Chapter 136: Neoplasms of the Thyroid

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The most common indication for thyroid surgery is the solitary nodule. An intelligent clinical approach to these patients depends on the otolaryngologist's thorough knowledge of thyroid anatomy, physiology, and pathology. For the past 5 years, the Index Medicus has listed over 350 papers each year in English under the heading "Thyroid Neoplasms", indicating the dynamic and often controversial natural of this subject.

Surgical Anatomy

Chapter 133 discussed thyroid anatomy; however, some points are worth highlighting.

Muscles

The sternohyoid and sternothyroid muscles (Fig. 136-1) are innervated by the ansa cervicalis, which descends along the lateral border of the sternohyoid to innervate both muscles low in the neck. If it is necessary to divide the sternohyoid and sternothyroid muscles for better exposure, this should be done high in the neck to protect the nerves.

Blood vessels

The superficial veins are readily visualized beneath the platysma and generally do not present a problem. The deep thyroid veins leave the gland in the same plane as the thyroid arteries. If they are inadvertently torn, extravasated blood can quickly obliterate important surgical landmarks (Fig. 136-2).

The superior thyroid artery as it penetrates the superior pole of the gland is just lateral and inferior to the external branch of the superficial laryngeal nerve, which innervates the cricothyroid muscle. Great care must be taken to avoid injury to that nerve during arterial ligation (Fig. 136-3). The inferior thyroid artery may divide into branches before entering the thyroid gland. Those branches can be intimately associated with the recurrent laryngeal nerve (Fig. 136-4). Thus ligation of the artery should be postponed until the recurrent nerve is clearly visualized.

Nerves

In the dissection of 400 specimens Fowler and Hanson (1929) found that both recurrent laryngeal nerves were located 1 to 2 cm lateral to the trachea in the region of the lower pole of the thyroid (Fig. 136-5). As the nerves ascend, they may anterior or posterior to the inferior thyroid artery (Fig. 136-4). Twenty-eight variations in the relationship of the recurrent laryngeal nerve to the inferior thyroid artery were described by Reed (1943); the most common ones are illustrated in Fig. 136-6. In 253 cadaver dissections (506 nerves), the relationship of the recurrent laryngeal nerve to the inferior thyroid artery was similar on the left and right sides in only 17%.

It is appropriate to search for the nerve caudad to the artery, since it rarely branches in that area. At the level of the inferior thyroid artery there may be branches of the recurrent nerve that are extralaryngeal in nature; this was true in 5.% of Reed's nerve dissections. All branches should be delineated and protected. The nerve continues very close to the posterior capsule of the thyroid gland as it ascends to enter the larynx between the inferior cornu of the thyroid cartilage and the arch of the cricoid. On rare occasions (less than 1%) the recurrent laryngeal nerve may pass directly from the vagus to the larynx close to the superior thyroid vessels. For this reason some surgeons advise first finding the nerve near its laryngeal entrance.

The superior laryngeal nerve divides into two branches at the level of the hyoid cornu. Both branches lie near the superior thyroid artery and may be injured if the artery is ligated too high above the thyroid gland (see Fig. 136-3).

Parathyroid glands

Identification of the parathyroid glands is imperative in cases of total thyroidectomy. The inferior parathyroid glands are usually located at the inferior pole of the thyroid, and they are supplied by the inferior thyroid vessels. The small branches to the parathyroid gland may be kept intact with careful dissection. Because of their migration (third branchial pouch derivatives), however, they may be found near the carotid bifurcation, or rarely they may descend into the thorax (for example, within thymus tissue).

The superior parathyroid glands are most commonly found near the cricothyroid joint posteriorly; their shorter migration (fourth branchial pouch derivatives) makes their location less variable. The superior glands may also be attached to the thyroid capsule posteriorly or posterosuperiorly. A more detailed anatomic description of parathyroid gland location is given in Chapter 137.

All four parathyroid glands are found in 75% of persons, whereas 5% to 10% of all persons have three and more than 10% have more than four parathyroid glands (Gilmour, 1933). As many as 10 parathyroid glands have been reported in a single patient.

Surgical Pathologic Findings

Unfortunately, there are several classifications of thyroid tumors, which adds to the difficulty of understanding thyroid pathologic conditions. The pathologic conditions discussed here are of specific interest to the thyroid surgeon.

Benign neoplasms

Adenomas are composed of glandular epithelium and are histologically nearly all follicular, although occasionally an adenoma will be papillary. Follicular adenomas are subclassified, by decreasing frequency, into fetal (microfollicular), colloid (simple or macrofollicular), embryonal (trabecular or atypical), and Hurthle (oxyphil cell). Adenomas are

solitary, well-circumscribed, encapsulated lesions and are the most common of all thyroid neoplasms (Sommers, 1982).

It is difficult on gross examination to differentiate between an adenoma and the nodule of an adenomatous goiter. If the gland appears otherwise normal, a solitary nodule is usually an adenoma. Follicular adenomas often function and will take up some radioiodine, but the "hot" nodule is with few exceptions an adenomatous goiter rather than a neoplasm.

Thyroid cyst is a term that is applied to any thyroid condition that appears largely cystic by ultrasound; 15% to 20% of thyroid nodules are cystic (Aschcraft and Van Herle, 1981b). In a group of cystic lesions selected for surgery on the basis of needle aspiration cytology, 25% were found to be colloid nodules, 43% to be adenomas, and 32% to be thyroid carcinomas (Rosen et al, 1986). The cystic degeneration is related to necrosis, liquefaction, and hemorrhage. These cysts usually undergo spontaneous resolution within 2 to 3 months; if they persist, a further evaluation for thyroid carcinoma is warranted.

Malignant neoplasms

Malignant neoplasms of the thyroid include papillary carcinoma, follicular carcinoma, Hurthle cell carcinoma, medullary carcinoma, anaplastic carcinoma, thyroid lymphoma, sarcomas, and metastatic carcinoma. The relative degree of malignancy is related to the histological classification. Papillary and follicular carcinomas are well-differentiated tumors with low-grade malignant behavior; their prognoses are related primarily to the patient's age and sex and to their size at the time of diagnosis (Cunningham et al, 1990). Medullary and anaplastic thyroid carcinomas are less differentiated and tend to be very aggressive; important prognostic factors for these patients are tumor size, direct extension into adjacent structures, and the presence or absence of distant metastases (Meissner and Warren, 1969; Woolner et al, 1961).

For purposes of discussion, the thyroid malignancies will be presented according to the 1981 revision of the World Health Organization histologic classification system (Hedinger et al, 1989).

Papillary carcinoma

Papillary carcinoma occurs as an irregular, solid or cystic mass that arises from follicular epithelium. The lesion is nonencapsulated but sharply circumscribed. The cut surface is rough, and if cysts are present, they contain a brown, watery fluid. Microscopically, the hallmark is papillary fronds of epithelium. They have distinct, relatively uniform cells, and mitoses are rare; this allows for microscopic diagnosis with a relatively small sample (for example, fine needle biopsy). Most papillary tumors contain both papillary and follicular components. Cells are generally large but can be of variable size and contain pink, finely granular cytoplasm with large, pale nuclei (ground glass or "Orphan Annie" appearance), which often contain nuclear grooves (Bhambhani et al, 1990; Chan and Saw, 1986). Rounded calcific deposits (psammoma bodies) can be found ni 50% of papillary carcinomas. Their significance is unknown, and although they

can be found occasionally in other thyroid tumors, they are highly characteristic of papillary carcinoma.

