TUMORS
of the
THYROID GLAND

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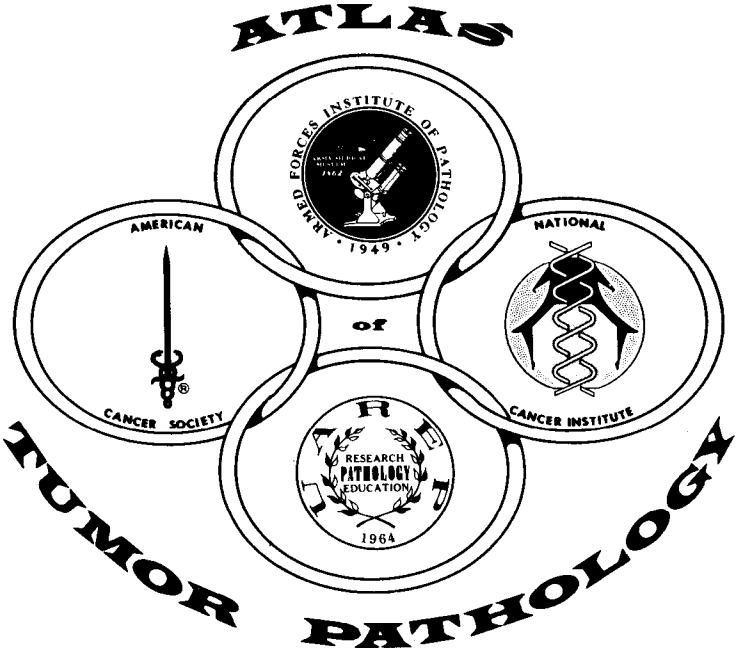

ATLAS OF TUMOR PATHOLOGY

Second Series

Fascicle 4

TUMORS OF THE THYROID GLAND

by

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EDITOR'S NOTE

The Atlas of Tumor Pathology was originated by the Committee on Pathology of the National Academy of Sciences—National Research Council in 1947. The form of the Atlas became the brain child of the Subcommittee on Oncology and was shepherded by a succession of editors. It was supported by a long list of agencies; many of the illustrations were made by the Medical Illustration Service of the Armed Forces Institute of Pathology; the type was set by the Government Printing Office; and the final printing was made by the press at the Armed Forces Institute of Pathology. The American Registry of Pathology purchased the fascicles from the Government Printing Office and sold them at cost, plus a small handling and shipping charge. Over a period of 20 years, 15,000 copies each of 40 fascicles were produced. They provided a system of nomenclature and set standards for histologic diagnosis which has received world-wide acclaim. Private contributions by almost 600 pathologists have helped to finance the compilation of an index by The Williams & Wilkins Company to complete the original Atlas.

Following the preparation of the final fascicle of the first Atlas, the National Academy of Sciences—National Research Council handed over the task of further pursuit of the project to Universities Associated for Research and Education in Pathology, Inc. Grant support for a second series was generously made available by both the National Cancer Institute and the American Cancer Society. The Armed Forces Institute of Pathology has expanded and improved its press facilities to provide for a more rapid and efficient production for the next series. A new Editor and Editorial Advisory Committee were appointed, and the solicitation and preparation of manuscripts continues.

This second series of the Atlas of Tumor Pathology is not intended as a second edition of the first Atlas and, in general, there will be variation in authorship. The basic purpose remains unchanged in providing an Atlas setting standards of diagnosis and terminology. Throughout this new series, the term chosen by the Committee on Tumor Nomenclature of the International Union Against Cancer is shown by an asterisk if it corresponds to the author's heading, or as the first synonym in italics if it differs from the author's first choice. Hematoxylin and eosin stained sections still represent the keystone of histologic diagnosis; therefore, most of the photomicrographs will be of sections stained by this technic, and only sections prepared by other technics will be specifically designated in the legends. It is hoped that in many of the new series a broader perspective of tumors may be offered by the inclusion of special stains, histochemical illustrations, electron micrographs, data on the biologic behavior, and other pertinent information for better understanding of the disease.

The format of the new series is changed in order to allow better correlation of the illustrations with the text, and a more substantial cover is provided. An index will be included in each fascicle.

It is the hope of the Editor, the Editorial Advisory Committee, and the Sponsors that these changes will be welcomed by the readers. Constructive criticisms and suggestions will be appreciated.

Harlan I. Firminger, M.D.

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William A. Meissner, M. D.

Shields Warren, M. D.

