Thyroid Diseases

The patient with thyroid disease is of concern to the dentist from several aspects. The dentist may detect early signs and symptoms of thyroid disease and may refer the patient for medical evaluation and treatment. In some cases, this may be lifesaving, whereas in others, quality of life can be improved and complications of certain thyroid disorders avoided. In this chapter, emphasis is placed on disorders involving hyperfunction of the gland (hyperthyroidism or thyrotoxicosis), hypofunction of the gland (hypothyroidism or myxedema or cretinism), thyroiditis, and the detection of lesions that may be cancerous. In an average dental practice, an estimated 20 to 150 patients will have a thyroid disorder.

THYROID GLAND

LOCATION

The thyroid gland, which is located in the anterior portion of the neck just below and bilateral to the thyroid cartilage, develops from the thyroglossal duct and portions of the ultimobranchial body It consists of two lateral lobes connected by an isthmus. The right lobe is normally larger than the left, and in some individuals, a superior portion of glandular tissue, or a pyramidal lobe, can be identifi ed. Thyroid tissue may be found anywhere along the path of the thyroglossal duct, from its origin (midline posterior portion of the tongue) to its termination (thyroid gland, in the neck).

ENLARGEMENT AND NODULES OF THE THYROID GLAND

Generalized enlargement of the thyroid gland, referred to as a *goiter,* may be diffuse, nodular, functional, or nonfunctional. On a functional basis, thyroid

enlargement can be divided into three types: primary goiter (simple goiter and thyroid cancer), thyrostimulatory secondary goiters (Graves' disease, Hashimoto's thyroiditis, and congenital hereditary goiter), and thyroinvasive secondary goiters (Hashimoto's thyroiditis, subacute painful thyroiditis, Riedel's thyroiditis, and metastatic tumors to the thyroid).

Laboratory Tests

Direct tests of thyroid function involve the administration of radioactive iodine. Measurement of thyroid radioactive iodine uptake (RAIU) is the most common of these tests. 131I has been used for this test, but 123I is preferred because it exposes the patient to a lower radiation dose. RAIU, which is measured 24 hours after administration of the isotope, varies inversely with plasma iodide concentration and directly with the functional state of the thyroid. In the United States, normal 24-hour RAIU is 10% to 30%. RAIU discriminates poorly between normal and hypothyroid states. Values above the normal range usually indicate thyroid hyperfunction. Several tests are available that measure thyroid hormone concentration and binding in blood. Highly specific and sensitive radioimmunoassays are used to measure serum T4 and T3 concentrations and rarely to measure rT3 concentration. The normal range for T4 is 64-154 nmol/L. (5-12 mg/dL). The normal range for T3 is 1.2-2.9 nmol/L (80-190 mg/dL). Elevated levels usually indicate hyperthyroidism, and lower levels usually indicate hypothyroidism. Free hormone levels usually correlate better with the metabolic state than do total hormone levels. Indirect assays are used to estimate the free T4 level. Measurement of basal serum TSH concentration is useful in the diagnosis of hyperthyroidism and hypothyroidism. Very sensitive methods, such as immunoradiometric or chemiluminescent techniques, are now available. to measure serum TSH. The normal range for

TSH is 0.5-4.5 mμ/L. In cases of hyperthyroidism, the TSH level is almost always low or nondetectable. Higher levels indicate hypothyroidism, and lower levels signify hyperthyroidism.

THYROTOXICOSIS (HYPERTHYROIDISM)

The term *thyrotoxicosis* refers to an excess of T4 and T3 in the bloodstream. This excess may be caused by ectopic thyroid tissue, Graves' disease, multinodular goiter, thyroid adenoma, subacute thyroiditis (painful and painless), ingestion of thyroid hormone (thyrotoxicosis factitia), food-containing thyroid hormone, or pituitary disease involving the anterior portion of the gland. In this section, the signs and symptoms, laboratory tests, treatment, and dental considerations for the patient with Graves' disease are considered in detail and serve as a model for other conditions that can result in similar clinical manifestations. It should be emphasized that multinodular goiter, ectopic thyroid tissue, and neoplastic causes of hyperthyroidism are rare compared with toxic goiter.. The basic cause of Graves' disease is not understood, but an immunoglobulin or a family of immunoglobulins directed against the TSH receptor mediate thyroid stimulation. These include TSHRAb and TSHR-blocking Ab, which inhibit the binding of TSH to its receptors. Graves' disease is now considered to be an autoimmune disease. The chief risk factor for Graves' disease is female gender, in part because of modulation of the autoimmune response by estrogen. This disorder is much more common in women (10:1) and may manifest during puberty, pregnancy, or menopause. Emotional stress such as severe fright or separation from loved ones has been reported to be associated with its onset. The disease may occur in a cyclic pattern and may then "burn itself out" or continue in an active state.