Prognosis is directly related to the size of the tumor; clinically small (less than 1.5 cm) or occult tumors have an excellent prognosis. About 5% of these tumors are encapsulated; these rarely metastasize and carry a very favorable prognosis. The prognosis becomes worse when the tumor extends beyond the thyroid capsule. Approximately 5% to 10% of papillary tumors are locally invasive, usually discovered at surgery. These tumors have a high recurrence rate, and patients with them have a high mortality; they may present with hemoptysis or dysphagia. The tumor may assume a more malignant character even 20 to 30 years after diagnosis. This often results in a more rapid deterioration of the patient's health, leading to death. For that reason application of the usual 5-year survival rate is unrealistic. Ten-year survival rates are 80% to 90%.

In one series, cervical metastases were found with 50% of occult and small tumors and with over 75% of palpable papillary thyroid carcinomas (Noguchi et al, 1987). The central cervical (level VI; see discussion of neck dissection below) and lateral jugular (levels II, III, and IV) chains are most often involved. The presence of cervical metastases causes a high recurrence rate but not a higher cancer mortality rate. The presence of extracapsular spread is not as ominous as it is in squamous cell carcinomas (Spires et al, 1989). Distant metastases are present in less than 1% of cases initially but in 5% to 10% of patients eventually (Ruegemer et al, 1988). Lung and bone are the most common sites. Total thyroidectomy reduces the rate of distant metastasis.

Tumors arising as a result of radiation exposure tend to be larger and multicentric and have a higher recurrence rate than other papillary tumors. They often show lymphocytic infiltration or Hashimoto's disease. Survival is similar to other papillary tumors. Papillary thyroid carcinoma may rarely arise within a thyroglossal duct cyst. These tumors are usually small but may be locally invasive. Wide local excision (Sistrunk procedure) is usually adequate treatment (Page et al, 1974).

Follicular carcinoma

Follicular carcinoma is the second most common malignancy and runs a low-grade course. Microscopically, this tumor has characteristics similar to those of benign follicular adenomas, and thus it is difficult to distinguish as malignant on frozen section or fine needle biopsy. This tumor is usually encapsulated and consists of highly cellular follicles and microfollicles with compact, dark-staining nuclei with fairly uniform size, shape, and location. Most follicular carcinomas are single, solid, noncystic tumors with no necrosis. Diagnosis is made when invasion of the capsule, adjacent glands, lymphatics, or blood vessels is seen. Follicular thyroid carcinomas are subdivided into minimally, moderately, or highly invasive; mortality is related to the degree of vascular invasion (Mazzaferri and Oertel, 1983).

When some or all of the cells in the tumor are noted to be oxyphilic (also called Askanazy or Hurthle cells), it is termed *Hurthle cell tumor*. This variant carries a less favorable prognosis than nonoxyphilic follicular carcinoma.

Age is the most important prognostic factor. Patients under 40 years of age at the time of diagnosis have the best survival rates. Follicular tumors in patients over 40 years of age are more aggressive and have higher recurrence rates; they also do not concentrate radioiodine very well.

Distant metastases are more common in follicular than in papillary thyroid carcinoma and may occur with a very small primary tumor. The most common sites, in descending order of frequency, are lung, bone, brain, and soft tissue (liver, bladder, skin). Bulky functional metastases may cause thyrotoxicosis, often primarily "T_3 toxic". Distant metastases are more common with highly invasive, large (more than 5 cm), and Hurthle cell tumor types and are associated with a poorer prognosis.

Medullary carcinoma

Medullary carcinoma is an ill-defined, nonencapsulated, invasive mass. It feels very hard, and the thyroid may be fixed to adjacent structures. Histologically, it is composed of columns of epithelial cells and dense stroma that typically stains for amyloid and collagen. The nuclei are frequently hyperchromatic, and mitoses are common. The cells are fusiform and may form a whorling pattern. Calcifications are seen in 50% of tumors. Calcitonin may be identified by immunohistochemical stains; a more intense, homogeneous uptake pattern is associated with a better prognosis. Stains for thyroglobulin are negative. Several histologic pattern variants have been described (Dominguez-Malagon et al, 1989). Recently, a few cases have been found to produce melanin (Eng and Chen, 1989; Kimura et al, 1989). The gene involved in inherited medullary thyroid carcinoma is probably located on chromosome 10 (Carson et al, 1990).

Regional metastases occur early in the course of the disease, often before the primary tumor reaches 2 cm in size; they are found in 50% of patients at the time of presentation. Cervical lymph nodes (levels II, III, IV, and VI) and upper mediastinal disease (occasionally massive) are the usual sites. Distant metastases occur late in the disease and are usually to the lungs; liver, bone, brain, and adrenal metastases also occur. The bone metastases may be blastic but are usually lytic and may cause pathologic fractures.

In the inherited forms of medullary carcinoma, C-cell hyperplasia usually occurs bilaterally and multicentrically; it precedes and later undergoes transformation toward medullary carcinoma. Histologically these tumors are very similar to the sporadic form.

Prognosis for medullary thyroid carcinoma falls between that for anaplastic tumors and the well-differentiated tumors. Poor prognostic factors include age greater than 50 years, male sex, the presence of metastases at the time of diagnosis, and multiple endocrine neoplasia (MEN), type II-B phenotype. Sporadic medullary cancer has the same prognosis as familial medullary

cancer when age-matched cases are considered. Overall 10-year survival rates are 90% when the disease is confined to the thyroid gland, 70% with cervical metastases, and 20% with distant metastases. Seventy percent of patients with MEN II-B have metastases at the time of diagnosis; less than 5% survive 5 years. The value of early detection and screening programs can be seen by considering the recurrence rates by decade of diagnosis given in table 136-1.

Table 136-1. Medullary thyroid carcinoma: value of early detection

Age at diagnosis (yr)	Recurrence rate
1-10	0%
11-20	33%
-	-
-	-
61-70	67%.

Anaplastic carcinoma

Undifferentiated tumors have few differentiated structures and do not form amyloid stroma. It may even be difficult to demonstrate their epithelial nature. They are usually subdivided into spindle, giant cell, and small cell types, the former two being the most malignant (giant cell is the worst). The tumor may stain positive for thyroglobulin. There is a high degree of nuclear aneuploidy. These tumors grow rapidly and are often inoperable. They invade adjacent structures and metastasize extensively to cervical nodes and distant sites. Most often these tumors present as large, fixed masses. Tracheal invasion is found in 25% at the time of presentation. Vocal cord paralysis from recurrent nerve invasion and superior mediastinal syndrome are also common. Regional lymph node metastases are present in 90% at diagnosis. Distant metastases to the lung are found in 50% at the time of diagnosis; many other sites have been reported.

