CHAPTER 166 ■ THYROID DISEASE IN THE INTENSIVE CARE UNIT

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The purpose of this chapter is to discuss thyroid disease as it may present in an intensive care unit (ICU). Interpretation of thyroid function tests in a critically ill patient requires knowledge of the perturbations of hormone synthesis that may occur with illness and certain medications. This text will also discuss the diagnosis and treatment of thyroid emergencies: myxedema coma, thyroid storm, postthyroidectomy hypocalcemia, and airway obstruction by goiter.

## THYROID FUNCTION TESTS

There are a myriad of tests that may be ordered to evaluate thyroid function, so finding the right test or set of tests can confound many physicians. Further complicating the comprehension is interpreting these values once they are obtained. The purpose of this section is to provide an overview of the most commonly ordered labs. A later section will delineate how to interpret these values in the critically ill patient.

### Serum Thyroid-stimulating Hormone

**Hormone/Free Thyroxine (FT<sub>4</sub>)** is sufficient to diagnose most thyroid disorders. It is recommended to use the now widely available ultrasensitive TSH (1). The normal reference range for this test is...
is an extensively debated issue among endocrinologists. Currently, the most widely accepted range of 0.45 to 4.12 mIU/L is based on values from the NHANES III (National Health and Nutrition Examination Survey) database (2). Fueling the controversy, however, was a study revealing that exclusion of patients with thyroid dysfunction and those taking medications known to affect thyroid tests yields an upper limit of normal at 2.5 mIU/L (3). The issue will require further investigation with larger studies. In this chapter, the normal range will be based on the NHANES data: 0.45 to 4.12 mIU/L.

### Total T₄ Measurement

Total T₄ (TT₄) measurement includes both bound and free thyroid. Therefore, conditions or medications that affect serum levels of thyroid-binding globulin will also affect the total T₄ value; use of FT₄ can eliminate this shortcoming. However, if FT₄ is not available, this level can be estimated by looking at the FT₃ index, FTI. This number is calculated by multiplying the total T₃ by the T₃ resin uptake, (T₃ RU) (see below for explanation). Many laboratories use this value when reporting a FTI.

### Serum Tri-iodothyronine (T₃)

Similar to thyroxine, serum tri-iodothyronine (T₃) may be measured in the free and bound fractions, although it is generally recommended that the total T₃ be used, as only a minute fraction of T₃ is free (4). T₃ levels should be measured in patients suspected of having hyperthyroidism, as some patients may have excess secretion of only T₃ early in the course of thyrotoxicosis. As a result, patients may have a suppressed TSH, normal free T₄, and an elevated total T₃ (T₃ toxicosis). Measurement of this hormone is not helpful, however, in hypothyroidism, as the elevated TSH stimulates preferential formation of T₄, typically maintaining these levels in the normal range (5,6).

### T₃ Resin Uptake

T₃ resin uptake is an indirect, inverse test to estimate the number of unoccupied serum protein-binding sites. Radiolabeled T₃ is added to the patient’s serum and distributed between unoccupied T₃-binding sites on thyroid-binding globulin (TBG) in the serum and an adsorbent that has been added to the solution. ¹²³I-T₃ binding to the adsorbent is increased if the number of unoccupied binding sites is decreased. This may be due to either low TBG levels such as in nephrotic syndrome or chronic liver disease, or increased thyroid hormone levels as in hyperthyroidism (7). In contrast, the T₃ RU is low if the number of unoccupied binding sites is increased. Low thyroid hormone concentrations (hypothyroidism or high TBG concentrations) estrogen therapy, or pregnancy may lead to a low T₃ RU (8).

### Reverse T₃

Reverse T₃ differs from T₃ in that the iodine is missing from the inner ring instead of the outer ring of T₃. It is largely bound to proteins in the serum. Its half-life in the serum is quite short (9), and furthermore, the biologic function of rT₃ is not completely understood in humans. The clinical utility of measuring these levels is chiefly in the setting of sick euthyroidism and will be discussed in greater detail in the section dealing with interpretation of thyroid function in critically ill patients. Table 166.1 details the interpretation of thyroid function tests.