Clinical Presentation

Signs and Symptoms. Direct and indirect effects of excessive thyroid hormones contribute to the clinical picture in Graves' disease. The most common symptoms are nervousness, fatigue, rapid heartbeat or palpitations, heat intolerance, and weight loss. These symptoms are reported in more than 50% of all patients in whom the disease is diagnosed. With increasing age, weight loss and decreased appetite become more common, and irritability and heat intolerance are less common. Atrial fibrillation is rare in patients younger than 50 years old but occurs in approximately 20% of older patients. The patient's skin is warm and moist and the complexion rosy; the patient may blush readily. Palmar erythema may be present, profuse sweating is common, and excessive melanin pigmentation of the skin occurs in many patients; however, pigmentation of the oral mucosa has not been reported. In addition, the patient's hair becomes fi ne and friable, and the nails soften. Graves' ophthalmopathy, which is identified in approximately 50% of patients, is characterized by edema and inflammation of the extraocular muscles, as well as an increase in orbital connective tissue and fat. Ophthalmopathy is an organ-specific autoimmune process that is strongly linked to Graves' hyperthyroidism. Although hyperthyroidism may be successfully treated, ophthalmopathy often produces the greatest long-term disability for patients with this disease. This disease may progress to visual loss through exposure keratopathy or compressive optic neuropathy. Most thyrotoxic patients show eye signs not related to the ophthalmopathy of Graves' disease. These signs (i.e., stare with widened palpebral fi ssures, infrequent blinking, lid lag, jerky movements of the lids, and failure to wrinkle the brow on upward gaze) result from sympathetic overstimulation and usually clear when thyrotoxicosis is corrected.

Another complication, which is found in about 1% to 2% of patients with Graves' disease, is dermopathy. In focal areas of the skin, hyaluronic acid and chondroitin sulfate concentrations in the dermis are increased. This may occur as the result of lymphokine activation of fi broblasts. Accumulation causes compression of the dermal lymphatics and nonpitting edema. Early lesions contain a lymphocytic infi ltrate. Nodular and plaque formation may occur in chronic lesions. These lesions are most common over the anterolateral aspects of the shin. Patients with dermopathy almost always develop severe ophthalmopathy. Increased metabolic activity caused by excessive hormone secretion increases circulatory demand; increased stroke volume and heart rate often develop in addition to widened pulse pressure, resulting in palpitations. Supraventricular cardiac dysrhythmias develop in many patients. Congestive heart failure may occur and often is somewhat resistant to the effects of digitalis. Patients with untreated or incompletely treated thyrotoxicosis are highly sensitive to the actions of epinephrine or other pressor amines, and these agents must not be administered to them; however, once the patient has been well managed from a medical standpoint, administration of these agents can be resumed. Dyspnea not related to the effects of congestive heart failure may occur in some patients. The respiratory effect is caused by reduction in vital capacity related to weakness of the respiratory muscles. Weight loss, even with an increased appetite, is a common finding in younger patients. Stools are poorly formed, and the frequency of bowel movements is increased. Anorexia, nausea, and vomiting are rare but, when they occur, may be forerunners of thyroid storm. Gastric ulcers are rare in patients with thyrotoxicosis. Many of these patients have achlorhydria, and about 3% develop pernicious anemia.Thyrotoxic patients tend to be nervous and often show a great deal of emotional lability, losing

their tempers easily and crying often; severe psychiatric reactions may occur. Patients cannot sit still and are always moving. A tremor of the hands and tongue, along with lightly closed eyelids, is often present; in addition, generalized muscle weakness may lead to easy fatigability

The effect of excessive thyroid hormone production on mineral metabolism is complex and not well understood. The role of calcitonin only complicates the problem. However, thyrotoxic patients have increased excretion of calcium and phosphorus into their urine and stools, and radiographs show increased bone loss. Hypercalcemia occurs sometimes, but serum levels of alkaline phosphatase usually are normal. The bone age of young individuals is advanced. Glucose intolerance and, rarely, diabetes mellitus may accompany hyperthyroidism. Those with diabetes who are treated with insulin require an increased dose of insulin if they develop Graves' disease. Individual red blood cells (RBCs) in patients with thyrotoxicosis are usually normal; however, the RBC mass is enlarged to carry the additional oxygen needed for increased metabolic activities. In addition to the increased total numbers of circulating RBCs, the bone marrow reveals erythroid hyperplasia, and requirements for vitamin B12 and folic acid are increased. White blood cell (WBC) count may be decreased because of a reduction in the number of neutrophils, whereas the absolute number of eosinophils may be increased. Enlargement of the spleen and lymph nodes occurs in some patients. The platelets and the clotting mechanism usually are normal, but thrombocytopenia has been reported. Increased metabolic activity associated with thyrotoxicosis leads to increased secretion and breakdown of cortisol; however, serum levels remain within normal limits.

Laboratory Findings. T4, T3, TBG, and TSH tests can be used to screen for hyperthyroidism. However, current practice is to screen patients suspected of being hyperthyroid with use of the TSH serum level and to measure or estimate the free T4 concentration. A low TSH level and a high free T4 concentration are classically combined in hyperthyroidism. Some patients are hyperthyroid with a low TSH level and a normal free T4 concentration, but they have an elevated free T3 level. A few patients have normal or elevated TSH and high free T4. These patients have a TSH-secreting pituitary adenoma or thyroid hormone resistance syndrome.