Treatment of any sort seldom results in cure; the 5-year survival rate is about 7%, and the mean survival after diagnosis is 6 months. Favorable prognostic factors include a small (less than 5 cm), unilateral tumor with no adjacent tissue invasion and no lymph node metastases; such anaplastic thyroid tumors are rare.

Shvero et al (1988) noted the importance of examining anaplastic thyroid tumors with immunohistochemical techniques for specific markers such as calcitonin and leukocyte common antigen. In their series, 5 of 26 cases of anaplastic thyroid carcinoma were reclassified on the basis of such markers to tumors with a better prognosis, clearly affecting treatment choices.

Lymphoma

Thyroid lymphoma may be primary or secondary. At autopsy the thyroid is involved in approximately 20% of patients with disseminated lymphoma. If the lymphoma is primary, it is usually a non-Hodgkin's, histiocytic lymphoma. Its peak onset is in the seventh decade, with a

6:1 female preponderance (Rasbach et al, 1985). There is often evidence of chronic lymphocytic thyroiditis and vessel wall invasion. Serum tests for antithyroid antibodies are positive in 83% of patients (Aozasa et al, 1986).

Prognosis is related to the extent of disease at the time of diagnosis. If the thyroid lymphoma is confined to the thyroid, the 5-year survival rate is 75% to 85% with radiation therapy; if there is extension into regional nodes, the rate is approximately 35%; and if there is disseminated disease, the rate is about 5%. The prognosis is much poorer for the immunoblastic subtype (5-year survival rate of 13%) than for the intermediate (79%) or low-grade (92%) subtype.

Taniwaki et al (1989) have demonstrated a correlation of chromosome abnormalities with the time of onset of thyroid lymphoma symptoms, suggesting the possibility of their role in the etiology of the disease.

Sarcoma

Primary sarcomas of the thyroid are extremely rare. Angiosarcomas (hemangioendotheliomas) and fibrosarcomas are the more likely sarcoma types, and immunologic and electron microscopic studies are recommended to confirm the diagnosis. A radiation-induced liposarcoma has been recently described (Griem et al, 1989). The prognosis for all thyroid sarcomas is very poor.

Metastatic carcinoma

The thyroid gland can be the site of metastatic lesions, either by lymphatic or hematogenous spread or by direct extension from nearby structures. Squamous cell carcinomas of the larynx, pharynx, trachea, and esophagus may extend into the thyroid directly or may spread via lymphatics. This is the most common type of carcinoma to metastasize to the thyroid; distinction from a thyroid primary is usually not difficult. Any type of malignancy may reach the thyroid by hematogenous spread; carcinoma of the kidney, colon, and breast and melanoma are the most common.

Clear cell neoplasms of the thyroid are usually metastatic renal cancer but may also be primary follicular-derived (papillary, follicular, or anaplastic), medullary, or parathyroid tumors that have clear cell metaplasia. The distinction of primary versus metastatic tumor in these cases may be difficult. The thyroid may be the first manifestation of a renal carcinoma and may be the only site of metastasis; the disproportionate frequency of this finding is poorly understood. Clear cells are formed from intracytoplasmic vesicles, glycogen or fat accumulation, or deposition of intracellular thyroglobulin. Special stains for thyroglobulin may be helpful in establishing the diagnosis.

Other malignancies

Squamous cell carcinoma of the thyroid has been reported sporadically but probably represents a true histologic primary tumor type (Korovin et al, 1989; Simpson and Caruthers, 1988). Although controversial, thyroid squamous cell carcinoma probably begins as squamous metaplasia of thyroid epithelial cells caused by an alteration in its physiologic environment. Most patients have had a longstanding goiter with a sudden recent increase in size. The diagnosis is made only after a diligent search rules out all other sites in the upper aerodigestive tract. The tumor tends to behave very aggressively, with invasion of adjacent structures present in over 50% of patients at the time of diagnosis. These lesions are usually unresectable, and most patients die within 1 year of diagnosis.

Mucoepidermoid carcinoma of the thyroid occurs but is extremely rare; only six cases are reported in the literature (Katoh et al, 1990). Its behavior tends to mimic its low-grade or high-grade salivary tumor counterparts. It should be noted that mucin is found in about 50% of differentiated thyroid tumors (Mlynek et al, 1985), complicating the histologic diagnosis. Another extremely unusual thyroid malignancy is the columnar cell carcinoma (Evans, 1986; Sobrihno-Simoes et al, 1988), which behaves as a poorly differentiated tumor and carries a poor prognosis.

Diagnostic Assessment

History

Thyroid nodules can occur with virtually any type of thyroid disease. The workup begins with a careful history and a thorough physical examination, both of which may provide clues for a specific diagnosis.

The patient's age and sex are an important part of the history. Nodules are three times more likely to be malignant in males than in females. Pregnancy may accelerate the development of thyroid carcinomas (Preston-Martin et al, 1987; Rosen and Walfish, 1986). Nodules in children under 20 years of age are also more likely to be malignant: the risk of malignancy in non-radiation-exposed children with nodules is 13% to 30%; whereas in radiation-exposed children the malignancy rate is 30% to 50%. Elderly patients have more nodules than younger adults, but the risk per nodule is not increased.

A history of childhood exposure to gamma radiation suggests the likelihood of a malignancy, usually of the papillary type. However, benign disease is three to four times more likely to be found in radiation-exposed patients with thyroid nodules. The nodule may present up to 30 years after the radiation exposure and is more common in women than in men (DeGroot et al, 1977). It may occur following low- or high-dose exposure. The exposure-risk curve rises in a linear manner to a peak at about 2000 rads and then flattens out at higher doses.

A positive family history for thyroid carcinoma suggests the possibility of medullary carcinoma, although most cases of medullary thyroid carcinoma occur sporadically. Papillary

carcinoma may occasionally exhibit a familial pattern as well.

A history of previous thyroid disease should also be investigated. A previous thyroid malignancy, whether treated adequately or inadequately, may have recurred; and well-differentiated thyroid cancers may degenerate into anaplastic tumors. Benign adenomas may also degenerate into carcinoma; usually angioinvasive follicular cancer. Patients with a history of Hashimoto's thyroiditis have a 70 times higher incidence of thyroid lymphoma than other patients (Holm et al, 1985).

In areas where dietary iodine deficiency is prevalent, follicular carcinoma is the most common thyroid malignancy (Belfiore et al, 1987). Among groups with a high dietary iodine content (for example, fisherman), papillary carcinoma occurs with greater frequency than in the general population. This apparent paradox has not been explained.

Other socioeconomic risk factors have been identified. Patients of Japanese, Chinese, and Filipino extraction living in the USA have twice the risk of thyroid cancer than they have in their native countries. Patients living in the "ring of fire" region of volcanic activity in the northern Pacific (for example, Hawaii) are also at increased risk of developing thyroid carcinoma (Arnbjornsson et al, 1986; Goodman et al, 1988). It is postulated that carcinogens from the volcanic eruptions are ingested by the fish that form a major part of the diet in these areas.