CONTENTS

TUMORS OF THE THYROID GLAND

INTRODUCTION

Clinical observations and experimental studies have contributed enough new information since publication of the first "Tumors of the Thyroid Gland" in 1953 to warrant a rather complete rewriting of the fascicle. The diagnosis and treatment of thyroid cancer have been improved with the introduction of new technics and with better understanding of the disease. The hormonal dependency of some thyroid tumors is appreciated. In 1963 the pharmacologists, Hirsch and associates, discovered a new thyroid hormone, thyrocalcitonin. More reliable statistics regarding incidence and death rates of thyroid cancer allow a better evaluation of the biologic behavior of these tumors. Many studies implicate radiation as having a role in the development of thyroid tumors in children. In addition to these and other developments, a specific type of thyroid carcinoma has been defined and established as a part of a new syndrome.

In this second writing, we have brought the previous classification and descriptions up to date. Most of the references are recent and many have particularly good bibliographies. Discussions of unusual tumors and tumor-like conditions have been expanded so that the fascicle might be of greater use as a reference. In the pathologic diagnosis of thyroid tumors there are particular problem areas for us, and apparently for our colleagues as well, as evidenced by cases sent for consultation; we have attempted to clarify such problem areas with more extensive discussion and additional photomicrographs.

In spite of great advances in the understanding of thyroid tumors, there are problems and unanswered questions. The great variety of types and the wide range of aggressiveness of thyroid cancers continue to complicate both diagnosis and management. It is a paradox that the low grade papillary adenocarcinoma and the highly malignant giant cell carcinoma both arise from the same follicular epithelium. Evaluation of different methods of therapy continues to be a problem partly because thyroid cancers are uncommon and partly because many of them are very low grade. Five or 10 years is insufficient time for adequate follow-up information for many thyroid tumors; clinical recurrences or death from the tumor may not take place until 20 or 30 years after the original diagnosis. Lastly, it should be stressed that it is still difficult clinically, and at times pathologically, to distinguish true neoplasm from a nodule of endemic goiter.

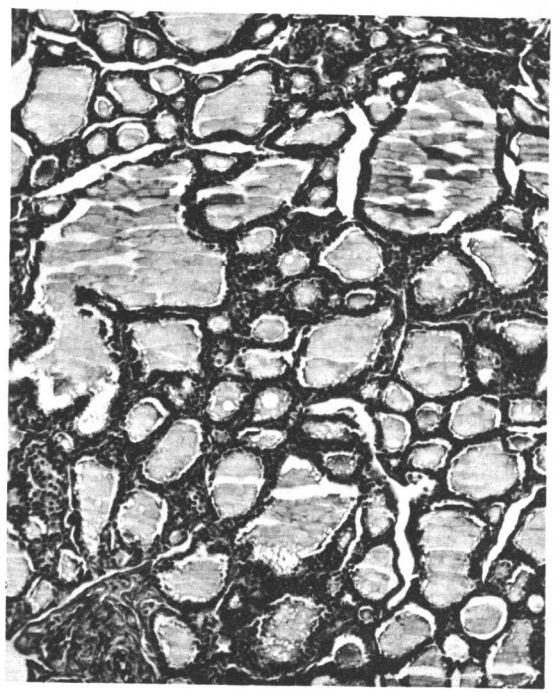
THE NORMAL THYROID

MORPHOLOGY (Figures 1–13)

The thyroid gland consists of two lateral lobes which usually are connected by an isthmus of variable size. In addition, a pyramidal lobe extends upward from the isthmus in about 40 per cent of persons. The right lobe is often somewhat larger than the left. The gland normally is soft, yellow-red and covered with a thin capsule. Cut surfaces glisten because of colloid. The rich blood supply comes from the superior and inferior thyroid arteries. Lymphatics drain to deep cervical nodes, to pretracheal nodes, and to retrosternal nodes.

The average weight of the normal thyroid generally has been considered to be 25 to 30 gm. with a range of 10 to 60 gm. Recent studies, however, give lower figures, perhaps because of the widespread use of iodized salt. Mochizuki and associates found that the mean weight of adult glands (18 years of age and over) in New York City was 16.7 $\pm$ 6.9 gm. (females 14.9 $\pm$ 6.7 gm. and males 17.5 $\pm$ 6.8 gm.). They estimated that one per cent of New York residents had thyroids weighing about one third of the mean. In children, according to Kay and associates, the average normal weight (again with a wide range) increases from 1.5 gm. at birth to 14.2 gm. in the 15 to 19 year age group.