### DRUGS AND THYROID FUNCTION

There are a number of drugs commonly used in the ICU that will interfere with thyroid homeostasis. Although many of these actions are viewed as detrimental, some effects may also be used for a therapeutic benefit, particularly in thyrotoxicosis. The vast majority of the effects of pharmacologic agents on thyroid hormone homeostasis may be divided into four different categories. First, they may alter the synthesis or secretion of thyroid hormones. Second, they may alter hormone concentration by changing serum levels of binding proteins or by competing for their binding sites. Third, the pharmacologic agents may modify the cellular uptake and metabolism of thyroid hormones. Fourth, drugs may interfere with thyroid hormone action at the tissue level. Typically these effects on thyroid hormone metabolism are transient, but they may complicate the interpretation of the thyroid function tests (10). The more commonly used compounds interfering with thyroid function and their mechanisms of action are listed in Table 166.2.
TABLE 166.2
COMMONLY USED DRUGS THAT AFFECT THYROID FUNCTION

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mode of action</th>
<th>Thyroid function abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>Inhibits cellular hormone uptake</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td></td>
<td>Alters hormone secretion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alters intracellular metabolism</td>
<td></td>
</tr>
<tr>
<td>Lithium</td>
<td>Reduced hormone secretion (acute)</td>
<td>Hypothyroidism (acute)</td>
</tr>
<tr>
<td></td>
<td>Autoantibody immune response (chronic)</td>
<td>Hypothyroidism (chronic)</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Reduced hormone secretion</td>
<td>Reduced TSH, T4</td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>Reduced absorption from gut</td>
<td>E elevated TSH, reduced T4</td>
</tr>
<tr>
<td>Ferrous sulfate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charcoal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucralfate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propylthiouracil</td>
<td>Altered hormone synthesis</td>
<td>Reduced T4-to-T3 conversion (13)</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Alters intracellular metabolism</td>
<td>Reduced total T4</td>
</tr>
<tr>
<td>Sodium iodide</td>
<td>Reduced hormone secretion</td>
<td>Reduced T4-to-T3 conversion (14)</td>
</tr>
<tr>
<td>Iopanoic acid</td>
<td>Altered hormone synthesis</td>
<td>Reduced total T4</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>Reduced TSH secretion</td>
<td>Reduced T4-to-T3 conversion (15)</td>
</tr>
<tr>
<td>Heparin</td>
<td>Inhibits T4 binding to TBG</td>
<td>Transient increase in fT4</td>
</tr>
<tr>
<td>Lasix</td>
<td>Inhibits T4 binding to TBG</td>
<td>Reduced total T4, total T3</td>
</tr>
<tr>
<td>Salicylates</td>
<td>Inhibits T4 binding to TBG</td>
<td>Increased free T3, free T3</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>Alters intracellular metabolism</td>
<td>Reduced total T4</td>
</tr>
<tr>
<td>Radiographic contrast</td>
<td>Alters hormone secretion</td>
<td>Increased free T4</td>
</tr>
<tr>
<td>contrast agents</td>
<td></td>
<td>Decreased free T3</td>
</tr>
<tr>
<td>Cytokines</td>
<td>Autoantibody immune response</td>
<td>Transient hypothyroidism or hypothyroidism (18)</td>
</tr>
</tbody>
</table>

Thyrotoxicosis

Clinical Presentation

In the ICU, patients with thyrotoxicosis may have an atypical presentation, with tachyarrhythmias or central nervous system disturbance as the primary sign. It is important for the intensivist to consider thyroid dysfunction in the differential diagnosis of such patients, since treatment with beta-blockers and antithyroid medications can rapidly improve the clinical course (19). The diagnosis may need to be a clinical one, as results of laboratory testing can take days. Table 166.3 lists the symptoms and signs that may be seen in a patient with thyrotoxicosis.

Cardiovascular Manifestations

Sinus tachycardia and atrial fibrillation are the most commonly seen cardiovascular disorders in hyperthyroidism. Since atrial fibrillation may be the only indication of thyrotoxicosis, it is important to screen such patients with a TSH and FT4. Congestive heart failure typically occurs only in patients with underlying heart disease, but may also manifest as a result of chronic tachycardia-induced cardiomyopathy (20). Physical examination findings in a thyrotoxic patient include widened pulse pressure, hyperdynamic precordium, tachycardia, and systolic ejection murmur. The pathogenesis of cardiovascular diseases from exposure to excessive thyroid hormone is not entirely understood. Thyroid hormone has both indirect and direct effects on vascular smooth muscle tone and increases cardiac output. Thyroxine also regulates expression of myocardial genes involved in the handling of calcium (21).

