Surgical literature is replete with discussions of surgical interventions and operative details of thyroid diseases. However, patients may present to the head and neck surgeon with thyroid diseases which require knowledge of thyroid physiology and endocrinology for diagnosis. In addition, it is incumbent upon any surgeon wishing to pursue surgery on the endocrine glands to understand the spectrum of diseases which may occur, and current alternative methods to treat these conditions. This will ensure both the best treatment for the patient, and help facilitate better understanding between the endocrine surgeon and the primary physician. This discussion is meant as an overview of thyroid physiology, and a brief discussion of common diseases of the thyroid gland which may present primarily to the head and neck surgeon or complicate surgical therapy of the thyroid gland.

History

The thyroid gland has long been recognized in medical literature due to the development of goiter in iodine deficient areas. The first description of thyroid goiter dates back to China around 2700 BC. Although it was recognized anatomically for centuries, the knowledge of its function was purely speculative. Da Vinci postulated that the gland was designed to fill a vacant space within the neck region. Parry believed that the heavy vascularity of the gland served as a buffer to prevent spikes in blood flow to the brain from the heart. Other physicians postulated the gland was used in lubrication of the neck tissues, or was an indicator of puberty. It was not until the practice of thyroidectomy became standard after the techniques of Bilroth, Kocher, and others, that the function of the thyroid became apparent. Kocher and other surgeons noted retrospectively that total thyroidectomy patients developed myxedema and cretinism. At this time, Halstead also noted a difference in the incidence of myxedema and tetany between Bilroth and Kocher. Bilroth usually performed a more rapid and bloody excision, but often left portions of the thyroid gland. His patients occasionally developed tetany, but rarely myxedema. Kocher used a more bloodless technique, excising the entire gland on its capsule. He rarely had cases of post-operative tetany, but had a higher incidence of myxedema. The cause of post-operative tetany was finally discovered in 1891 by Eudene Gley, who attributed this to parathyroid
removal. While surgical advances were leading to great improvements in the survivability of thyroid procedures, advances in knowledge of thyroid function and diseases were also being made. In the 1820’s it was discovered that the use of seaweed (iodine) lead to a decrease in goiter size, and in the 1830’s, the disease we now refer to as Graves’ disease was first described. These rapid advances into the later half of the 19th century made our current understanding of thyroid diseases and treatments possible.

**Thyroid Physiology**

The thyroid gland is made up of cells arranged into follicles. Each of these cells takes up inorganic iodine through a Sodium/Iodine symporter. This process in stimulated by TSH. Once the iodine is within the cell, thyroid peroxidase, an apical membrane protein, catalyzes a reaction to organify the iodine and move it into the follicular space (colloid). While in this space, thyroid peroxidase (TPO) also catalyzes a reaction which links two of these molecules together, thus forming T3 and T4. These two steps which utilize TPO are important, because they are the site of function for the anti-thyroid medications PTU and methimazole, both of which inactivate TPO. After hormone production, it is kept in the colloid until a stimulus (TSH) induces its release. The hormone is then endocytosed, the excess protein is removed, and then the hormone is secreted into the bloodstream. This release step is also affected by the medication lithium, and when taken chronically, can lead to goiter due to inability to release stored hormone.

In areas of normal iodine intake, this cycle occurs without problems. However, if the thyroid is suddenly given a large bolus of iodine, several effects may occur. First, the thyroid may begin to produce and store more hormone; but as the iodine builds up within the gland, it actually causes the thyroid to stop producing more hormone. This is known as the Wolff-Chaikoff effect. In some instances, this can lead to chronic suppression of thyroid hormone formation, and result in goiter. If the patient has an underlying hyperthyroid disorder where the gland is chronically stimulated, such as Graves’ disease, then a bolus of iodine may have an opposite effect, and stimulate a sudden increase in the formation and release of hormone leading to thyrotoxicosis. This is known as the Jod-Basedow phenomenon.

Thyroid hormones are controlled through a feedback inhibition model, where the final product, T3, inhibits the release of thyrotropic factors. The initiating factor in the cascade is TRH, which is produced in the hypothalamus. This then stimulates the release of TSH. However, the release of TSH is influenced more by the circulating T3 levels than the TRH. Once TSH is produced, it then acts at on the thyrocytes directly to stimulate growth, iodine uptake, and colloid endocytosis. Once the colloid is endocytosed and released, it circulates as T3 and T4, with 98% of the hormone in circulation being T4. The hormones then circulate in the serum in bound and free components. The bound component comprises the vast majority of circulating hormone, and the binding proteins include thyroid binding globulin, transthyretin, and albumin. Changes in the concentrations of these proteins, such as in liver failure, can alter the total amount of hormone circulating in the system. This occurs because the body regulates the free component of the hormone, and the free/total ratio remains the same, regardless of total hormone in circulation. This is why certain disease states necessitate measurement of the free T3 and T4 rather than the total values. Medications such as anticonvulsants can also compete for the binding sites of thyroid hormones, causing displacement of hormone, and thus give a false impression of thyroid function.
When assessing thyroid function, the most practical method is measurement of the TSH level, since this is indicative of the thyroid state. If the TSH results are abnormal, or if clinical exam is suggestive, then T3 and T4 levels (total or free) can be obtained to further delineate the exact thyroid state. TRH levels or stimulation tests are rarely needed due to the rarity of central axis thyroid dysfunction.