Medical Management

Treatment of patients with thyrotoxicosis may involve antithyroid agents that block hormone synthesis, iodides, radioactive iodine, or subtotal thyroidectomy. The antithyroid agents most often used in the United States are propylthiouracil and methimazole, both of which inhibit thyroid peroxidase and thus the synthesis of thyroid hormone. Propylthiouracil also blocks extrathyroidal deiodination of T4 to T3. Carbimazole is the drug of choice in the United Kingdom, and propylthiouracil is the drug of choice in North America. The usual length of treatment ranges up to 18 months. When the “block-replace” regimen is used, no added benefi t occurs after 6 months of treatment with an antithyroid agent that is given along with T4. Antithyroid agents may cause a mild leukopenia, but drug therapy is not stopped unless the WBC count is more severely depressed. In rare cases, agranulocytosis may occur. If sore throat, fever, and/or mouth ulcers develop, most physicians advise the patient to stop the antithyroid medication and have a WBC count performed. Radioactive iodine is the preferred initial treatment for patients with Graves’ disease in North America. It is contraindicated in pregnant women and in those who are

breast feeding. Radioactive iodine can induce or worsen ophthalmopathy, particularly in smokers. Weetman recommends antithyroid drug treatment for patients younger than 50 years of age at their first episode of Graves' disease; radioactive iodine is recommended for those older than 50 years of age. The main adverse effect associated with radioactive iodine treatment is hypothyroidism. The incidence of cancer is unchanged or slightly reduced in patients treated with radioactive iodine, but the risk of death from thyroid cancer and possibly other cancers is slightly increased. Patients with severe hyperthyroidism should be treated with an antithyroid drug for 4 to 8 weeks before radioactive iodine therapy is initiated This approach reduces the slight risk of thyrotoxic crisis if radioactive iodine was given initially. Subtotal thyroidectomy is preferred by some patients with a large goiter and is indicated in those with a coexistent thyroid nodule whose nature is unclear. The patient is first treated with an antithyroid drug until euthyroidism is achieved. Then, inorganic iodide is administered for 7 days before surgery. In major centers, hyperthyroidism is cured in more than 98% of cases, and low rates of operative complications are reported. Postoperative hypothyroidism is a complication of more frequent surgical treatment as near-total thyroidectomy is approached. If exophthalmos is present, it follows a course independent of the therapeutic metabolic response to antithyroid treatment modalities and usually is irreversible. The adrenergic component in thyrotoxicosis can be managed with beta-adrenergic antagonists such as propranolol. Propranolol alleviates adrenergic manifestations such as sweating, tremor, and tachycardia. A delay in recovery of the hypothalamus-pituitarythyroid axis occurs in most patients with Graves' disease who are treated with 131I and manifests as a transient central hypothyroid phase. The clinical presentations of thyroid disorders

often are subtle in older adults and may be confused with "normal" aging. To avoid delay in diagnosis, some authors recommend routine TSH screening in the primary care practice of all patients age 60 and older. When hyperthyroidism is caused by Graves' disease, symptomatic therapy with a beta blocker or antithyroid drugs is initiated and is followed by definitive thyroid ablation with radioiodine.

Management of Thyrotoxic Crisis. Patients with thyrotoxicosis who are untreated or incompletely treated may develop thyrotoxic crisis, a serious but fortunately rare complication of abrupt onset that may occur at any age. Thyrotoxic crisis occurs in less than 1% of patients hospitalized for thyrotoxicosis. Most patients who develop thyrotoxic crisis have a goiter, wide pulse pressure, eye signs, and a long history of thyrotoxicosis. Precipitating factors include infection, trauma, surgical emergencies, and operations. Early symptoms of extreme restlessness, nausea, vomiting, and abdominal pain have been reported; fever, profuse sweating, marked tachycardia, cardiac arrhythmias, pulmonary edema, and congestive heart failure soon develop. The patient appears to be in a stupor, and coma may follow. Severe hypotension develops, and death may occur. These reactions appear to be associated, at least in part, with adrenal cortical insuffi ciency. Immediate treatment for the patient in thyrotoxic crisis consists of large doses of antithyroid drugs (200 mg of propylthiouracil), potassium iodide, propranolol (to antagonize the adrenergic component), hydrocortisone (100 to 300 mg), dexamethasone (2 mg orally every 6 hours, to inhibit release of hormone from the gland and peripheral conversion of T4 to T3), intravenous (IV) glucose solution, vitamin B complex, wet packs, fans, and ice packs. Cardiopulmonary resuscitation is sometimes needed.

Thyrotoxicosis Factitia. Thyrotoxicosis that results from the ingestion, usually chronic, of excessive quantities of thyroid hormone is referred to as *thyrotoxicosis factitia*. This condition usually occurs in patients with underlying psychiatric disease, or in individuals such as nurses and physicians who have access to the medication. In other cases, patients may not be aware that they are taking the hormone or some other thyroid active agent (iodocasein) as part of a we ight reduction program.

Other Causes of Thyrotoxicosis. Thyrotoxicosis has been reported to occur in patients who ate ground beef containing large quantities of bovine thyroid. Functional ectopic thyroid tissue can cause thyrotoxicosis. Thyroid tissue may be found in ovarian teratomas (struma ovarii). In rare cases, hyperfunctioning metastases of follicular carcinoma may cause thyrotoxicosis.

