Chapter

21 Thyroid Gland

Surgical thyroid disease encompasses those conditions in which partial or complete removal of the thyroid gland is required due to goiter and hyperthyroid conditions that are unresponsive to medical management and to benign and malignant neoplastic disease.

ANATOMY AND PHYSIOLOGY

The thyroid gland is derived embryologically from an evagination of the floor of the pharynx at the base of the tongue. The developing thyroid descends along a midline course to its final position as a bilobed gland overlying the lower half of the thyroid cartilage. The two lateral lobes of the fully developed gland are connected by a median isthmus. In 75% of individuals, the distal thyroglossal remnant extends superiorly from the isthmus and is called the *pyramidal lobe*. Arterial blood is supplied via the paired superior and inferior thyroid arteries, and venous drainage is via the paired superior, middle, and inferior thyroid veins (Figure 21-1).

Of key importance to the surgeon is anatomic knowledge of the recurrent laryngeal nerve. Bilateral vagus nerves descend from the neck into the chest. The right vagus branches into the right recurrent laryngeal nerve, which loops under the right subclavian artery from anterior to posterior and ascends superiorly in the right tracheoesophageal groove. In 5% of patients, the right laryngeal nerve may be nonrecurrent, taking a more direct course into the larynx. The left vagus branches into the left recurrent laryngeal nerve, which loops in a similar anterior-to-posterior fashion around the arch of the aorta and ascends along the left tracheoesophageal groove. The recurrent laryngeal nerves travel posteromedial to their respective thyroid lobes and enter the larynx via the cricothyroid membrane to innervate the abductor muscles of the true vocal cords. Injury during thyroidectomy results in ipsilateral vocal cord paralysis and subsequent hoarseness (Figure 21-2).

As a result of aberrant migration of the developing thyroid gland, several anatomic variances can be seen. Complete failure of migration from the base of the tongue results in a *lingual thyroid*. The entire mass of thyroid tissue is located in the posterior tongue, and airway obstruction may result if goiter develops. Incomplete migration can result in thyroid tissue being found anywhere between the base of the tongue and the root of the neck. Lastly, thyroid tissue may migrate beyond the level of the thyroid cartilage into the substernal region, where occasionally a *substernal goiter* develops.

Persistence of the thyroglossal duct results in a *thyroglossal cyst* or *fistula*. Thyroglossal cysts are most commonly seen in children and appear as a single painless lump in the midline that moves with swallowing. Surgical excision of the cyst is corrective. Thyroglossal duct fistulae appear as midline sinus tracts. As the fistula is an embryologic remnant, it ascends superiorly through the middle of the hyoid bone, often to its origin at the base of the tongue. Surgical excision of the fistula requires resection of the middle portion of the hyoid bone (Figure 21-3).

The thyroid gland determines the metabolic pace of the body. Increased levels of thyroid hormone and loss of the normal negative feedback mechanism result in hyperthyroidism. The main etiologies of hyperthyroidism are (a) diffuse toxic goiter (Graves' disease), (b) toxic multinodular goiter (Plummer's disease), and (c) toxic adenoma. Surgical treatment of these disorders involves either excision of localized diseased tissue, as in the case of adenoma, or complete excision of the majority of the gland, as in Graves' disease or toxic multinodular goiter.