Signs and symptoms suggestive of malignancy should also be elicited. A change in size of the mass, hoarseness, dysphagia, and dyspnea are nonspecific symptoms more commonly associated with malignancy. Pain may be produced by stretching of the thyroid capsule by the tumor but may occur with benign processes as well. Intractable diarrhea may occur in patients with medullary thyroid carcinomas that secrete certain hormones (see below).

Physical examination

Thyroid nodules are most commonly identified as an incidental finding on a routine physical examination. In general, the nodule's characteristics do not predict whether it is benign or malignant. The neck examination is particularly important; the finding of discrete, firm, nontender, 1 to 2 cm lymph nodes in conjunction with a thyroid nodule suggests a malignancy. Other findings suggestive of malignancy include (1) rapid growth; (2) vocal cord paralysis, (3) presence of a firm, large nodule (Staunton and Greening, 1973); (4) fixation of the nodule to surrounding structures; and (5) tracheal deviation. Patients with medullary carcinoma may exhibit mucosal neuromas, especially on the tongue and conjunctiva. Tenderness of the nodule is more commonly found with thyroiditis than with malignancy.

Fine needle biopsy

Fine needle biopsy is the "gold standard" diagnostic technique for evaluating a thyroid nodule (Backdahl et al, 1987). The accuracy of diagnosis with this technique depends on the experience of the cytopathologist; it may approach 97% (Lowhagen et al, 1979; Mazzafierri et

al, 1988). The procedure is performed in the office with the patient under local anesthesia. A 22-gauge needle is passed into the mass, and negative pressure is applied with a syringe. The needle is withdrawn, and the pressure is released when the tip of the needle reaches the edge of the gland. At least six passes should be made in this manner before removing the needle from the skin. The aspirated cells are then pushed from the needle onto a slide and immediately fixed for cytopathologic processing. With this technique, specimens should be considered inadequate or unsatisfactory no more than 10% of the time, although this also depends on the experience of the clinician performing the biopsy (Hall et al, 1989).

With an adequate specimen, diagnostic accuracy depends on the tumor type (Frable, 1986). Medullary carcinoma and undifferentiated tumors are easily recognized and approach 90% accuracy. A diagnosis of papillary carcinoma is about 80% accurate, and follicular carcinoma can be accurately diagnosed in about 40% of cases (Mazzaferri et al, 1988). If all thyroid nodules are considered, a diagnosis of benign should be returned in about 60% to 75% of cases. There is a false-negative rate of 8% to 10%; therefore these patients must be watched very closely (Hamburger, 1987). About 5% of cases will be found to be definitely malignant with fine needle biopsy, but 10% of these will be false-positive readings. Over 20% of cases will be returned as "suspicious"; these patients require surgical resection, at which time 20% to 40% will prove to be malignancies (Gardiner et al, 1986; Hawkins et al, 1987). Cohen and Cho (1988) point out that fine needle biopsy is unnecessary when clinical conditions mandate surgery, such as with airway compression or mediastinal extension, but that 50% of other patients should expect fine needle biopsy to affect the choice of treatment.

Complications of fine needle biopsy are rare (less than 2%) and most often involve hemorrhage into the nodule. A deep biopsy with hemorrhage may result in a transient recurrent laryngeal nerve injury. Tumor seeding of the aspiration tract was not reported through several thousand fine needle biopsies of proven malignancies (Lowhagen et al, 1979) until a recent report of a single case (Hales and Hsu, 1990).

Thyroid scanning

Radionuclide scintigraphy (Fig. 136-7) is the best method of defining active thyroid tissue, but nodules less than 1 cm are not detected with current techniques. Most nonfunctional or "cold" nodules are benign but as many as 20% may be malignant (Messaris et al, 1974). Other causes of cold nodules are congenital anomalies or asymmetries, tortuous innominate artery, fibrosis, cysts, hemorrhage, thyroiditis, and adenomas. Hyperfunctioning "hot" nodules make up 5% of cases and are almost never malignant (Katz and Bronson, 1978). The degree of hyperfunction may be such that the patient is clinically hyperthyroid; the rest of the gland may be suppressed as a result.

A number of radionuclides may be used for thyroid scintigraphy. The most commonly used agent is technetium 99m pertechnetate, which has a half-life of 8 hours. Iodine-123 is better for visualizing substernal thyroid tissue; and I-131 is used for total body scanning, looking for active metastatic tumors. Other agents, such as thallium-201, are being developed (Bleichrodt et

al, 1987).

Thyroid nodules located at the periphery of the gland are not well visualized with this technique. Oblique views are required to demonstrate a cold nodule surrounded by normal-functioning gland (Fig. 136-8).

Intraoperative thyroid scintigraphy has been reported (Lennquist et al, 1988) for the identification of residual tissue after thyroidectomy. This technique permitted the identification and removal of residual tissue in 77% of patients, resulting in no uptake on postoperative scans. Further development of this technique may lead to wider use.

Ultrasonography

Ultrasonography can effectively differentiate a solid from a cystic lesion (Fig. 136-9) with greater than 90% accuracy (Clark et al, 1975; Rosen et al, 1975). It is also the best study available to measure nodule size and may detect nodules as small as 1 mm. Thus it may be used to detect a tiny nodule in a lobe contralateral to a larger tumor. Up to 40% of patients with a clinically solitary nodule will have multiple nodules by ultrasound examination (Rojeski and Gharib, 1985). The technique may also be used to guide fine needle biopsies and may be useful in cases of recurrent disease (Simeone et al, 1987).

Nearly all (96% to 98%) purely cystic lesions less than 4 cm are benign (Miller et al, 1974); they can be needle evacuated and observed using ultrasound. Cysts larger than 4 cm are frequently (20% to 25%) malignant. The benign or malignant nature of complex cysts and solid lesions cannot be accurately assessed using ultrasound.

Thyroid suppression therapy

Solitary ("cold," solid) nodules have been singled out for surgical removal (when fine needle biopsy is nondiagnostic) because of their relatively high incidence of malignancy when compared to multinodular lesions. The very low incidence of malignancy associated with multinodular goiters is such that the proponents of suppression therapy as an alternative to surgery point to the finding that approximately 35% of thyroid glands removed for solitary nodules are actually multinodular (Kambal, 1969; Liechty et al, 1965; Miller, 1955). Problems with thyroid suppressive therapy relate to a low frequency of involution in treated nodules and the fact that a carcinoma may decrease in size during suppressive therapy (Friedman et al, 1980; Hill et al, 1974; Mazzaferri et al, 1977). Thus in order to eliminated the suspicion of malignancy, a nodule must totally disappear. The usual dose of levothyroxine is 100 to 200 microg daily (Dunn, 1986).

Soft tissue roentgenograms

Standard roentgenograms of the neck are of limited value, but incidental findings may be noted in some patients with thyroid nodules. Scattered, fine calcifications are associated with

papillary carcinoma and may represent psammoma bodies. "Eggshell" calcifications usually represent benign hard nodules. A finding of tracheal deviation may also be seen.