The typical electrocardiographic changes seen in thyrotoxicosis are sinus tachycardia and atrial fibrillation (20). Patients may also present with complete heart block, and cases have been reported that showed reversal with treatment of the underlying thyroid disorder (22–25).

TABLE 166.3
SIGNS AND SYMPTOMS OF THYROTOXICOSIS

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Hyperdefecation</td>
<td>Lumbar/lower back pain</td>
</tr>
<tr>
<td>Sweating/heat intolerance</td>
<td>Proximal muscle weakness</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Tachycardia/arrhythmias</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Tachycardia/arrhythmias</td>
</tr>
<tr>
<td>Weakness</td>
<td>Hyperreflexia</td>
</tr>
<tr>
<td>Increased appetite</td>
<td>Thyroid bruit</td>
</tr>
<tr>
<td>Scant/absent menses</td>
<td>Dermopathy</td>
</tr>
</tbody>
</table>
Pulmonary Manifestations

Dyspnea on exertion is a common presenting symptom of patients with hyperthyroidism. Respiratory muscle strength is significantly reduced in thyrotoxicosis and improves with reduction of thyroid hormone levels (26). Several studies have also shown that thyrotoxicosis is a risk factor for the development of pulmonary hypertension (27–29). Pulmonary emboli may be seen in patients with atrial fibrillation who are not on anticoagulation therapy (30). Furthermore, pulmonary edema has been described in uncontrolled thyrotoxic patients (31–34).

Laboratory Findings

The laboratory findings in hyperthyroidism are the combination of a low TSH and a high FT4 (Table 166.1). If the FT4 is normal and TSH suppressed in a patient suspected of having thyrotoxicosis, it is important to check a T3 level, as this may be elevated in early Graves disease or in T3-secreting toxic adenomas. In the event that the patient presents with an elevated T3 or T4 and a detectable or “normal” TSH, the clinician should consider the effects of nonthyroidal illness (see below) or drugs (Table 166.2) on thyroid function testing. Rarely, the patient may have a TSH-secreting pituitary tumor or thyroid hormone resistance (33). Consultation with an endocrinologist may be warranted if the patient has unusual thyroid function tests that cannot be readily corroborated with the entire clinical picture.

Etiology

The two most common causes of thyrotoxicosis in the outpatient setting are Graves disease and toxic multinodular goiter. Elderly patients tend to have a solitary or multiple nodules that become autonomously functioning and lead to hypersecretion of thyroid hormone. The goiter may not always be palpable if the offending nodule is small or if the patient has a substernal goiter. Tracheal deviation on chest radiograph may be the only finding to alert the physician of the underlying disease process. By way of contrast, young women are more likely to present with the classic stigmata of Graves disease: thyroid bruit, ophthalmopathy, and diffuse goiter. In the ICU, however, it is important to consider other causes of hyperthyroidism. Factitious thyrotoxicosis is rare but should be considered in a patient with a history of taking herbal supplements or overthe-counter weight loss medications (36). Surrupitious use of thyroid hormone may be diagnosed by measurement of serum thyroglobulin levels. If low, this would indicate that the patient is self-medicating (37). Typically, the thyroglobulin levels are high in patients with true thyroid disorders. Iodinated contrast media as used with computed tomography or cardiac catheterization may also cause hyperthyroidism because these agents contain free iodine (38). Generally, patients with normal thyroid function are not at risk of this complication. However, patients with a history of Graves disease, multinodular goiter, or even subclinical hyperthyroidism may develop frank thyrotoxicosis several days after the administration of contrast media (see below for further discussion of contrast media and thyroid function) (38,39).

Treatment

The treatment of thyrotoxicosis is based on the underlying pathophysiology. Patients with Graves disease, toxic multinodular goiter, or toxic adenoma should be started on a thionamide, such as methimazole (MMI) or propylthiouracil (PTU). The dosage of antithyroid medication should be tailored to the degree of thyrotoxicosis; hence, consultation with an endocrinologist is advisable. Patients with peripheral manifestations of hyperthyroidism may also benefit from the addition of a beta-adrenergic antagonist drug. This agent will assist with the symptoms of agitation, tremor, palpitations, and diarrrhea. Propranolol is the drug most commonly used in the United States. Patients who have overdosed on thyroid hormone or are taking a supplement with thyroid hormone extract should be counseled regarding the complications of taking thyroid hormone supplements in excess, and the offending agent should be discontinued. If the patient requires treatment, beta-adrenergic antagonists and bile acid sequestrants—for example, cholestyramine—may be used.

