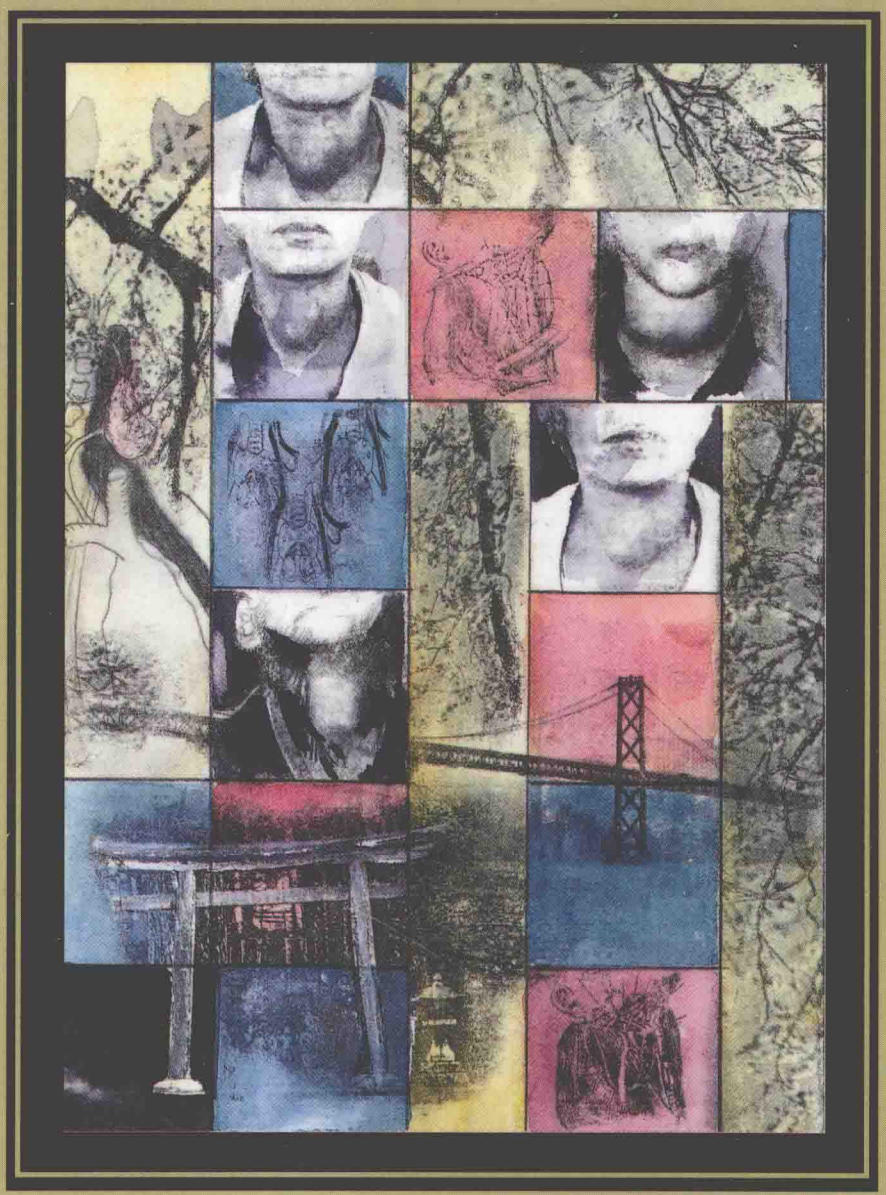
Thyroid Cancer

Diagnosis and Treatment



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Foreword

Two of the world's leading thyroid cancer experts, Shiro Noguchi of Beppu, Japan, and Orlo Clark of San Francisco have combined forces with their colleagues to produce the definitive text on this subject. Although thyroid cancer is a rare disease, it is a topic worthy of study; research and clinical work in this area has had widespread implications. Many of the new techniques and breakthroughs in understanding disease processes as a whole have grown out of advances in thyroidology, which continues to pioneer medical advances.

A compendium such as this allows the reader to gain a wider perspective of this topic. This book recalls John Keats' line, "I stood tip-toe upon a little hill." In similar fashion, this book permits us to climb a metaphoric hill and view the spectrum of progress to date in the understanding of thyroid cancer and its treatment. I heartily commend this work to you.