Computerized tomography (CT) and magnetic resonance imaging (MRI) provide additional information about the sites of infiltration of extensive, hard tumors that are difficult to evaluate clinically (Crow et al, 1989; Takashima et al, 1990). These studies (particularly CT) are also useful for assessing clinically occult cervical node involvement, including substernal and upper mediastinal lymph nodes.

Serologic studies

With the exception of calcitonin levels for the detection of medullary carcinoma, serologic studies are of limited diagnostic usefulness in thyroid carcinoma. Thyroxin (T_4, T_3, T_3 resin uptake) and thyroid-stimulating hormone (TSH) are measured to determine the patient's status relative to the euthyroid state and are mainly used in evaluating patients with toxic hot nodules (Beckers, 1979). Thyroglobulin assay is used to detect residual or recurrent carcinoma after a total thyroidectomy or I-131 ablation (Harley et al, 1988; Harvey et al, 1990; LoGerfo et al, 1977); the sensitivity for recurrent disease is enhanced by TSH stimulation (Muller-Gartner and Schneider, 1988). Non-functioning metastases, which will not be seen on whole-body radionuclide imaging, may be detected because of their production of thyroglobulin (Pacini et al, 1985; Panza et al, 1987).

Provocative tests are more accurate than measurements of basal levels of calcitonin for detecting medullary thyroid carcinoma. Intravenous pentagastrin or calcium or both are administered, and immunoreactive calcium (iCT) is measured at intervals of 0, 2, and 5 minutes (Sizemore, 1987). This test is abnormal in patients with medullary thyroid carcinoma or C-cell hyperplasia long before the disease is clinically apparent and serves as a useful screening test for family members of an affected patient or for observing known cases that have to be treated. False-positive tests may occur in patients with breast and lung cancers, thyrotoxicosis, or hypothyroidism (Oishi et al, 1984). The recommended screening for family members at risk includes repeating the provocative testing every 6 months until 30 years old; this program will identify 95% of affected family members (Gagel et al, 1982).

Medullary carcinomas have been found to be associated with expression of other substances (Mansson et al, 1990). Carcinoembryonic antigen (CEA) levels have been found to be elevated in some patients (DeLellis et al, 1978). Levels of the peptides PDN (peptide)(P)-aspartic acid(D)-asparagine(N)) and CGRP (calcitonin gene-related peptide) have been found to be consistently elevated (Sikri et al, 1985). Other neuroendocrine peptides such as chromogranin A can be specifically assayed (Deftos et al, 1988). A new DNA marked (DI0S94) has recently been linked to the gene locus identified for MEN, type II-A (Goodfellow et al, 1990).

Epidermal growth factor-specific receptors have been identified on the surface of normal and neoplastic thyroid tissue (Duh et al, 1985; Makinen et al, 1988; Masuda et al, 1988). Other surface receptors identified include estrogen receptors (Chaudhuri and Prinz, 1989; Miki et al,

1990) and an insulin-like growth factor receptor (Yashiro et al, 1989). Endothelial growth factor has been isolated from anaplastic thyroid carcinoma (Itoh et al, 1989) and is probably responsible for tumor angiogenesis. It is not yet known how these factors may be used in the diagnosis or follow-up of human thyroid tumors.

Oncogenes

A number of oncogenes have been identified in patients with thyroid carcinomas (Table 136-2). The clinical value of this finding has not yet been determined, but in the future the level of oncogene activation may be useful for observing patients who have been treated for thyroid carcinoma or for determining prognosis.

Management

Much controversy has surrounded the surgical aspects of treating thyroid carcinoma. Some surgeons advocate less surgery and more adjunctive therapy, such as thyroid suppression and radioiodine, citing reduced risk to the recurrent laryngeal nerves and parathyroid glands. Others promote total thyroidectomy for nearly all cases, pointing to improved disease-free (and possibly survival) rates and better response to radioiodine in the absence of uptake by normal gland tissue. Several large series have been published with multivariate analyses of risk and prognostic factors (Brooks et al, 1988; Simpson et al, 1987; Thoreson et al, 1989). A recent series by Jensen and coworkers (1990) reviews 5287 cases and compares treatment and survival. The following recommendations are based on these and other experiences.

Papillary carcinoma

Clinical aspects

Papillary and predominantly papillary (mixed papillary-follicular) thyroid carcinomas are the most common thyroid malignancy, accounting for over 70% of cases. Among patients with radiation-induced thyroid carcinoma, papillary carcinoma accounts for 85% of cases. Radiation-induced tumors tend to be larger at presentation, are associated with higher recurrence rates, but have the same survival statistics as spontaneously occurring tumors (Friedman et al, 1986; Schneider et al, 1986). Occult tumors have been reported in up to 10% of autopsies (Lang et al, 1988). The peak onset is in the third and fourth decades, with a female to male predominance of 3:1. In children, there is no sex predominance, probably because most cases are related to radiation exposure. The disease is rarely familial, although this has been reported (Christensen and Ljungberg, 1983; Ozaki et al, 1988).

The most commonly cited prognostic factors are age at time of diagnosis (younger is better), tumor stage, and histological classification. Other factors include sex (males worse), degree of differentiation, presence of anaplastic cells, tumor size, and presence of lymph node and distant metastases.

Therapy

Surgical therapy is based on the finding that more complete ablation of disease results in fewer cancer recurrences and deaths. It is also desirable to reduce the amount of normal gland tissue that will take up radioiodine. Although more complete resection of the thyroid (for example, total thyroidectomy) is associated with a higher rate of complications (recurrent laryngeal nerve injury, postoperative hypoparathyroidism), in experienced hands this should not be significant.

Based on these rationales, tumors that are well circumscribed, isolated, small (less than 1.0 cm), and in young patients (between 20 and 40 years of age) without a history of radiation exposure can be treated by hemithyroidectomy with isthmusectomy. All other papillary thyroid carcinomas should be treated with total thyroidectomy (Arnold and Edge, 1989). All patients should have excision of paratracheal (level VI) and involved cervical lymph nodes ("node plucking" from levels II, III, and IV) or ipsilateral functional neck dissection (McGuirt, 1989; Noguchi and Murakami, 1987; Noguchi et al, 1990; Sako et al, 1985).

Radioiodine (I-131) is taken up well by papillary thyroid carcinoma and is a useful adjunct to total thyroidectomy for microscopic metastases (Connor et al, 1988; McHenry et al, 1989). Uptake is enhanced in the absence of normal thyroid tissue and in the presence of high TSH levels; thus patients should not be taking thyroid replacement hormone when given radioiodine. A low-iodine diet for 1 week before therapy is also helpful. The usual dose is 50 to 150 mCi and is given 6 weeks postoperatively. Complications of therapy are related to tumor edema: hemorrhage within distant metastases may cause local complications (for example, brain, spinal cord); and cumulative doses of 300 to 400 mCi are associated with a high incidence of radiation pulmonary fibrosis when there are lung metastases (Edmunds and Smith, 1986). Radioiodine therapy may be repeated every 6 months if there continues to be uptake in a metastatic lesion; longer intervals (eg, 1 year) may allow a higher total dose to be given (Brown et al, 1984).