Thyroid Storm

Thyroid storm is a rare but life-threatening syndrome of exaggerated clinical manifestations of thyrotoxicosis. There are no universally accepted criteria for its diagnosis, and consequently, the incidence is unknown. Laboratory testing is unreliable in distinguishing patients with thyrotoxicosis and thyroid storm; thus the diagnosis of thyroid storm is primarily a clinical one. It is a medical emergency typically caused by exacerbation of hyperthyroidism following a precipitating event or illness; Table 166.4 lists the precipitants of thyroid storm. The clinical picture is one of decompensation of one or more organ systems (40). There are four main features noted in thyroid storm: tachycardia, fever, central nervous system disturbances, and gastrointestinal symptoms. The CNS symptoms vary from marked hyperirritability and anxiety, to confusion and coma. Mortality rates range from 20% to 100%, so prompt, multifaceted therapy is essential (41).

Management

The treatment of thyroid storm takes a four-pronged approach (Table 166.5). First, an antithyroid drug must be given.
reduce thyroid hormone production and peripheral conversion of \( T_4 \) to \( T_3 \). Second, supportive care must be administered against the systemic disturbances of fever, hypovolemia, and cardiovascular compromise. Third, the peripheral actions of thyroid hormone should be blocked. Finally, any precipitating factors should be addressed.

A thionamide is given to block synthesis of \( T_3 \) and \( T_4 \). PTU is the favored agent because it also inhibits peripheral conversion of \( T_4 \) to \( T_3 \). By reducing \( T_3 \) concentrations in the serum, it is postulated that the manifestations of thyrotoxicosis are more rapidly improved with PTU than with MMI (41). Neither of these drugs is available parenterally; so administration is typically by mouth or nasogastric (NG) tube. In patients with altered mental status, or in whom an NG cannot be placed, rectal administration of PTU has been reported to be used successfully in a few patients (44,45). It is conventional to use high doses of antithyroid drugs, such as 200 to 400 mg PTU every 4 hours or 20 mg MMI every 4 hours.

Thionamides do not inhibit the release of preformed \( T_3 \) and \( T_4 \) from the thyroid. Inorganic iodide, however, can accomplish this goal. It may be administered orally as Lugol solution (ten drops every 8 hours) or as saturated solution of potassium iodide (SSKI, five drops every 6 hours). Oral radiographic contrast agents, sodium ipodate or iopanoic acid, may be substituted for iodine. These drugs block the release of preformed thyroid hormone from the gland and inhibit the extrathyroidal conversion of \( T_4 \) to \( T_3 \) (41). It is critical to administer thionamide therapy about an hour before the iodide or contrast agent is given, because the sudden influx of iodide into the thyroid can lead to increased thyroid hormone production and thereby prolong the thyrotropic axis (46). However, when the iodide or contrast agent is given after the antithyroid drug, serum \( T_3 \) and \( T_4 \) levels are substantially reduced in 2 to 3 days and may reach the normal range in 5 to 7 days (41,47).

If the patient has an allergy to iodide or cannot tolerate thionamides, lithium may be substituted to inhibit \( T_3 \) and \( T_4 \) synthesis (48). It may be given initially at a dose of 300 mg every 6 hours and titrated to maintain serum lithium concentrations around 1 mEq/L.

Supportive care should also be provided. Fever is preferentially treated with acetaminophen. Salicylates should not be used as they competitively inhibit \( T_3 \) and \( T_4 \) binding to serum proteins and thus increase serum free \( T_3 \) and \( T_4 \) levels (49). The patient’s fluid losses should be appropriately replaced, bearing in mind the insensible losses from high fever and, if present, diarrhea. Hypercalcemia, if present, will usually be reversed by adequate hydration. High-dose glucocorticoids have been given historically for empiric treatment of relative adrenal insufficiency. Such treatment also has the added benefit of inhibition of peripheral conversion of \( T_4 \) to \( T_3 \). In patients with Graves disease, glucocorticoids also directly inhibit secretion of thyroid hormone. A loading dose of hydrocortisone 200 mg may be given initially followed by 100 mg every 8 hours; this therapy can be tapered rapidly after 2 to 3 days. Dexamethasone or methylprednisolone at equivalent doses may be substituted for hydrocortisone if preferred.