THYROIDITIS

Thyroiditis is infl ammation of the thyroid gland that may occur for a variety of reasons. Five types of thyroiditis have been identifi ed: Hashimoto's, subacute painful, subacute painless, acute suppurative, and Riedel's . Radiation therapy and drugs such as lithium, interlukin-2, interferons, and amiodarone also may cause thyroiditis iatrogenically. In some cases (subacute painful thyroiditis), infl ammation may result from transient hyperthyroidism due to follicle damage and release of preformed thyroid hormone. In contrast, Hashimoto's thyroiditis (chronic autoimmune thyroiditis) results in progressive hypothyroidism. Hashimoto's thyroiditis is the most common cause of primary hypothyroidism in the United States. It is an autoimmune disorder that presents most often as an asymptomatic diffuse goiter. High titers of circulating thyroid autoantibodies and thyroid antigen–specific T cells are observed. It usually affects young and middleaged

women. However, it can occur in men (3 to 4 times more common in women) and persons at any age. By the time the diagnosis has been established, most patients are hypothyroid. A family history of Hashimoto's thyroiditis or other autoimmune thyroid disorders is often reported. It may be associated with other autoimmune diseases such as pernicious anemia and type 1 diabetes mellitus. Early in the disease course, the thyroid becomes enlarged and firm and may have a nodular consistency.

Late in the disease, the gland may become atrophied and no longer palpable.Subacute painful thyroiditis is uncommon and often follows upper respiratory tract viral infection. Patients often present with an enlarged, painful, tender gland with signs and symptoms of hyperthyroidism. A marked increase in erythrocyte sedimentation rate (ESR) occurs, along with a low radioactive iodine uptake. A brief phase of hypothyroidism may be noted. Recovery of normal thyroid function can be expected. Subacute painful thyroiditis has a peak incidence in the third through fifth decades. It is about 4 times more common in women than in men. Subacute painless thyroiditis is another autoimmune disorder. Patients usually present with signs and symptoms of hyperthyroidism without thyroid pain or tenderness or fever. ESR is normal, and radioactive iodine uptake is abnormally low. Transient hypothyroidism may occur before normal thyroid function returns. This condition occurs in up to 5% of postpartum women and is more common among women than men.

Acute suppurative thyroiditis is caused by microbial infection of the thyroid. Patients present with severe neck pain, fever, focal thyroid tenderness, and erythema of the overlying skin. This acute infection may require fine-needle aspiration and culture for determination of the appropriate antibiotic therapy. It may also require surgical incision and drainage if an abscess is present.

This condition is rare and, when found, is seen in immunocompromised individuals and those with penetrating neck wounds. Riedel's thyroiditis is fi brous infi ltration of the thyroid gland of unknown origin. This condition, which may represent a variant of Hashimoto's thyroiditis, presents as a slowly enlarging stony neck mass, which may extend beyond the thyroid gland. As it gets larger, it may cause compressive symptoms such as dyspnea, dysphagia, hoarseness, and a sensation of choking. The clinical course is unpredictable, and patients may require surgery. It occurs predominantly in women and may eventually lead to clinically significant hypothyroidism. Because Hashimoto's thyroiditis is the most common type of thyroiditis, it is discussed in greater detail in the following section.

CLINICAL PRESENTATION—

HASHIMOTO'S THYROIDITIS

Signs and Symptoms

Goiter is the hallmark of Hashimoto's thyroiditis. The goiter is usually moderate in size and rubbery firm in consistency, and it moves freely with swallowing. In cases of sudden onset, the clinical picture suggests subacute thyroiditis with pain. Patients may be euthyroid during early phases of the disease. Over time, most patients develop hypothyroidism as lymphocytes replace functioning tissue. In a few cases, the patient develops transient hyperthyroidism, to be followed later by hypothyroidism.

Laboratory Findings

Early in the course of Hashimoto's disease, the patient is euthyroid, but TSH level is often slightly increased and RAIU is increased. Increasing titers of autoantibodies are found early in the disease; anti-TPOAb and anti-TgAb are the most important from a clinical standpoint. Fine needle biopsy of the

thyroid gland at this stage helps to confirm the diagnosis. Later in the disease, serum levels of T4 and T3 start to fall, and the level of TSH continues to increase. At this stage the patient is hypothyroid and requires treatment with hormone replacement

MEDICAL MANAGEMENT

Early in the course of the disease, patients with Hashimoto's disease have small goiters, are asymptomatic, and do not require treatment. Patients with larger goiters and/or mild hypothyroidism are treated with thyroid hormone replacement. More recent goiters usually respond by decreasing in size. Long-standing goiters often do not respond to hormone treatment. In these cases, unsightly goiters or those compressing adjacent structures may be treated by surgery after an attempt has been made to decrease their size with the use of hormone therapy. Patients with full-blown hypothyroidism require hormone replacement treatment.