Thyroid hormone in suppressive doses is used postoperatively based on research indicating that the tumor may depend on endogenous TSH (Komlos et al, 1988). Recurrences and mortality rates have been demonstrably lower in patients receiving thyroid suppression (Mazzafierri et al, 1977).

Follow-up

Routine follow-up includes physical examination, chest radiographs, and whole body I-131 nuclear scans. Serum thyroglobulin level, measured when the patient is off thyroid hormone replacement, is the most reliable tumor marker after total thyroid ablation (Aschcraft and Van Herle, 1981a). Chest radiographs and serum thyroglobulin levels should be obtained annually. Most recurrences occur within 10 years but may occur as much as 30 to 40 years later (Powell et al, 1990; Schlumberger et al, 1988). Initial follow-up is every 2 months for the first year, every 3 months for the next 2 years, every 6 months for the next 2 years; and then annual follow-up

is recommended for life.

Follicular carcinoma

Clinical aspects

Follicular thyroid carcinomas comprise about 15% of all thyroid carcinomas (Samaan et al, 1983). Compared to papillary thyroid carcinoma, follicular thyroid carcinoma occurs in a slightly older age group and is less common in children. It occurs rarely after radiation exposure and is rarely an occult autopsy finding.

Hurthle cell carcinoma occurs in an older age group, with a mean age of 55 years (Chonkich et al, 1987). Although they do not appear more invasive or less differentiated, they do have a less favorable prognosis than other follicular tumors.

Therapy

Surgical options and rationale are somewhat similar to papillary thyroid carcinoma. It must be kept in mind, however, that the diagnosis may not be ascertained by frozen section at the time of surgery, and therapeutic decisions should await a definitive diagnosis. Patients with minimally invasive, small (less than 1.0 cm) tumors who are less than 40 years old may be adequately treated with hemithyroidectomy with isthmusectomy. All other patients should undergo total thyroidectomy. If the intraoperative frozen section pathologic finding is uncertain, a hemithyroidectomy with isthmusectomy should be performed. When the diagnosis of follicular carcinoma is confirmed postoperatively, completion thyroidectomy should be performed.

All patients (including those with metastases) should be evaluated for uptake of radioiodine, and ablative I-131 therapy should be carried out if uptake is present. Metastatic lesions that do not take up radioiodine should be locally resected, followed by external beam radiation therapy. All patients should also receive suppressive postoperative thyroid hormone therapy unless they are already thyrotoxic from bulky metastases.

Follow-up

Follow-up for follicular carcinoma is the same as that for papillary thyroid carcinoma (see above).

Medullary carcinoma

Clinical aspects

Medullary thyroid carcinoma accounts for about 5% to 10% of all thyroid malignancies. There are four clinical settings. Sporadic medullary thyroid carcinoma comprises 80% of cases; these tumors are unilateral, and there are no associated endocrinopathies. The peak onset is in

the fourth through sixth decades, and there is a female/male predominance of 3:2 (Chong et al, 1975). One third of patients with sporadic medullary thyroid carcinoma present with intractable diarrhea.

The second and third types of medullary thyroid carcinoma are those that occur with the multiple endocrine neoplasia (MEN) syndromes, types II-A and II-B. The clinical features of these syndromes are listed in Table 136-3. The abnormal phenotype of MEN II-B may include multiple mucosal ganglioneuromas (especially of the tarsus and anterior tongue), musculoskeletal abnormalities (Marfan-like habitus), and hyperplastic corneal nerves. The peak age of onset is in the third decade, and because of the autosomal-dominant pattern of inheritance, the female/male ratio is 1:1. Adrenal disease is present in 50% to 80% of patients with type II-A. The most sensitive test is the epinephrine/norepinephrine ratio, because total urine catecholamines may be normal. Patients with pheochromocytoma are at risk for an intraoperative hypertensive crisis; thus it is important to identify these patients and begin prophylactic treatment preoperatively. Parathyroid disease is present in up to 70% of patients with type II-A; this is most likely caused by gene mutation rather than being secondary to calcitonin hypocalcemia.

Table 136-3. Multiple endocrine neoplasia syndromes

	Type II-A (Sipple syndrome)	**Type II-B**
Bilateral medullary thyroid carcinoma or C-cell hyperplasia or both	+	+
Pheochromocytoma or adrenal medullary hyperplasia or both	+	+
Hyperparathyroidism	+	Rare
Phenotype	Normal	Abnormal
Inheritance	Autosomal dominant	Autosomal dominant *or* sporadic.

The fourth type of medullary thyroid carcinoma appears to be an inherited type with no associated endocrinopathies (Farndon et al, 1986); two kindreds with 178 members have thus far been identified. These patients have no extra-thyroid manifestations. The age of onset is higher than that for MEN, type II-A. This appears to be the least aggressive form of medullary thyroid carcinoma; there have been no cancer deaths reported in these two kindreds.

Diarrhea in medullary thyroid carcinoma is caused by increased gastrointestinal secretion or hypermotility from calcitonin, prostaglandins, serotonin, or vasoactive intestinal peptide (VIP) secreted by the tumor. Evidence in support of the humoral mechanism is that the diarrhea stops after tumor resection, and it is stimulated by the administration of calcitonin. A number of humoral secretions are found to be elevated in medullary thyroid carcinoma; these are listed in the box.

Box: Humoral secretions in medullary thyroid carcinoma

Immunoreactive calcitonin (iCT)*
Calcitonin gene-related peptide (CGRP)*
Katacalcin
L-dopa decarboxylase*
Serotonin
Prostaglandin
Adrenocorticotropin (ACTH)
Histaminase*
Carcinoembryonic antigen (CEA)*
Gastrin-releasing peptide
Nerve growth factor
Vasoactive intestinal peptide
Substance P

* Secretions not seen in other types of thyroid carcinoma.

Therapy

All patients with medullary thyroid carcinoma should undergo total thyroidectomy with dissection of lymph nodes in the central (level VI, paratracheal) cervical compartment (Duh et al, 1989). Lateral neck dissection (levels II, III, and IV) should be added if any involved lymph nodes are found; alternatively, some authors advocate bilateral functional neck dissection in all cases. If the patient has a pheochromocytoma, this should be resected first to minimize operative risk during thyroidectomy.

Medullary thyroid carcinomas rarely take up radioiodine. Patients with inoperable or recurrent disease may be treated with external beam radiation therapy for localized disease or with doxorubicin for widely disseminated disease, although both have poor response rates.

Follow-up

Periodic physical examinations and chest radiographs are required as in other thyroid tumors. Serum immunoreactive calcitonin (iCT) measurements have proven very useful. The basal and provoked levels of iCT should return to normal within 6 months of treatment; such a return usually indicates a cure. As a follow-up screening test, iCT should be repeated every 6 months and a metastatic workup initiated if the iCT level becomes elevated. Such elevation may indicate the occurrence of microscopic metastases, which may be controlled with a meticulous neck dissection (if not already performed) (Tisell et al, 1986). Any iCT elevation should be rechecked several times, since some patients may have occasional iCT elevation without ever manifesting any metastases.