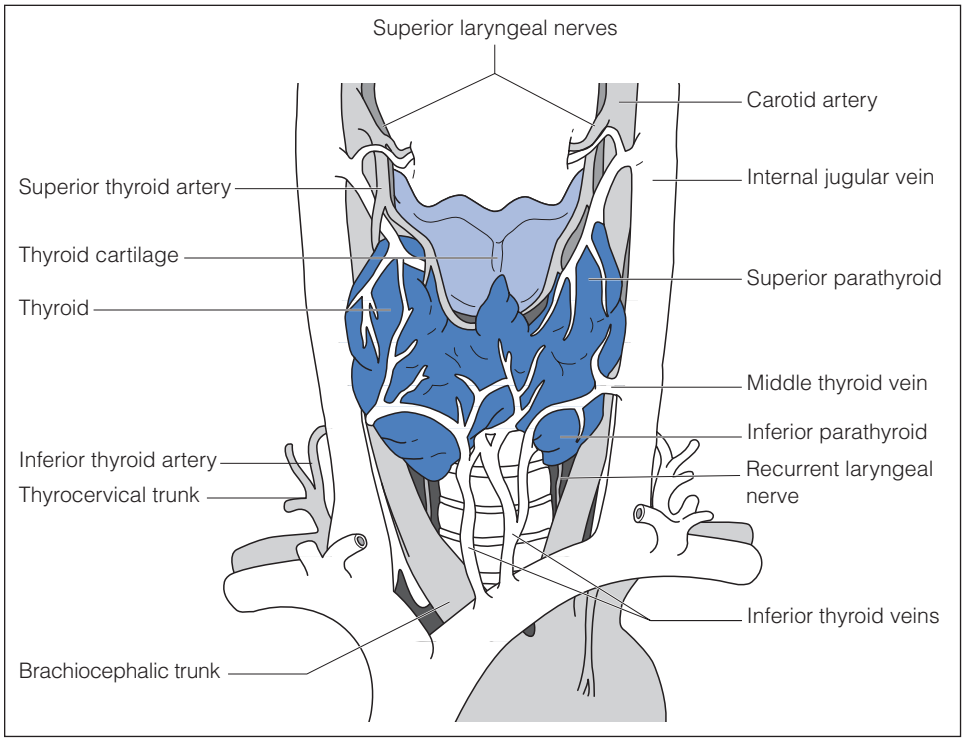

Figure 21-1 • Anatomy of the thyroid gland.

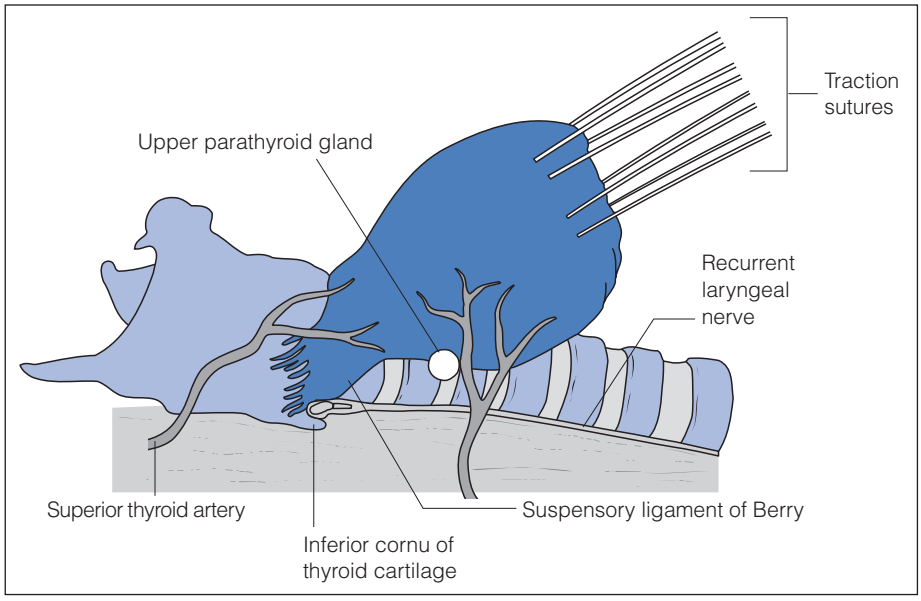

Figure 21-2 • Course of the recurrent laryngeal nerve.

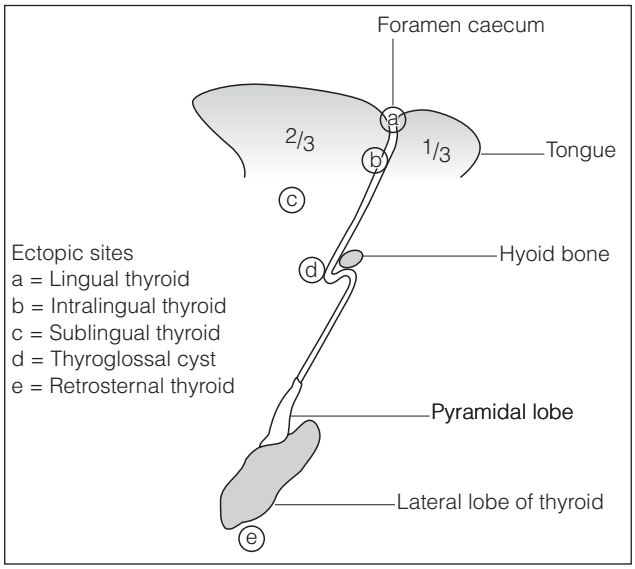

Figure 21-3 • Migration of the thyroid via the thyroglossal duct and possible ectopic sites of development and duct remnants.