HYPOTHYROIDISM

DEFINITION

The causes of hypothyroidism can be divided into four main categories :

1. Primary atrophic
2. Secondary
3. Transient
4. Generalized resistance to thyroid hormone

Ninety-five percent of cases of hypothyroidism are caused by primary and goitrous hypothyroidism. Acquired impairment of thyroid function affects about 2% of adult women and about 0.1% to 0.2% of adult men in North America.Hypothyroidism may be congenital or acquired. Permanent hypothyroidism occurs about once in every 4000 live births in the United States. Transient hypothyroidism occurs in 1% to 2% of newborns. Most

infants with permanent congenital hypothyroidism have thyroid dysgenesis, that is, ectopic, hypoplastic, or thyroid agenesis. The acquired form may follow thyroid gland or pituitary gland failure. Radiation of the thyroid gland (radioactive iodine), surgical removal, and excessive antithyroid drug therapy are responsible for most of these cases of hypothyroidism; however, some occur with no identifi able cause. Subclinical hypothyroidism is a prevalent condition that is characterized by elevated serum TSH concentration and normal serum FT4 and T3. It occurs in about 75 of 1000 women and in 28 of 1000 men. It is most common in women and older adults and is caused by chronic autoimmune thyroiditis, postpartum thyroiditis, 131I therapy, thyroidectomy, and antithyroid drugs. Subclinical hypothyroidism caused by chronic autoimmune thyroiditis has a predictable clinical course. Spontaneous return to normal TSH values occurs in 5% to 6% of cases. Progression to overt hypothyroidism occurs at a rate of about 5% per year. Some patients report fatigue, weight gain, poor memory, poor ability to concentrate, and depressed feelings.

CLINICAL PRESENTATION

Signs and Symptoms

Neonatal cretinism is characterized by dwarfism; being overweight; a broad, flat nose; wide-set eyes; thick lips; a large, protruding tongue; poor muscle tone; pale skin; stubby hands; retarded bone age; delayed eruption of teeth; malocclusions; a hoarse cry; an umbilical hernia;and mental retardation. All of these characteristics can be prevented by early detection and treatment . The onset of hypothyroidism in older children and adults is characterized by a dull expression; puffy eyelids; alopecia of the outer third of the eyebrows; palmar yellowing; dry, rough skin; dry, brittle, and coarse hair; increased

size of the tongue; slowing of physical and mental activity; slurred, hoarse speech; anemia; constipation; increased sensitivity to cold; increased capillary fragility; weight gain; muscle weakness; and deafness. Accumulation of subcutaneous fl uid (intracellularly and extracellularly) is usually not as pronounced in patients with pituitary myxedema as it is in those with primary (thyroid) myxedema. Serum cholesterol levels are elevated in thyroid myxedema and are closer to normal values in patients with pituitary myxedema. Untreated patients with severe myxedema may develop hypothermic coma that usually is fatal. T4, T3, TBG, and TSH tests are used to screen for hypothyroidism

MEDICAL MANAGEMENT

Patients with hypothyroidism are treated with synthetic preparations that contain sodium levothyroxine (T4) or sodium liothyronine (T3). The usual prescription for patients of ideal body weight for sodium levothyroxine is 75 μg to 100 μg per day. Hypothyroid patients receiving warfarin or other related oral anticoagulants when treated with T4 may have further prolongation of prothrombin time and could be at risk for hemorrhage. In addition, hypothyroid patients with diabetes with a decreased need for insulin or sulfonylureas may become hyperglycemic when treated with T4.

Congestive heart failure may occur in severe cases of myxedema. Levothyroxine therapy can correct this condition. The treatment of hypothyroid children with levothyroxine can result in a dramatic reversal of the signs and symptoms. Patients with untreated hypothyroidism are sensitive to the actions of narcotics, barbiturates, and tranquilizers, so these drugs must be used with caution. Smoking can worsen the disease. Stressful situations such as cold, operations, infections, or trauma may precipitate a

hypothyroid (myxedema) coma in untreated hypothyroid patients. External manifestations of severe myxedema, bradycardia, and severe hypotension are just about always present. Myxedematous coma occurs most often in severely hypothyroid elderly patients. It is more common during the winter months and has a high mortality rate. Hypothyroid coma is treated by parenteral levothyroxine (T4) and steroids; the patient is covered to conserve heat and artificial respiration. Hypertonic saline and glucose may be required to alleviate dilutional hyponatremia and occasional hypoglycemia.

THYROID CANCER

DEFINITION

Three main histologic types of thyroid cancer have been identifi ed: differentiated, medullary, and anaplastic. Differentiated cancers are subdivided into papillary, follicular, mixed, and Hürthle cell carcinomas. In addition, primary lymphomas may occur in the thyroid gland, and other cancers may metastasize to the thyroid. An important neoplastic syndrome, multiple endocrine neoplasia type 2 (MEN2), involves the thyroid gland. MEN2 consists of medullary thyroid carcinoma (MTC), pheochromocytoma in 50% of cases, and parathyroid hyperplasia/adenoma in 10% to 35% of cases. In rare cases, cancer from other locations may metastasize to the thyroid gland. The kidney is the most common site of origin for metastasis to the thyroid gland; other sites include cancer of the breast and lung, and melanoma.