Goiter

The term goiter refers to a chronic enlargement of the thyroid gland. This condition is frequently broken down into endemic goiter and sporadic goiter. Endemic goiter is strictly defined as goiter in a region where >5% of children age 6-12 have a goiterus condition. Sporadic goiter occurs as goiter occurring in any area where the incidence is less than 5% of children 6-12 years. Areas of endemic goiter include china and central Africa, and are commonly due to iodine deficiency.

There are multiple causes of goiter. Hashimoto’s thyroiditis can cause a goiter in its early stages, but usually results in an atrophic gland in the later stages. Graves’ disease commonly results in goiter due to excess stimulation of the TSH receptor. Certain diets that are high in cabbage, broccoli, or cassava can lead to goiter. In addition, chronic ingestion of high doses of iodine (seaweed) can lead to thyroid enlargement, as can chronic use of lithium.

Once goiter is diagnosed, the status of the thyroid function should be assessed, since it can greatly impact the treatment recommended. If a patient is found to have a low TSH, they can be grouped as having clinical hyperthyroidism (low T3, T4), or subclinical hyperthyroidism (normal T3, T4). Both conditions may require treatment due to the long-term effects of hyperthyroidism, which include the risk of atrial fibrillation, congestive heart failure, and bone loss.

If the patient has goiter with normal thyroid functions, this condition is simply termed non-toxic goiter. For these patients, which usually have a multinodular goiter, the workup for cancer should be performed just like any solitary nodule. The nodule size should be measured and followed. FNA is recommended once the nodule increases >1.5 cm, while nodules >4cm are difficult to asses and require definitive treatment. If a nodule less than 4cm is found to be normal, then simple yearly follow-up with ultrasound to detect enlargement can be done. When the goiter does not cause compression, periodic observation is usually the treatment of choice. However, if the patient has any risk factors for carcinoma, such as rapid enlargement, history of radiation, suspicious neck lymphadenopathy, or papillary carcinoma on FNA, then surgery may be indicated. Thyroid suppression therapy for benign non-toxic goiter is not commonly done due to the high dose of thyroid hormone needed, and the rapid recurrence of the goiter following withdraw of therapy. If symptoms of compression are present, treatment is indicated. The most common treatment for compressive non-toxic goiter is surgery. This rapidly reverses the symptoms, and avoids the complications of ablation. For patients that are not as healthy or that opt for ablation, I131 may be given. The treatment reduces the gland size by 33% - 66% in most patients, and the symptoms improve in 70%-90%. However, radioactive iodine for a non-toxic goiter can result in permanent hypothyroidism in up to 80% of patients, and post-RAI Graves’ disease in 10%.
For patients with thyroid goiter and hyperthyroidism, the term toxic goiter is used. These conditions may include Graves’ disease, toxic adenoma, thyroiditis, or recent administration of iodine. For toxic conditions, FNA evaluation is not needed for treatment planning, since hyperactive nodules often mimic follicular neoplasms on FNA, and have a low potential for malignancy. In clinical or subclinical hyperthyroid conditions, the disease warrants treatment due to the risks for atrial fibrillation, heart failure, and bone loss. For toxic multinodular goiter, the preferred treatments are surgery and radioiodine. Anti-thyroid medications are not recommended for long-term use due to their side effects, such as agranulocytosis. Treatment with radioiodine may reduce the gland size by 40% within the first year, and the risk of post RAI ablation is only 11% - 24% for toxic goiter. Some patients will require a second dose if a problem persists. Surgery is also a viable option; however, the risk for post-operative hypothyroidism in subtotal thyroidectomy is higher than RAI, so RAI is often the first line of treatment. Patients that are undergoing surgery should have their hyperthyroid symptoms controlled prior to treatment with a short course of methimazole or PTU.

If the patient has toxicity due to Graves’ disease, then the treatment recommendations may differ. Since Graves’ disease has a chance for remission, most recommend beginning a non-ablative therapy initially. This is commonly done with methimazole or PTU. These medications will control the hyperthyroidism, and may be stopped after several months to check for disease remission, which may occur in 40% - 60%. Complications of therapy, such as agranulocytosis should be monitored for during therapy. RAI may also be employed. This therapy is usually effective, but it is also permanent, with a 55% - 75% incidence of hypothyroidism which requires lifetime hormone therapy. RAI must be avoided in children or pregnancy. Surgery is also an option, but is usually reserved for goiters that are too large for RAI, or goiters in children or goiters with compressive symptoms. The hypothyroid rate for surgery is almost equal to the RAI rate for this condition.