GRAVES' DISEASE

The most common cause of hyperthyroidism in the United States and Europe is Graves' disease. This autoimmune disorder is caused by thyroid-stimulating immunoglobulins that target the thyroid-stimulating hormone (TSH) receptor of the thyroid gland. The hyperstimulated gland releases excessive amounts of hormone, resulting in the classic clinical picture of goiter, exophthalmos, pretibial myxedema, and the signs and symptoms of hyperthyroidism. The exact pathogenesis remains unclear; however, evidence of a genetic component exists in many cases. Families with Graves' disease exhibit an overall increased incidence of thyroid disorders and increased levels of circulating antithyroid antibodies. Individuals and families with Graves' disease also have higher incidences of other autoimmune disorders, such as insulin-dependent diabetes mellitis, rheumatoid arthritis, and Addison's disease.

History

The typical presentation of hyperthyroidism involves complaints of unexplained nervousness and sweating, heat intolerance, weight loss, palpitations, an enlarging neck mass, and ocular prominence. As patients present at different stages of disease, the subtle findings of early disease differ dramatically from the florid exophthalmos, dyspnea, and agitation of more advanced cases.

Physical Examination

Patients are generally agitated, irritable, or nervous. The enlarged gland is palpable and often visibly apparent. Due to increased vascularity, a thrill may be felt or a bruit auscultated over the enlarged lobes.

The most notable and dramatic finding is exophthalmos, caused by edema of the retrobulbar fat pad forcing the globe anteriorly. Increased sympathetic tone secondary to excess thyroid hormone causes eyelid retraction, leading to the pronounced Graves' "stare."

Skin examination reveals myxedema, a raised plaquelike skin change seen typically in a pretibial distribution. Cardiac examination demonstrates sinus tachycardia, hyperdynamism, systolic flow murmurs, and occasionally atrial fibrillation.

Diagnostic Evaluation

Thyroid function tests yield the information necessary for making the diagnosis of Graves' disease. T3 and T4 levels are elevated due to gland hyperstimulation, and the TSH level is low due to the negative feedback exerted by circulating thyroid hormones. If T3 and T4 levels are within normal limits, radioactive iodide uptake testing (RAIU) will show increased uptake secondary to increased glandular activity.

Thyrotropin-releasing hormone (TRH) testing shows a negative response in Graves' disease. TSH does not rise in response to intravenous infusion of TRH, because pituitary secretion has been inhibited by negative feedback.

Differential Diagnosis

In addition to hyperthyroidism, one should consider thyroiditis, factitious hyperthyroidism, and anxiety disorder as possible diagnoses.

Treatment

Hyperthyroidism of Graves' disease is treated by

1. Antithyroid medication to reduce glandular hormone secretion,

2. Radioiodine ablation to reduce the functional glandular mass, or
3. Surgical excision.

The appropriate treatment choice is determined by considerations such as pregnancy status, surgical risk, and treatment side effects.

Antithyroid Medication

The goal of antithyroid medication is to return the patient to a euthyroid state. Two thiocarbamide medications, propylthiouracil (PTU) and methimazole (Tapazole), inhibit thyroid hormone synthesis. Additionally, propylthiouracil inhibits peripheral conversion of T4 to T3. Despite the ability of antithyroid medications to control the signs and symptoms of hyperthyroidism, there is a high recurrence rate. Hence, such medications are used for long-term treatment of patients who are expected to undergo remission as indicated by mild laboratory abnormalities and a small goiter.

Adjunctive drug therapy includes beta blockers to control the signs and symptoms of thyrotoxicosis. Propranolol is used to dampen the increased sympathetic tone brought on by circulating thyroid hormones. Iodide is used to inhibit thyroid hormone release directly and treat patients with severe disease rapidly. Potassium iodide (Lugol's solution) can also be used preoperatively before elective thyroidectomy to reduce glandular vascularity.