Etiology and Clinical Findings

External radiation to the cervical region is believed to be one cause of thyroid cancer. Children who underwent thymic irradiation are at increased risk. Teenagers with acne that was treated by irradiation also are at greater risk for thyroid cancer. Patients with other types of neck cancer treated with

irradiation have increased risk for thyroid cancer. Children exposed to radioactive fallout from Chernobyl have been found to have an increase in thyroid cancer. External medical diagnostic radiation can add to the risk for thyroid cancer; however, dental radiographs do not appear to add to this burden. Radiation to the thyroid from internal sources and diagnostic or therapeutic doses of 131I have not been associated with an increased risk for thyroid cancer. Environmental factors such as high dietary iodine intake (papillary cancer) or a very low iodine intake (follicular cancer) appear to increase the risk for thyroid cancer. A genetic factor is suggested by an increased risk for thyroid cancer when a family member has had thyroid cancer or In some cases, no risk factor can be identified. On physical examination, manifestations of thyroid malignancy, including firm consistency of the nodule, irregular shape, fixation to underlying or overlying tissue, and suspicious regional lymphadenopathy, should be sought.Signs and symptoms that may be associated with thyroid cancer include a lump in the region of the gland, a dominant nodule(s) in multinodular goiter, a hard painless mass, fi xation to adjacent structures, enlarged cervical lymph nodes, a rapidly growing mass,hemoptysis, dysphagia, stridor, and hoarseness.

DIAGNOSIS

The cornerstone for the diagnosis of thyroid nodules is ultrasonography and fi ne-needle aspiration biopsy (FNAB). Clinically detected nodules should be evaluated through ultrasonography. Hypoechoic nodules should be submitted for FNAB. Ultrasound also can be used in cases of nonpalpable nodules, to guide FNAB. Overall rates of sensitivity and specificity for FNAB of thyroid nodules exceed 90% in iodinesufficient areas. FNAB is easy to perform and safe; very few complications have been reported. The

key to accuracy of the technique is to obtain an adequate specimen. This usually involves obtaining three to six aspirations that will contain at least fi ve or six groups of 10 to 15 well-preserved cells.15 Nodules found in patients living in iodine-defi cient areas may require surgical removal before a diagnosis can be established.

TREATMENT

For most papillary carcinomas, surgery is the indicatedtreatment. Options include lobectomy and total thyroidectomy. The recurrence rate is higher for lobectomy, but complications are fewer. Radioiodine ablation of residual thyroid tissue does not improve survival but does allow for interpretation of thyroglobulin levels. Radioiodine ablation is useful in metastatic disease and locally invasive disease, and in cases where cervical lymph nodes cannot be resected. Suppression of levothyroxine can be used to limit thyrotropin stimulation of tumor growth, but adverse effects may be difficult for the patient to deal with. Treatment of follicular carcinomas involves surgery, followed by radioiodine ablation and lifelong thyrotropin suppression through levothyroxine replacement therapy. Initial surgery may consist of thyroid lobectomy or total thyroidectomy. Other available options for minimally invasive disease include lobectomy and levothyroxine suppression of thyrotropin secretion alone; if cancer recurs, the rest of the thyroid is surgically removed, and radioiodine scanning for recurrence or radioiodine ablation of remaining thyroid tissue is performed. Hürthle cell cancers and medullary carcinomas are treated by total thyroidectomy with cervical lymph node dissection. Patients with medullary carcinoma should undergo regular monitoring of serum calcitonin for evidence of recurrence.The main objective of treatment for patients with anaplastic carcinomas is to control symptoms and relieve airway obstruction. Any

combination of surgery, external beam radiotherapy, and chemotherapy may be used. However, at best, these treatments occasionally may add several months to the life span. External beam radiotherapy is used to manage bony pain caused by metastases. Complications associated with total or subtotal thyroidectomy are hypoparathyroidism, recurrent laryngeal nerve damage, hemorrhage, and general risks associated with surgery. Complications of external beam radiotherapy include damage to the spinal cord, skin damage, and mucosal ulceration. Complications associated with chemotherapy include nausea and vomiting, mucosal damage, hair loss, infection, and bleeding.

PROGNOSIS

The best prognosis for differentiated cancers is based on age of the patient, metastases, and extent and size of the lesion. The best outlook is projected for young people with localized cancers that are smaller than 2 cm. Overall 10-year survival rates for papillary carcinoma are 80% to 90%, follicular carcinoma 65% to 75%, and medullary carcinoma 60% to 70%. Involvement of cervical nodes predicts recurrence in older patients (older than 45 years) but does not predict overall survival. Patients with distant metastases of a differentiated carcinoma have a long-term survival of 43%. The prognosis for anaplastic carcinoma is very poor, and 5-year survival is rare.

DENTAL MANAGEMENT

Clinical Examination Examination of the thyroid gland should be included as part of a head and neck examination performed by the dentist. The anterior neck region may be scanned for indications of old surgical scars, the posterior dorsal region of the tongue should be examined for a nodule that could represent lingual thyroid tissue, and the area just superior and lateral to the thyroid cartilage should be palpated for the presence of a

pyramidal lobe. Although difficult to detect, the normal thyroid gland can be palpated in many patients. It may feel rubbery and may be more easily identifi ed by having the patient swallow during the examination. As the patient swallows, the thyroid rises; lumps in the neck that may be associated with it also rise (move superiorly). Nodules in the midline area of the thyroglossal duct move upward with protrusion of the patient's tongue. An enlarged thyroid gland caused by hyperplasia (goiter) feels softer than the normal gland. Adenomas and carcinomas involving the gland are firmer on palpation and are usually seen as isolated swellings. Patients with Hashimoto's disease or Riedel's thyroiditis have a gland that on palpation is much fi rmer than the normal gland. If a diffuse enlargement of the thyroid is detected, auscultation should be used to examine for a systolic or continuous bruit that can be heard over the hyperactive gland of thyrotoxicosis or Graves' disease as a result of engorgement of the gland's vascular system.