Another tumor marker being developed is calcitonin gene-related peptide (CGRP). This peptide is elevated in patients with medullary thyroid carcinoma but does not vary with calcium levels as does iCT (Poston et al, 1987). The clinical usefulness of this marker is still being established.

Anaplastic carcinoma

Anaplastic carcinomas comprise less than 10% of all thyroid carcinomas. They most commonly (more than 50%) arise as a degeneration of a more differentiated thyroid tumor or goiter; but they may also occur following low- or high-dose radiation exposure. The peak age of onset is the seventh decade, and the female/male ratio is 1:2. The incidence of anaplastic thyroid cancer is higher in areas of low dietary iodine and endemic goiter.

The most common presentation is one of a growing mass with neck tightness. Other symptoms, in decreasing order of frequency, are dysphagia, hoarseness, dyspnea, neck pain, sore throat, and cough.

In select cases, surgery followed by radiation therapy may be attempted for cure. If the carotid arteries are uninvolved, the entire cervical viscera may be excised, provided such excision will entirely encompass the tumor mass. The prognosis is generally poor even with such heroic measures. Tallroth et al (1987) have reported a combination "triple" therapy, using hyperfractionated radiation therapy and three-drug chemotherapy followed by surgery during remission periods, resulting in a 12% 3-year survival.

Lymphoma

Thyroid lymphoma has been increasing in incidence over the last 20 years; it currently represents about 8% of thyroid malignancies. The mean age of onset is the seventh decade. The female/male sex ratio varies with age: for patients over 60 years of age, the ratio is about 5:1; but for patients under 50 years of age, it is 3:2. There is a clear association with Hashimoto's thyroiditis; these patients are at a seventyfold higher risk for developing thyroid lymphoma (Holm et al, 1985). Most patients present with a rapidly enlarging mass, often in a preexisting goiter, which causes neck swelling, tenderness, hoarseness, dysphagia, and neck pressure. In advanced cases, there may be facial edema and Horner's syndrome. Fifty percent will be hypothyroid by serologic measures. It is important to carefully assess for metastases, especially to the gastrointestinal tract.

Surgery is indicated only to relieve airway obstruction or to make the diagnosis and to check tumor markers. In the absence of distant metastases, radiation therapy cures most patients.

Thyroid Surgery

Thyroid surgery should be performed with exquisite care to minimize morbidity. Several techniques have been described. Developing a routine is useful, but the surgeons may have to

design an approach to suit unusual cases. The patient must be very carefully prepared preoperatively. The surgeon, endocrinologist, anesthesiologist, and pathologist act as a team for maximum patient benefit.

Skin incision

A gently curved incision is recommended (Fig. 136-10), placed approximately one finger-breadth above the sternal notch in a suitable skin crease. It should be symmetric about the midline. Every effort should be made to keep the scar as cosmetically acceptable as possible.

Flap elevation

The flap consists of skin, subcutaneous tissue, and platysma. The superficial veins are not elevated. It is important to raise the flap to the level of the thyroid notch to achieve adequate exposure at the superior pole of the thyroid. The lower flap can be elevated slightly if necessary. Dural hooks are useful as skin retractors (Fig. 136-11).

Muscles

The sternohyoid and sternothyroid muscles are separated in the midline and dissected laterally. It is not necessary to transect them unless the thyroid gland is so large that additional exposure is required. If muscle transection is necessary, the muscles should be cut high to avoid injury of the ansa cervicalis nerves. The prethyroid muscles should be elevated sufficiently to exposure the superior pole of the thyroid (Fig. 136-11).

Thyroid dissection

The lateral thyroid veins are identified, cross-clamped, and tied. The thyroid is then displaced upward by gentle retraction. Lateral muscle retraction by an assistant is essential for exposure. There are usually one or two lateral thyroid veins, with a plexus of veins near the inferior pole. The gland is rotated medially and upward as the dissection continues. The compartment between the carotid artery laterally and the trachea medially contains both the inferior thyroid artery and the recurrent laryngeal nerve. Dissection in this region must be meticulous and delicate. Using either mosquito forceps or fine dissecting scissors, the surgeon separates the connective tissue along a vertical plane in order to identify the recurrent laryngeal nerve (Fig. 136-12). It is most important to look specifically for the recurrent nerve rather than the inferior thyroid artery. The inferior thyroid artery is not clamped and ligated until the nerve is identified and protected. The nerve is invariably close to a plexus of delicate inferior thyroid veins. Careful dissection is necessary to prevent bleeding that may obscure the surgical field.

The lower pole of the thyroid gland is then mobilized. The plexus of vessels at the inferior pole of the thyroid can be isolated individually or cross-clamped and secured with a suture ligature (Fig. 136-13). The trachea and isthmus are defined. The isthmus can be cross-clamped and divided at this stage. The recurrent nerve is kept in constant view during these

maneuvers. As the gland is mobilized cephalad, it is important to protect the recurrent laryngeal nerve when the suspensory ligament is divided (Fig. 136-14). The recurrent nerve can then be traced to its laryngeal entry between the inferior cornu of the thyroid cartilage and the arch of the cricoid cartilage.

The superior vessels are more readily identified with countertraction downward on the superior pole (Fig. 136-15). The vessels are either doubly ligated above, or a suture ligature is used. The superior thyroid vessels should be ligated at the capsule of the thyroid gland to avoid injury to the external branch of the superior laryngeal nerve, which innervates the cricothyroid muscle. The cricothyroid muscle elongates the vocal cord and is therefore very important to normal speech production.

Parathyroid gland identification (also see Chapter 137)

It is impossible to predict preoperatively whether a hemithyroidectomy will suffice unless the fine needle biopsy is definitive. The pathology report on frozen section may indicate the need for a total thyroidectomy; thus it is important to preserve at least one parathyroid gland and its blood supply on the ipsilateral side. The superior parathyroid gland is usually at the border of the middle and upper thirds of the thyroid gland posteriorly, near the cricothyroid joint. The inferior parathyroid gland is usually near the junction of the recurrent laryngeal nerve and the inferior thyroid artery posteriorly (Fig. 136-16). These glands are tan to brown, pea sized, and located close to the thyroid capsule. They can be carefully elevated from the thyroid gland and left with their vessel and connective tissue attachments (Schwartz and Friedman, 1987). If the integrity of the parathyroid vascularity is uncertain, a portion of the gland in question should be transected, minced into several small (< 1mm) pieces, and implanted within the body of the sternocleidomastoid muscle (Smith et al, 1990). This provides a potential secondary source of parathyroid function if the vascularity of the native glands is compromised.

Wound closure

Before closure the wound is irrigated and the meticulous search for bleeding points is made. Once the wound is completely dry, the neck is flexed slightly to remove tension, and the strap muscles are closed in the midline with interrupted mattress sutures. A small suction drain is brought out through a separate stab wound below and lateral to the incision line. Our preference for skin closure is subcuticular sutures. Whatever the choice of skin closure, it must be done very carefully to provide the best eventual cosmetic result.