The unit of thyroid structure is the follicle, a closed sac lined with epithelium and containing colloid (figs. 1, 2). Individual follicles are roughly spherical and vary considerably in size with an average diameter of about 200 micra. Thyroid lobules consist of 20 to 40 follicles bound together by a thin sheath of connective tissue and supplied by a lobular artery; it is possible that nodules develop from such an anatomical unit. In spite of the great vascularity and the close relationship of small vessels and capillaries to the follicles, neither blood vessels nor interfollicular stroma are conspicuous in the normal gland.

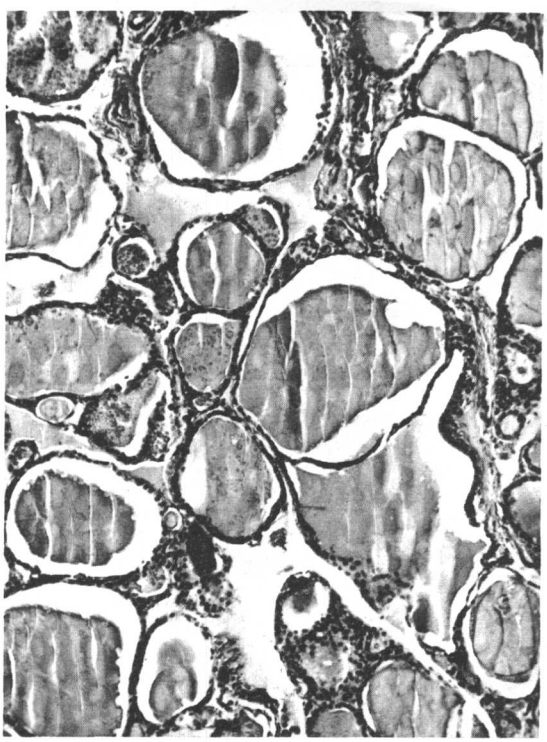


NORMAL THYROID

Figure 1. This thyroid when removed at autopsy from an 8-year-old child was considered to be normal. There was no clinical evidence of thyroid disease. Hematoxylin and eosin stain.* × 100. A.F.I.P. Atlas No. 67-3-1.

* Throughout the fascicle where the stain is not so designated, hematoxylin and eosin stain has been used.

The epithelium of the follicle is usually single-layered, cuboidal, and rests on a basement membrane. Electron microscopic studies (figs. 3–5) (Klinck; Heimann) show that the basement membrane envelops the entire follicle, extending without interruption along the bases of the follicular cells, but never into the intercellular spaces. The lateral borders and the base of the cell are covered with a plasma membrane, with the membranes of adjacent cells separated by a space of relatively constant width. On the colloid surface of the cells, there is a brush border composed of cytoplasmic extensions or microvilli which project into the colloid. The microvilli are up to 0.2 microns long.