MEDICAL CONSIDERATIONS

Thyrotoxicosis

The dentist should be aware of the clinical manifestations of thyrotoxicosis, so that undiagnosed or poorly treated disease can be detected and the patient referred for medical evaluation and treatment. By doing this, dentists may be able to help reduce the morbidity and mortality rates associated with thyrotoxicosis. Patients with untreated or poorly treated thyrotoxicosis are susceptible to developing an acute medical emergency called *thyrotoxic crisis,* which is another important reason for detection and referral. Symptoms include restlessness, fever, tachycardia, pulmonary edema, tremor, sweating, stupor, and finally, coma and death, if treatment is not provided. If a surgical procedure is performed on these patients, a crisis may

then be precipitated. In addition, an acute oral infection could precipitate a crisis. If a crisis occurs, the dentist should be able to recognize what is happening, begin emergency treatment, and seek immediate medical assistance. The patient can be cooled with cold towels, given an injection of hydrocortisone (100 to 300 mg), and started on an IV infusion of hypertonic glucose (if equipment is available). Vital signs must be monitored, and cardiopulmonary resuscitation initiated, if necessary. Immediate medical assistance should be sought, and, when available, other measures such as antithyroid drugs and potassium iodide may be started. Although the role of chronic infection and thyrotoxicosis is unclear, these conditions should be treated, as in any other patient. Once the patient has been identified and referred for medical management, oral foci of infection can be treated. Patients with extensive dental caries or periodontal disease, or both, can be treated after medical management of the thyroid problem has been effected. The use of epinephrine or other pressor amines (in local anesthetics or gingival retraction cords, or to control bleeding) must be avoided in the untreated or poorly treated thyrotoxic patient. However, the well-managed or euthyroid thyrotoxic patient presents no problem in this regard and may be given normal concentrations of these vasoconstrictors.Care must be taken with patients who are being controlled with nonselective beta blockers.When epinephrine is given to these patients, it is possible that blood pressure can be increased through inhibition of the vasodilatory action of epinephrine attained through blocking of beta2 receptors. Clinical experience has shown that small amounts of epinephrine can be used safely in these patients. More concentrated preparations of epinephrine (retraction cords and those used to control bleeding) should be avoided. Adverse reactions to propylthiouracil include agranulocytosis and leukopenia . If these should occur, the patient is

at risk for serious infection. The physician should monitor the patient for these adverse reactions. The dentist can consult with the patient's physician, or he or she can order a complete blood count to rule out the presence of these complications prior to undertaking surgical procedures. It has been reported that propylthiouracil can induce sialolith formation. This drug also can increase the anticoagulant effects of warfarin. Aspirin and nonsteroidal anti-infl ammatory drugs can increase the amount of circulating T4 and make control of thyroid disease more difficult. Once the thyrotoxic patient is under good medical management, the dental treatment plan can proceed without alteration. If acute oral infection occurs, however, consultation with the patient's physician is recommended as part of the management program. lists the medical concerns the dentist should be aware of regarding the hyperthyroid patient.

Hypothyroidism

In general, the patient with mild symptoms of untreated hypothyroidism is not in danger when receiving dental therapy. Central nervous system (CNS) depressants, sedatives, or narcotic analgesics may cause an exaggerated response in patients with mild to severe hypothyroidism. These drugs must be avoided in all patients with severe hypothyroidism and must be used with care (reduced dosage) in patients with mild hypothyroidism; however, a few patients with untreated severe symptoms of hypothyroidism may be in danger if dental treatment is rendered This is particularly true of elderly patients with myxedema. A myxedematous coma can be precipitated by CNS depressants, surgical procedures, and infections; thus, once again, the major goal of the dentist is to detect these patients and refer them for medical management before any dental treatment is rendered. If myxedema coma should occur, the dentist should call for medical aid; while waiting for

this assistance, the dentist can inject 100 to 300 mg of hydrocortisone, cover the patient to conserve heat, and apply cardiopulmonary resuscitation (CPR) as indicated. Once medical aid becomes available, parental levothyroxine is administered, and IV hypertonic saline and glucose are given as needed. Patients with less severe forms of hypothyroidism should be identified when possible, because the quality of their life can be greatly improved with medical treatment. In young individuals, permanent mental retardation can be avoided with early medical management. In addition, oral complications of delayed eruption of teeth, malocclusion, enlargement of the tongue, and skeletal retardation can be prevented through early detection and medical treatment. Once the hypothyroid patient is under good medical care, no special problems in terms of dental management remain, except for the need to address malocclusion and enlarged tongue, if they are present.

Thyroid Cancer

Palpation and inspection of the thyroid gland should be included as part of the routine head and neck examination performed by the dentist. If thyroid enlargement is noted, even though the patient may appear euthyroid (normal thyroid function), a referral should be made for evaluation before dental treatment is rendered. A diffuse enlargement may be a simple goiter, subacute thyroiditis, or chronic thyroiditis. The patient may be hyperthyroid, hypothyroid, or euthyroid. Isolated nodules may turn out to be an adenoma or carcinoma. Growing nodules in diffusely enlarged glands or in glands with multinodular involvement may be the manifestation of thyroid carcinoma and must be evaluated by a physician.