Substernal thyroid

If the thyroid gland is in a substernal position, finger dissection is used to remove it. Finger dissection is made outside the thyroid capsule; great care is required to avoid tearing veins. If there is considerable venous bleeding during the maneuver, the gland must be delivered as quickly as possible; otherwise, the veins can become further engorged and bleed more severely because of the pressure of the thyroid in the thoracic inlet producing a tourniquet effect.

Transsternal mediastinotomy is seldom required for removal of malignant disease, but the surgeon should be prepared to do so when necessary (Niederle et al, 1985). The technical aspects of this procedure are beyond the scope of this chapter, but they are well described in the general literature. The assistance of a thoracic surgery colleague is advisable.

Neck dissection

Neck dissection terminology has been standardized by the American Academy of Otolaryngology - Head and Neck Surgery's Committee for Head and Neck Surgery and Oncology (Robbins et al, 1991) based on the Sloan-Kettering Memorial Group's level system of cervical lymph node groups (Fig. 136-17) (Shah et al, 1981). All cases of malignancy of the thyroid should have level VI nodes dissected (perithyroid, paratracheal, precricoid, and other midline visceral nodes). A "selective" neck dissection should also be done to include any involved nodes in levels II, III, and IV identified by careful intraoperative palpation. The sternocleidomastoid muscle, spinal accessory nerve, internal jugular vein, and nodal region I and V will rarely need to be included in the dissection.

Postoperative care

Sutures are removed on the fifth postoperative day, and skin-colored Steri-strips are placed across the incision line to prevent wound tension. These are left in place for at least 1 week.

Serum calcium levels are measured daily for the first 2 to 4 postoperative days in all patients who have undergone total thyroidectomy or who have had both thyroid lobes dissected in a subtotal operation. There is usually a small drop in serum calcium (to as low as 7.0 mg/dL) as the remaining parathyroid tissue takes a few days to recover fro the "shock" of surgical dissection before resuming normal function. This mild hypocalcemia needs to be treated only if it is symptomatic (positive Trousseau's or Chvostek's sign, cardiac arrhythmia, tingling about the lips). Intravenous calcium gluconate is used when rapid calcium replacement is indicated (severe arrhythmias, impending tetany). Total parathyroidectomy patients will require lifelong calcium supplementation; the usual requirement is oral calcium carbonate, 2 g/day. Vitamin D2 (calciferol) must also be carefully administered.

Patients who have had total thyroidectomy also require thyroid hormone supplementation, which is begun within the first few days postoperatively. The usual dose of synthetic oral levothyroxine is 100 to 200 microg/day (Dunn, 1986). Thyroid hormone supplementation is withheld in patients who will be receiving postoperative radioiodine treatment, since this therapy is optimal when TSH levels are maximized; a level greater than 30 microU/mL is desirable. This is usually reached 3 to 6 weeks after total thyroidectomy. After radioiodine treatment, many authors advocate suppression therapy for differentiated thyroid cancers, to keep TSH levels minimal; the typical dose is 300 microg/day. The suppressive dose is withheld for 6 weeks before obtaining follow-up nuclear scans; with its shorter half-life, liothyronine (synthetic T_3, Cytomel), 25 microg/day, may be substituted during this interval and discontinued 2 weeks before testing. This regimen maximizes the period in which there is no suppression while maximizing the uptake

of the radionuclide used in the scan.

Complications

Postoperative stridor indicates upper airway obstruction caused either by tracheal compression from wound hemorrhage or by bilateral vocal cord paralysis. The status of the vocal cords should be determined immediately by fiberoptic laryngoscopy. Bilateral paralysis may be temporary, from paresis, or permanent; but when it causes stridor a tracheotomy is usually required urgently. In cases of permanent bilateral paralysis, arytenoidectomy (Ossoff et al, 1984; Woodman, 1946) or vocal cord lateralization (Kirchner, 1979; Remsen et al, 1985) may allow eventual decannulation.

Unilateral paresis or paralysis of the recurrent laryngeal nerve occurs in up to 5% of thyroid lobectomy patients, even in the most experienced hands. Postoperatively, paresis should be sought routinely by examination, even if there is no hoarseness. If the recurrent laryngeal nerve is found to be transected intraoperatively, it should be reanastomosed microscopically. This technique results in improved muscle tone of the paralyzed vocal cord or rarely in some degree of normal function (Crumley, 1990). If the vocal cord is noted to be immobile immediately postoperatively, it may be impossible to distinguish paresis from paralysis. Symptomatic patients (aspiration, severe persistent hoarseness) may be treated with temporary vocal cord medialization using Gelfoam injection (Schramm et al, 1978). The Gelfoam is gradually reabsorbed over a 1- to 3-month period and may be repeated if necessary. If there is no spontaneous resolution within 12 months, symptomatic patients (aspiration, persistent hoarseness) may have the involved vocal cord medialization by Teflon injection (Sadek, 1987; Ward et al, 1985), collagen injection (Ford and Bless, 1986), or thyroplasty procedures (Isshiki et al, 1975; Koufman, 1986).

The external branch of the superior laryngeal nerve is damaged in up to 15% of thyroid lobectomies. The main symptom is a breathy voice or an inability to raise vocal pitch. Examination of the larynx reveals the vocal cord to be shorter on the injured side, with the posterior aspect of the larynx rotated toward that side. Most patients with this injury compensate well, and no treatment is required. If there is a coexistent recurrent nerve injury, aspiration is more likely to be a problem that will require treatment. Identification and preservation of the external branch of the superior laryngeal nerve may improve the postoperative voice results (Kark et al, 1984).

Tracheal compression from wound hemorrhage usually indicates a nonfunctioning suction drain. The Valsalva maneuver of a cough may cause a silk tie to come loose from a ligated vein. The wound must be explored immediately and bleeding controlled; tracheotomy is usually not necessary.

Thyrotoxic storm, although rare, is a surgical emergency with which the thyroid surgeon must be familiar. It is more common in patients who are hyperthyroid preoperatively but may occur in any patient whose thyroid gland is subjected to the stress of surgery (Peele and Wartofsky, 1990). The presentation includes fever, tachycardia, agitation, disorientation, frequent

watery stools, and congestive heart failure; it may progress to coma and death if not recognized and treated. The key to effective therapy is early diagnosis and treatment. The patient may develop hyperpyrexia and tachycardia intraoperatively; the procedure must be stopped, the wound closed, and emergency therapy initiated. Intensive care unit monitoring is required. Additional postoperative treatment includes immediate administration of anti-thyroid drugs (propylthiouracil), iodides, beta blockers (propranolol), and large volumes of intravenous fluids and glucose to combat hypermetabolism. Steroids are used to reduce the conversion of T_4 to T_3 and to reduce the hyperthermia. Cooling blankets, alcohol washes, ice packs, and acetaminophen are also used to combat the fever. The incidence and mortality of this condition have been reduced markedly since the advent of modern thyroid function testing to identify thyrotoxic patients preoperatively.