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Preface

Thyroid cancer is the most common endocrine neoplasm, excluding ovarian neoplasms. Despite the overall excellent outcome for patients diagnosed with this disease, death is a more common outcome than with other endocrine cancers. This text is written to help clarify the best methods for the immediate management of patients with thyroid neoplasms for all of the team members involved in the care of patients with this diagnosis. General, head and neck, and endocrine surgeons as well as surgical residents who treat patients with thyroid neoplasms are our intended audience as are thyroidologists, endocrinologists, nuclear medicine specialists, and other physicians.

This book reflects contributions from an international group of authorities. Together they provide a rationale for the various approaches to the management of thyroid nodules and thyroid cancer. Although there is general agreement regarding the evaluation of the patient with a thyroid nodule, the extent of thyroid gland resection, the need for central or lateral neck dissection, the use of postoperative radioiodine therapy, external radiation therapy, and TSH suppressive therapy remain controversial. In Japan, the emphasis is on subtotal thyroidectomy with regional node dissection without the use of post-thyroidectomy treatment with ^{131}I for patients with differentiated thyroid cancer of follicular cell origin. In the United States, the preferred treatment is total or near total thyroidectomy with postoperative radioiodine with TSH therapy. Prophylactic nodal dissection is not usually recommended for patients with papillary thyroid cancer in the United States.

Our text provides the data to document why various diagnostic and therapeutic methods are used. Chapters regarding cytologic and histologic evaluation, application and value of imaging studies, recent advances in the diagnosis and treatment of medullary thyroid cancer, angiogenesis, TSH suppression therapy, and thyroid oncogenes are included. Our goal is to present our readers with an international perspective on the current management of patients with thyroid neoplasms.

Orlo H. Clark, M.D.
Shiro Noguchi, M.D., Ph.D.

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The writing or editing of any book requires the help of many individuals. Endocrine surgery has afforded both Professor Noguchi and I with the opportunity to interact with talented surgeons, endocrinologists, nuclear medicine physicians, radiologists, and pathologists who have provided tremendous intellectual stimulation and friendship over the years. We have benefited from the educational opportunities in our respective medical centers and countries. We also have been extremely fortunate to have been exposed to the inspired teachings of Mr. Selwyn Taylor and Professor Richard Welbourne at the Royal Postgraduate Medical Center, Hammersmith Hospital, London.

I (O.C.) would also like to pay tribute to my father, Orlo Holly Clark, M.D., and uncle, William Fischer Clark, M.D., both general surgeons, whose love of medicine and surgery and desire to help people influenced me in my career selection. My wife, Carol, deserves my greatest appreciation; she is a consummate source of inspiration and encouragement.

I (S.N.) would like to dedicate this book to my foster father, the late Dr. Akito Noguchi, and Dr. Hideo Kurihara, who introduced me to the basic skills of thyroid surgery, and to my wife, Ryoko, who has continuously encouraged me over the past 30 years.

Thyroid Cancer

Diagnosis and Treatment

Contents

PART

I

Overview and Epidemiology, Cytologic, and Histologic Evaluation

CHAPTER 1

Overview

SHIRO NOGUCHI, M.D., Ph.D.

EPIDEMIOLOGY

Clinically evident thyroid cancer represents an uncommon disease in the general population, with an annual incidence of about 2 to 4 new cases per 100,000 population in countries in which adequate amounts of iodine are ingested. Microscopic thyroid carcinoma, however, is extremely prevalent. The highest prevalence rate of 35.6% was reported by Harach et al.[1] in 101 consecutive autopsies. The difference in the prevalence rate among the reported autopsy series may be partly the result of the method of examination, the diagnostic criteria, and real geographic differences (Table 1-1).

