuate into carcinoma of the thyroid after a succession of

pathogenic events which include intense follicular hyperplasia, hypertrophy and nodule and adenoma formation. The evidence in man for an etiologic association between severe iodine deficiency and thyroid cancer has consisted of increased thyroid cancer incidence and mortality, particularly of the follicular and anaplastic types, in geographic areas considered to be at high risk for adenomatous or nodular goiter. The foci of carcinoma have usually been located in otherwise normal parenchyma rather than within hyperplastic nodules.^{46,47} It has even been suggested that the frequency of goiter and thyroid cancer in Switzerland diminished after the introduction of iodized table salt. Those who argue against a direct causal relationship between endemic goiter and thyroid carcinoma point to prior studies in geographic areas where there was no correlation (i.e., Australia, Austria, Finland and the United States), or where the frequency of goiter was low and thyroid cancer was high (i.e., Hawaii, Iceland and Newfoundland).⁴⁸ Other reports from Switzerland subsequent to the introduc-

	All Ages		Under 25		25-44	
	Male	Female	Male	Female	Male	Female
Percent at 5 years	75	85	96	99	92	98
Percent at 10 years	74	86	96	99	91	96
	45-54		55-64		65+	
	Male	Female	Male	Female	Male	Female
Percent at 5 years	76	91	61	67	39	46
Percent at 10 years	70	89	49	65	33	44

Source: End Results in Cancer, Report No. 4, End Results Section, Biometry Branch, National Cancer Institute, 1972, p. 164.

tion of iodized table salt do not substantiate a continuing trend of decreasing frequency of thyroid cancer, but rather emphasize the stable rates of thyroid cancer mortality, decreasing incidence of goiter, and increasing proportion of thyroid cancers that are classified as papillary.^{49,50} The observation of increased thyroid cancer mortality in an endemic goiter area, i.e., where the prevalence of goiter is 10 percent or greater, may be due to the higher proportion of anaplastic carcinomas.* In addition, thyroid enlargement due to iodine deficiency may obscure the existence of a cancer, and because of delay in seeking medical care, the majority of malignant tumors are diagnosed at more advanced stages.⁵¹ In studies conducted in the United States during 1939-1951, the average annual age-

adjusted mortality due to thyrotoxicosis (secondary to toxic nodular goiter and the diffuse hyperplasia of Graves' disease) diminished significantly in relation to the decreasing prevalence of endemic goiter; during the same period of time, the age-adjusted mortality due to thyroid cancer increased slightly.⁵² To summarize, the epidemiologic evidence that endemic iodine deficiency may serve as a necessary and sufficient cause of the follicular type of thyroid carcinoma is unconvincing, although iodine prophylaxis may alter the histologic pattern of thyroid cancer, and ultimately diminish the mortality due to thyrotoxicosis.

Graves' Disease and Hashimoto's Thyroiditis

The coincidence of thyrotoxicosis and thyroid cancer was considered to be extremely rare. In more recent statistical surveys, the prevalence of thyroid carcinoma in patients with toxic goiter has been reported variously as being between 0.2 and 5.0 percent.⁵³ The average prevalence

*It has also been suggested that the highly malignant hemangioendothelioma of the thyroid occurs in geographic areas where iodine is deficient and particularly in older patients with chronic goiter. (Cubilla, A.: *Personal Communication*, 1977.)