Therapy directed against the peripheral actions of thyroid hormone should be administered as well. \( \beta \)-Adrenergic antagonists can provide rapid amelioration of many of the symptoms of thyroid storm and should be dispensed immediately. Propranolol is the most commonly used agent, and may be given intravenously or orally depending on the clinical setting. If the oral route is used, the patient may be given between 80 and 120 mg every 6 hours. It is important to consider that in the thyrotoxic state, drug clearance is increased and higher-than-usual doses are necessary to achieve the desired effect. If rapid beta-blockade is necessary to reduce heart rate, or if the patient’s mental status precludes oral drugs, intravenous

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**TABLE 16-5**

**SUMMARY OF TREATMENT FOR THYROID STORM**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose and route of administration</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>0.3–1 mg IV over 10 min, then 1–3 mg IV as needed 80–120 mg PO q8h</td>
<td>( \beta )-Adrenergic blockade and inhibition of ( T_4 )-to-( T_3 ) conversion</td>
</tr>
<tr>
<td>Methimazole</td>
<td>200–400 mg PO/NG/PR q8h</td>
<td>Inhibit hormone synthesis and block conversion of ( T_4 ) to ( T_3 )</td>
</tr>
<tr>
<td>Iodine(^a)</td>
<td>20 mg PO/NG q8h</td>
<td>Inhibits hormone synthesis</td>
</tr>
<tr>
<td>SSKI</td>
<td>5 drops PO/NG q8h</td>
<td>Blocks release of thyroid hormone</td>
</tr>
<tr>
<td>Iodinated contrast agents(^a)</td>
<td>10 drops PO/NG q8h</td>
<td>Blocks release of thyroid hormone and conversion of ( T_4 ) to ( T_3 )</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>200 mg IV load, then 100 mg IV q8h</td>
<td>Stress-dose steroids and blocks conversion of ( T_4 ) to ( T_3 )</td>
</tr>
<tr>
<td>Lithium</td>
<td>300 mg PO/NG q8h titrate to lithium level of 1 mEq/L</td>
<td>Inhibits hormone synthesis</td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>4 g PO/NG q6h</td>
<td>Lowers serum ( T_3 ) and ( T_4 )</td>
</tr>
</tbody>
</table>

\(^{a}\)Either iodine or iodinated contrast agents should be used, but not both. Administration of iodide should be preceded by PTU by 2–3 hours to avoid enhancement of thyroid hormone synthesis.
(IV) administration is preferred. The initial dose should be 0.5 to 1 mg given over 10 minutes while continuously monitoring the patient’s cardiac rhythm, and subsequently, 1 to 3 mg may be given over 10 minutes every several hours as needed. Propranolol attenuates the effects of catecholamines and weakly inhibits the peripheral conversion of T₄ to T₃. This inhibition occurs over a period of a week, however, and thus does not solely account for the beneficial effects of propranolol in the thyrotoxic patient.

In extreme cases, it may be beneficial to use a method to remove T₄ and T₃ from the patient’s serum. The simplest approach is to administer oral cholestyramine. This drug binds the hormones in the GI tract, interrupting the enterohepatic circulation (50). Plasmapheresis has also been used successfully to lower T₄ and T₃ levels (51,52), although other studies were unable to confirm the beneficial effects (53).

Finally, it is important to search for and treat underlying illnesses that may have precipitated the thyroid storm. This process can be difficult in obtunded patients, but a systematic approach is usually successful in uncovering the cause.