ORAL COMPLICATIONS AND MANIFESTATIONS

Thyrotoxicosis

Osteoporosis involving the alveolar bone may occur, and dental caries and periodontal disease appear rapidly in these patients. The teeth and jaws develop rapidly, and premature loss of deciduous teeth with early eruption of permanent teeth is common. Euthyroid infants of hyperthyroid mothers have been reported to have erupted teeth at birth. A few patients with thyrotoxicosis have been found to have a lingual "thyroid," consisting of thyroid tissue below the area of the foramen cecum. If the dentist detects a lingual tumor in a euthyroid patient, a physician should examine the patient before the mass is surgically removed. This usually is done with radioactive iodine scanning.

Hypothyroidism

Infants with cretinism may present with thick lips, enlarged tongue, delayed eruption of teeth, and resulting malocclusion. The only specifi c oral change manifested by adults with acquired hypothyroidism is an enlarged tongue.

Thyroiditis

The pain associated with subacute painful thyroiditis may radiate to the ear, jaw, or occipital region. Hoarseness and dysphagia may occur. Patients may report palpitations, nervousness, and lassitude. On palpation, the thyroid is enlarged, fi rm, often nodular, and usually very tender.

Dental Management of the Patient With Thyroid Disease

Clinical Setting	Hyperthyroid	Hypothyroid
Detection of undiagnosed disease	Symptoms Signs Refer for medical Dx and Rx	Symptoms Signs Refer for medical Dx and Rx
Diagnosed disease	Determine original diagnosis and Rx Past treatment Current treatment Lack of signs and symptoms Presence of any complications	Original diagnosis and Rx Past treatment Current treatment Lack of signs and symptoms Presence of any complications
Untreated or poorly controlled	Avoid surgical procedures Treat any acute infection Avoid use of epinephrine or pressor amines	Avoid surgical procedures Treat oral infection Avoid central nervous system (CNS) depressants such as narcotics, barbiturates, etc.
Well controlled	Treat acute infection (avoid if possible) Treat chronic infection Implement normal procedures and management	Avoid oral infections Implement normal procedures and management
Medical crisis (rare)	Recognition and initial management of **thyrotoxic crisis** Seek medical aid Wet packs, ice packs Hydrocortisone (100-300 mg) Cardiopulmonary resuscitation Propylthiouracil Intravenous (IV) glucose solution	Recognition and initial management of **myxedema coma** Seek medical aid Cover to conserve heat Hydrocortisone (100-300 mg) Cardiopulmonary resuscitation Parental levothyroxine IV saline and glucose

BOX 17-2

Treatment of Thyrotoxicosis[8,9]

SEVERE THYROTOXICOSIS

- Propylthiouracil (PTU)—100 to 150 mg q 8 hr; in some cases, PTU 200 to 300 mg q 6 hr.
- With improvement of symptoms, PTU dosage can be lowered. As improvement continues, can switch to once-a-day methimazole (MMI) 2.5 to 5.0 mg once per day for 12 to 24 months.

MODERATE THYROTOXICOSIS

- Start with methimazole (MMI), which is 10 times more potent than propylthiouracil (PTU). MMI also has longer intrathyroid residence time but does not inhibit conversion of T_4 to T_3 as PTU does. Start with 20 to 30 mg once per day. Within 4 to 6 weeks, the patient will be euthyroid. Reduce dosage to 2.5 to 5 mg per day for 12 to 24 months.
- No surgical complications or radiation hazards. Frequent relapses occur, and drug adverse effects may complicate treatment.

^{131}I THERAPY

- This is the most common form of treatment in the United States. Antithyroid drugs are given to make the patient euthyroid. The antithyroid medicine is stopped for 3 to 5 days, and then 6000 to 8000 rad dosage of ^{131}I is given. More than 80% of patients are cured with a single dose of ^{131}I.
- Delayed control of thyrotoxicosis, lower efficacy in large goiters, easy to perform, no surgical risk, questionable radiation hazard, and transient worsening of preexisting eye disease. Rare, mild, and transient adverse effects.

SURGERY

- Patient must be euthyroid before surgery is performed. This is usually done with one of the antithyroid drugs (PTU or MMI). Subtotal thyroidectomy is the treatment of choice.
- Hypoparathyroidism occurs in 0.9% to 2.0% of cases, and recurrent laryngeal nerve damage is found in 0.1% to 2.0% of cases. Bleeding, infection, and anesthetic complications may occur. Results in fast correction of thyrotoxicosis but at a high cost.

BOX 17-5

Medical Problems of Concern to the Dentist in Treating a Patient With Undiagnosed or Poorly Controlled Thyroid Disease

HYPERTHYROIDISM

- Adverse interaction with epinephrine
- Life-threatening cardiac arrhythmias
- Congestive heart failure
- Complications of underlying cardiovascular pathologic conditions
- Thyrotoxic crisis can be precipitated by the following:
  - Infection
  - Surgical procedures

HYPOTHYROIDISM

- Exaggerated response to central nervous system (CNS) depressants
- Sedatives
- Narcotic analgesics
- Myxedematous coma can be precipitated by the following:
  - CNS depressants
  - Infection
  - Surgical procedures

Suggestive Reading

James W Little, Craig S Miller, Nelson L Rhodus. Dental management of medically compromised patient, 9th edition, Elsevier, 2018