Radioactive Iodine Therapy

Radioactive ablation of the thyroid with iodine-131 is simple and effective. The goal of therapy is to reduce the functional mass of thyroid tissue to achieve a euthyroid level of secretion. However, the final result is often complete glandular ablation, with subsequent permanent hypothyroidism requiring lifelong thyroid hormone replacement. Radioactive iodine therapy is useful for most patients, except pregnant women and newborns.

Subtotal Thyroidectomy

Surgical intervention is appropriate for patients with contraindications to radioactive iodine therapy and for those who are unable to tolerate or are unresponsive to antithyroid medications. Children and young adults are the majority of such patients. As with radioiodine therapy, the goal of surgical treatment is to reduce the mass of thyroid tissue to a level at which euthyroid levels of hormone are secreted by residual tissue. Despite the low operative risk of the procedure, significant complications can include recurrent laryngeal nerve injury with vocal cord paralysis, permanent hypothyroidism, and surgical hypoparathyroidism. Despite undergoing surgery, recurrent hyperthyroidism occurs in approximately 5% of patients.

The operation is performed through a curvilinear "necklace" incision extending to the sternocleidomastoid muscles bilaterally. Of key importance is to avoid injury to the recurrent laryngeal nerves, parathyroid glands, and external branches of the superior laryngeal nerves.

Follow-Up

After treatment, thyroid function tests should be used to ensure that the patient is euthyroid. This is important because up to 50% of patients may develop postoperative hypothyroidism and require thyroid hormone replacement therapy.

THYROID CANCER

Thyroid cancers are relatively uncommon because they account for only approximately 1% of all malignancies. The four thyroid cancer types are papillary, follicular, medullary, and anaplastic. The tumor types differ in histologic appearance, malignant behavior, and treatment response. Indolent papillary cancer carries a favorable 80% 10-year survival rate, whereas undifferentiated anaplastic cancer is invariably fatal. Anaplastic thyroid cancer is one of the most lethal cancers known, with an average life expectancy of 5 months from the time of diagnosis. Follicular and medullary cancers occupy the middle ground. Depending on the tumor type, surgical therapy has variable success.

Pathogenesis

Although the etiology of most thyroid cancer is unknown, cancer of the thyroid has been experimentally induced by exposure to radiation, goitrogenic medications, and iodide deficiency. Knowledge of radiation-induced carcinogenesis evolved from experience with the use of external-beam radiation as medical therapy earlier this century. It was noted that thyroid cancer, usually of the papillary type, subsequently developed in a significant number of chil-

dren irradiated for the treatment of acne, enlarged tonsils, or hemangiomas. A direct dose-response relationship was identified, showing that the incidence of malignancy was proportional to the radiation dose received. Eventually it was discovered that ionizing radiation exerts a dual carcinogenic role: the disruption of cellular deoxyribonucleic acid (DNA) and the inducement of chronic TSH stimulation of the thyroid gland by damaging the capacity to produce thyroid hormone, which is necessary for negative feedback.

History

Patients usually present for surgical evaluation after an asymptomatic painless *thyroid nodule* is discovered on routine physical examination. A systemic workup for a newly diagnosed thyroid nodule is necessary to determine the biologic nature of the nodule and to rule out cancer. Important historic information includes the duration of nodule existence, rate of enlargement, presence of voice changes, dysphagia, prior radiation exposure from medical or military sources, radioiodine therapy in childhood, family history of medullary cancer, and history of iodide deficiency suggested by residence in a geographic area of endemic goiter.

Physical Examination

Physical findings may range from a single discrete nodule in a single lobe to large bulky disease with evidence of distant metastasis. Generally, carcinomas are nontender on palpation; however, pain may arise after hemorrhage into a necrotic tumor or by compression of local structures. Hoarseness is often a sign of malignancy, indicating involvement of the recurrent laryngeal nerve. An enlarging fixed nodule with associated adenopathy and symptoms of dysphagia also suggests malignancy.

Differential Diagnosis

The differential diagnosis of a thyroid nodule includes follicular adenoma, multinodular goiter, colloid nodule, Hashimoto's thyroiditis, thyroid cyst, thyroid lymphoma, papillary thyroid cancer, follicular thyroid cancer, medullary thyroid cancer, anaplastic thyroid cancer, metastatic cancer, and parathyroid mass.