Hyperthyroidism and goiter may also be due to a large gland with a solitary hyperfunctioning adenoma. This condition is much less common than Graves’ or toxic MNG, but requires treatment due to the same risks of hyperthyroid states. In general, nodules <3cm do not require treatment since they are usually asymptomatic. Treatment with anti-thyroid medications is not advised due to their complications. Radioactive iodine is recommended and has a low hypothyroidism rate due to selective nodule uptake. Surgery can be done, but is generally reserved for adolescents or pregnant patients. For patients who have severe toxic symptoms, these should be controlled with a short course of anti-thyroid medications prior to RAI or surgery.

Thyroiditis

For patients with hypothyroidism, there are several common causes depending on the geographic origin of the patient. For people in iodine deficient areas of the world, iodine deficiency is the most common cause of hypothyroidism. However, for people in industrialized nations, the most common cause is from some form of thyroid destruction, due to Hashimoto’s disease, surgery, or radioactive iodine. If the patient’s history is negative for surgical conditions or radioactive iodine administration, then Hashimoto’s disease is the most common cause in the U.S. This involves a painless enlargement of the thyroid gland initially, but later results in a painless atrophic gland. Thyroid functions show a high TSH, and a low or normal T3, T4.
Patients may also have demonstrable antibodies to TPO or TBG. Treatment involves thyroid hormone replacement with levothyroxine for most patients. Treatment with T3 may be needed for patients with myxedema.

Several other forms of thyroiditis also occur, however, with much less frequency than Hashimoto’s disease. Most of these diseases involve several phases. The first phase may involve a hyperthyroid state due to acute inflammation of the thyroid gland with release of pre-formed hormone. The next phase usually involves a period of resolution as the gland recovers from the inflammation and the patient exhibits euthyroidism. Some patients then progress to a hypothyroid state while the gland recovers from the insult, and final resolution to a euthyroid state may take up to a year.

Silent thyroiditis is one of these inflammatory conditions. It occurs spontaneously, and may be termed post-partum thyroiditis if it occurs within one year of delivery. Thyroid functions are initially elevated, and patients often present with hyperthyroidism and a non-tender gland on exam. Treatment is usually supportive, with beta blockers for symptoms. Severe toxicity may require iodine administration. The resolution phase may be prolonged requiring treatment with thyroid hormones for up to a year.

Subacute thyroiditis is similar in course to silent thyroiditis. However, the presentation of this disease is its defining element. These patients present with acute hyperthyroidism and a painful enlarged thyroid gland. Patients often need beta blockers for symptoms, and may require iodine if severe symptoms develop. Treatment involves salicylates or steroids for severe swelling and pain. Pain and symptoms generally resolve within a few weeks, and most people will return to normal thyroid function within a year.

Acute thyroiditis is an uncommon condition that also presents with a painful thyroid. This condition involves an acute infection of the thyroid gland itself. It may be related to an infection of the deep neck spaces, or a pyriform sinus fistula. Regardless of the cause, it requires hospital admission and IV antibiotic therapy on diagnosis. Failure to diagnose and treat this disease in a timely fashion is associated with a high mortality rate. FNA can be done if clinical abscess is present, or to obtain a culture to guide treatment. At some point in the treatment course, a barium swallow or direct laryngoscopy is recommended due to the frequency of pyriform sinus fistula with this condition. If treated promptly, most cases return to normal function after the insult.

The least common of all thyroiditis conditions is termed Reidel’s thyroiditis. This entity involves a replacement of the thyroid gland with dense scar tissue creating a gland with the consistency of hard wood. Patients may complain of pain or dysphagia as the gland enlarges, and may progress to hypothyroidism is the gland is replaced by scar. This syndrome is associated with other focal sclerosis syndromes such as retroperitoneal fibrosis. Treatment involves open biopsy for diagnosis, surgical debulking for compressive symptoms, and thyroid hormone for hypothyroidism. The main therapy for this disease is chemotherapy utilizing tamoxifen or methotrexate to prevent recurrence.
Conclusions

Thyroid disease is common in clinical practice. It is important for any surgeon who wishes to treat thyroid disorders to understand the common problems associated with the thyroid gland, and the medical or surgical therapy that each disorder entails. This will improve understanding and communication between the endocrinologist and surgeon, since most operative patients will need to be followed for life. In addition, thyroid disorders may present primarily to head and neck surgeons with complaints of neck pain or dysphagia. It is important that these patients are properly diagnosed, and that the indications for surgical and medical therapy are well understood.

Bibliography