Kugimoto et al.[15] performed an epidemiologic survey of 30,359 subjects (which is 86.4% of the total inhabitants of the studied area, in Nagano, Japan), 1965 through 1967. The method of detection was palpation by experienced surgeons; they found thyroid cancer in 0.08% of males and 0.18% of females. Ishida et al.[16] examined 152,651 subjects and found 0.14% of them to have small but detectable thyroid carcinomas by mass screening. Omata et al.[17] reported an incidence of 0.58% in 19,821 subjects. The different incidence of thyroid cancer in these Japanese mass screenings is primarily related to the method of the survey. In the study of Omata et al.,[17] ultrasonographic examination, which can

TABLE 1-1 Prevalence of Cancer by Autopsy Studies

Author	Year	Geographic Area	No. of Autopsies	Prevalence (%)
Silverberg and Vidone[2]	1966	Connecticut, USA	300	2.70
Farooki[3]	1969	Philadelphia, USA	220	0.50
Sampson et al.[4]	1969	Hiroshima and Nagasaki, Japan	1096	17.90
Sampson et al.[5]	1974	Minnesota, USA	157	5.70
Fukunaga and Yatani[6]	1975	Columbia	607	5.60
	1975	Hawaii (Japanese)	298	24.20
	1975	Ontario, Canada	100	6.00
	1975	Poland	110	9.10
	1975	Sendai, Japan	102	28.40
Sobrinho-Simoes et al.[7]	1979	Portugal	600	6.50
Bondeson and Ljungberg[8]	1981	Sweden	500	8.60
Pingitore[9]	1982	Toscana, Italy	111	3.60
Arellano and Ibarra[10]	1984	Chile	274	3.60
Harach et al.[1]	1985	Finland	101	35.60
Franssila and Harach[11]	1986	Finland	93	27.00
Lang et al.[12]	1987	Hannover, Germany	1020	6.20
Ottino et al.[13]	1989	La Plata, Argentina	100	11.00
Yamamoto et al.[14]	1990	Tokushima, Japan	408	11.30

detect lesions larger than 4 mm, was used. The incidence of thyroid cancer detected by mass screenings is about 1 of 100 microscopic thyroid cancers observed in an autopsy series.[2-14] Clinically evident thyroid cancer incidences appearing in the cancer registry are also about 1 of 100 ultrasonographically detectable thyroid cancers. Therefore about 1 of 10,000 microscopic cancers may eventually become clinical carcinoma.

ETIOLOGIC FACTORS

In the vast majority of thyroid cancers, it is hard to assign a specific etiologic factor in a routine clinical setting. Genetic factors may play some role in the etiology of thyroid cancer, not to mention the medullary, but also in papillary cancer, since there is a significant difference in standardized incidence ratios by ethnicity in the United States.[18] The occurrence of thyroid cancer in recognized familial syndromes was reported as Pendred's syndrome,[19] Gardner's syndrome,[20] chemodectoma,[21] and familial adenomatous polyposis.[22] Women under 35 years of age with familial adenomatous polyposis have been estimated to have a 160-fold higher risk of thyroid carcinoma than the general population[23] and familial clusters of nonmedullary cancer are also reported.[24-39] However, a responsible gene is not yet identified.

One of the most well-studied causes is therapeutic-dose radiation for enlarged thymus, tonsils, adenoids, acne vulgaris, lymphoid hyperplasia, and hyperthyroidism in childhood. In 1949, the relationship between irradiation and thyroid cancer was first noted by Quimby and Werner.[40] Carefully designed epidemiologic studies have confirmed the relationship between radiation treatment and thyroid neoplasms. Ron et al.[41] showed that children who received 6 mGy to the thyroid had a fourfold increase in the rate of thyroid cancer. Shore et al.[42] followed up 2650 subjects who underwent irradiation for an enlarged thymus, 90% of whom were treated at 1 year of age, compared with 4800 nonirradiated siblings. Mean follow-up for the exposed subjects was 24 years. In the irradiated group, 30 had thyroid cancer, contrasting with only one in the nonirradiated group. Schneider et al.[43] followed up 3042 irradiated patients and found 37.6% had developed thyroid nodules; among those, 318 (10.5%) had thyroid cancer 3 to 42 years later. In our study of thyroid cancer patients under 20 years old, 3 of 27 had a history of diagnostic-dose irradiation (2 to 9 mGy) to the head, neck, or chest during their infancy or childhood, and one had a therapeutic dose (0.4 mGy). Sixty-nine age- and sex-matched control subjects were randomly selected from patients who visited the same hospital in the same calendar year. The only