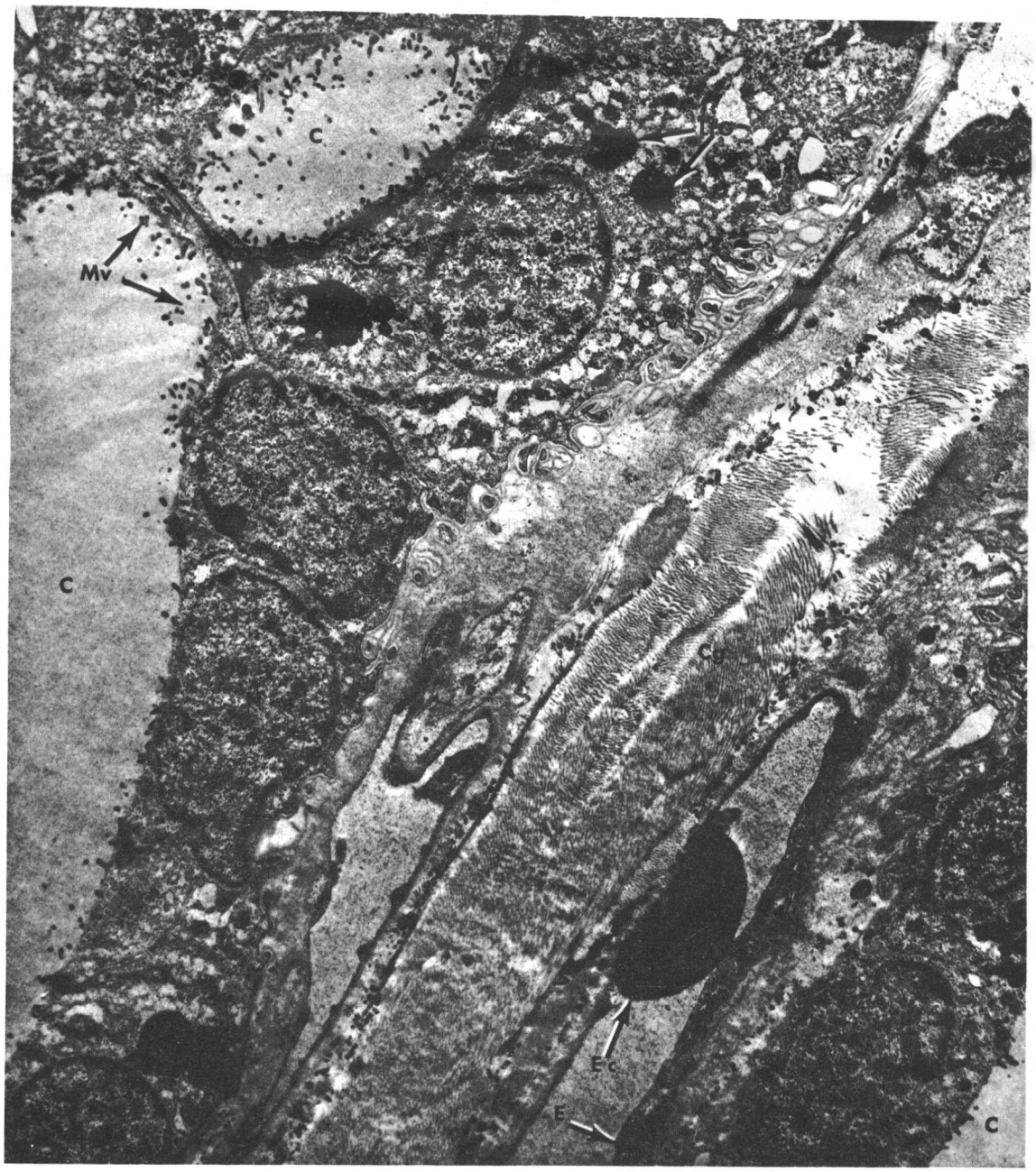
NORMAL THYROID

Figure 2. The thyroid gland from an 80-year-old man was removed at autopsy. It weighed 15 gm. and was considered to be grossly and microscopically normal. There was no clinical evidence of thyroid disease. On the average, the follicles are somewhat larger than those in the 8-year-old child and the epithelium tends to be more flattened, indicating decreased activity. × 100. A.F.I.P. Atlas No. 67-3-2.

In the resting cell the nucleus is usually central, roughly spherical, and about one-third the diameter of the cell. The nucleolus is not prominent. Mitochondria are evenly distributed throughout the cytoplasm. They are rod-shaped with the cristae oriented at right angles to the long axis. The endoplasmic reticulum is conspicuous, widely distributed, and predominantly of the rough-surfaced type. Ribosomes lie both free in the cytoplasm and along the covering membranes of the cisterns. The colloid is uniform in density and slightly acidophilic. With the light microscope, vacuoles are often seen at its periphery, giving a scalloped appearance. By electron microscopy, such vacuoles are not found.