Diagnostic Evaluation

Standard thyroid function tests reveal the functional status of the gland; results are rarely abnormal in patients with thyroid cancer. The single most important diagnostic study is percutaneous fine-needle aspiration (FNA) because it provides a tissue diagnosis. Other studies include radionuclide thyroid scanning, which only demonstrates the functional status of a nodule by showing whether a nodule is "hot" or "cold." A hot functioning nodule takes up high levels of radioactive iodide tracer, and a cold nodule indicates low uptake and minimal function. Overall, the majority of hot nodules are benign, and approximately 5% of cold nodules are malignant. Thyroid ultrasound is used to determine whether a nodule is solid or cystic, to assess nodule size, or to identify impalpable nodules. Solid nodules are more likely to be cancerous than are cystic lesions. For patients suspected of having medullary cancer based on family history, serum calcitonin levels should be checked after a calcium-pentagastrin infusion test. An elevated calcitonin level defines a positive result and obviates the need for FNA.

Treatment

Papillary

Usually associated with exposure to ionizing radiation, papillary thyroid cancer is often multicentric and bilateral, spreading slowly via lymphatic channels to lymph nodes and by direct extension into surrounding structures. Only 5% of patients with papillary cancer present with distant metastases. For tumors less than 1.5 cm and for disease confined clinically to one lobe with no extracapsular extension, thyroid lobectomy is generally performed. However, due to the multicentric and often bilateral nature of the disease, some surgeons advocate total thyroidectomy, because a more extensive operation is associated with lower rates of recurrence and better long-term survival.

Follicular

Found more commonly in iodide-deficient regions, follicular thyroid cancer usually manifests as a solitary thyroid mass. FNA cytology is unable to distinguish follicular adenoma from carcinoma, as angioinvasion and capsular invasion can only be seen histologically. Tumors invade vascular structures, and

metastasis is by hematologic spread to brain, bone, lungs, and liver. Total thyroidectomy is indicated, and radioactive iodine ablation is usually performed postoperatively.

Medullary

Typically seen as part of multiple endocrine neoplasia disease, heritable medullary thyroid cancer is usually multicentric and bilateral, with early metastasis to cervical lymph nodes. Sporadic cases comprise the majority of medullary cancers. Total thyroidectomy is performed, with additional neck dissection if lymph node metastases are present.

Anaplastic

Lethal cancers seen more frequently in regions with endemic goiter, anaplastic thyroid cancers usually present as rapidly enlarging neck masses. Extremely aggressive tumor invasion into vital neck structures may cause dysphagia and dyspnea. Tracheal invasion is common, and tracheostomy may be required to maintain airway patency. Such invasiveness usually precludes surgical resection, and attempts at palliation with radiation therapy and chemotherapy have limited success.

KEY POINTS

1. The thyroid gland is derived from an evagination at the base of the tongue followed by migration into the neck via the thyroglossal duct. Failure of thyroid migration results in a lingual thyroid, whereas persistence of the thyroglossal duct results in a thyroglossal cyst or fistula.
2. The recurrent laryngeal nerve may be damaged during surgery, causing ipsilateral vocal cord paralysis and hoarseness.
3. Graves' disease, toxic multinodular goiter, and toxic adenoma are the main etiologies of hyperthyroidism.
4. Graves' disease is an autoimmune disorder caused by thyroid-stimulating immunoglobulins that target thyroid-stimulating hormone (TSH) receptors of the thyroid gland.
5. T3 and T4 levels are elevated in Graves' disease, whereas the TSH level is low due to negative feedback.
6. Management of Graves' disease includes antithyroid medications, radioiodine ablation, or surgical excision.
7. Complications of subtotal thyroidectomy include recurrent laryngeal nerve injury, permanent hypothyroidism, and surgical hypoparathyroidism.
8. The four types of thyroid cancer in order of increasing malignancy are papillary, follicular, medullary, and anaplastic.
9. Fine-needle aspiration is the most important diagnostic study for evaluation of a thyroid nodule.
10. Patients with heritable medullary cancer have an elevated calcitonin level on calcium-pentagastrin testing.