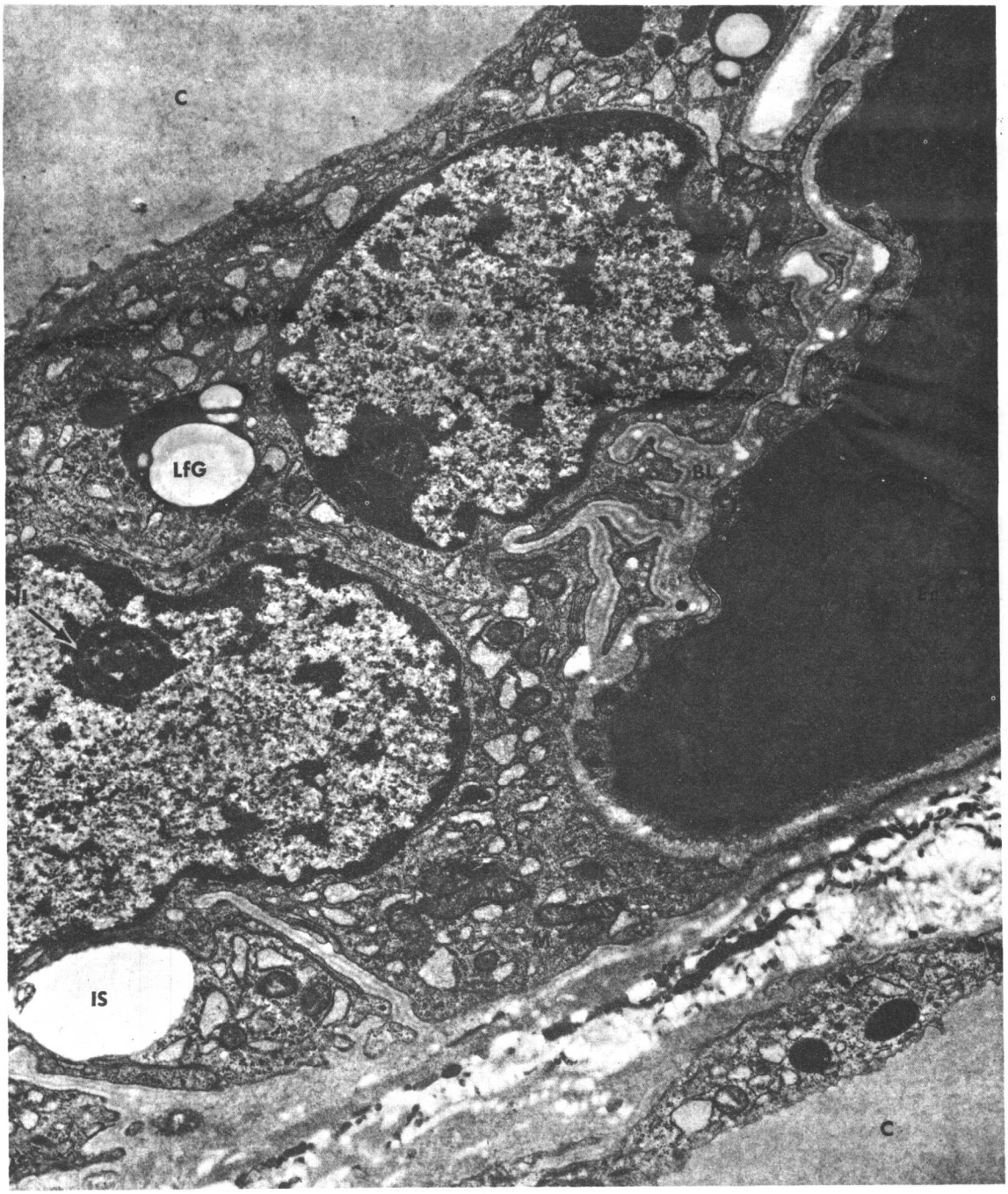
When stimulated to increased activity, the follicle becomes smaller, colloid diminishes, the follicular cells become tall columnar, and the nuclei enlarge and lie nearer the base. There is an increase in endoplasmic reticulum and in ribosomes, and the Golgi apparatus hypertrophies. Microvilli are greatly increased both in number and in length. Intracytoplasmic droplets appear which apparently are colloid droplets and represent colloid that has been engulfed by cytoplasmic pseudopod streamers.

With decreased activity the follicles enlarge and accumulate more colloid; the epithelium changes to a low cuboidal or flat type. In older individuals the follicles become less active, presumably because of diminished requirements; some, but not all, glands in older persons show a mild increase of stromal connective tissue.



NORMAL THYROID

Figure 3. An electron micrograph shows portions of two adjoining follicles. The microvilli projecting into the colloid are clearly visible. The structures are identified as follows: C, colloid; Cg, collagen; E, endothelium; Ec, erythrocyte; LfG, lipofuscin granule; Mv, microvilli; N, nucleus. Approx. × 4500. (Courtesy of the Armed Forces Institute of Pathology.) A.F.I.P. Atlas No. 67-3–3.



NORMAL THYROID

Figure 4. This electron micrograph also shows portions of two adjacent follicles. The epithelial layer of the lower follicle is flat. These structures are identified as follows: BL, basal lamina; C, colloid; Cg, collagen; Ec, erythrocyte; IS, intercellular space; LfG, lipofuscin granule; M, mitochondria; N, nucleus; N1, nucleolus. × 10,000. (Courtesy of the Armed Forces Institute of Pathology.) A.F.I.P. Atlas No. 67-3-4.