Patients treated with the above regimen usually recover in 1 to 24 hours if the syndrome is recognized and treated in a timely fashion. As the patient’s condition stabilizes, it is important to wean the glucocorticoids, switch to oral rehydration, and taper the beta-blocking drugs. Long-term treatment is important to wean the glucocorticoids, switch to oral rehydration, and taper the beta-blocking drugs. Long-term treatment with glucocorticoids and by discontinuation of the amiodarone, although in some cases, it is reasonable to continue the antiarhythmic medication (59). In patients in whom chronic therapy with amiodarone is essential, thyrotoxicity is a potential option for treatment of AIT (54). Radioiodine ablation is not an option given the low iodine uptake as a result of the iodine deficiency. In iodine-deficient regions, it is more common to see hyperthyroidism as a result of amiodarone therapy (56). There are two mechanisms (Table 166.6) of amiodarone-induced thyrotoxicosis (AIT). Distinction of these two disorders is relevant because their treatment differs. Type I AIT occurs in glands with an underlying abnormality. Areas of autonomy, such as a toxic nodule or autoimmune disease in the thyroid, produce increased levels of hormone in response to the excess iodine released from the amiodarone (55). Type II AIT develops as a result of a direct cytotoxic effect of amiodarone on the thyrocyte (57). Treatment of type I AIT is difficult because most patients do not respond to thionamides, as these drugs have decreased efficacy in states of iodine excess (58). Use of potassium perchlorate (KClO₅) may enhance the efficacy of thionamides (54). It is important to note that both thionamides and KClO₅ may cause agranulocytosis, so serial monitoring of blood counts is advisable. If possible, it is also important to discontinue the amiodarone. The treatment of type II AIT is primarily with glucocorticoids and by discontinuation of the amiodarone, although in some cases, it is reasonable to continue the antiarhythmic medication (59). In patients in whom chronic therapy with amiodarone is essential, thyrotoxicity is a potential option for treatment of AIT (54). Radioiodine ablation is not an option given the low iodine uptake as a result of the iodine deficiency.

Drugs induced Alterations in Thyroid Function

Amiodarone

Amiodarone is a lipophilic drug that contains 75 mg iodine per 200-mg tablet. The drug has a half-life of several months, and, during that time, it releases approximately 9 mg of inorganic iodine per day. In euthyroid patients, chronic administration of the drug results in increased serum FT₄ and FT₃ levels; lower T₃ concentrations; and normal TSH (54). The reason for these changes is the drug’s strong inhibition of 5′-deiodinase, the enzyme responsible for conversion of T₄ to T₃ and rT₃ to T₂. Most patients remain euthyroid while on amiodarone despite the hormonal derangements that may be seen; on the other hand, about 14% to 18% of patients develop either hypothyroidism or hyperthyroidism while on amiodarone (55). Hypothyroidism is more commonly encountered in iodine-deficient areas, such as the United States (56). Treatment is aimed at normalization of the TSH with levothyroxine replacement while the amiodarone therapy is continued. On discontinuation of the amiodarone, most patients return to euthyroidism, although it may take several months because of the prolonged half-life of the drug.

Disorders associated with amiodarone-induced thyrotoxicosis can be divided into two types (Table 166.6) of amiodarone-induced thyrotoxicosis (AIT). Distinction of these two disorders is relevant because their treatment differs. Type I AIT occurs in glands with an underlying abnormality. Areas of autonomy, such as a toxic nodule or autoimmune disease in the thyroid, produce increased levels of hormone in response to the excess iodine released from the amiodarone (55). Type II AIT develops as a result of a direct cytotoxic effect of amiodarone on the thyrocyte (57). Treatment of type I AIT is difficult because most patients do not respond to thionamides, as these drugs have decreased efficacy in states of iodine excess (58). Use of potassium perchlorate (KClO₅) may enhance the efficacy of thionamides (54). It is important to note that both thionamides and KClO₅ may cause agranulocytosis, so serial monitoring of blood counts is advisable. If possible, it is also important to discontinue the amiodarone. The treatment of type II AIT is primarily with glucocorticoids and by discontinuation of the amiodarone, although in some cases, it is reasonable to continue the antiarhythmic medication (59). In patients in whom chronic therapy with amiodarone is essential, thyrotoxicity is a potential option for treatment of AIT (54). Radioiodine ablation is not an option given the low iodine uptake as a result of the iodine deficiency.

**Table 166.6**

<table>
<thead>
<tr>
<th>Features of Amiodarone-Induced Thyrotoxicosis</th>
<th>Iodine-induced thyrotoxicosis (Type I)</th>
<th>Destructive thyrotoxicosis (Type II)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underlying thyroid abnormality</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Goiter</td>
<td>Diffuse or multinodular usually present</td>
<td>Occasionally small, firm goiter</td>
</tr>
<tr>
<td>RAIU concentrations</td>
<td>Low/normal/high</td>
<td>Low</td>
</tr>
<tr>
<td>Pathogenic mechanism</td>
<td>Excessive thyroid hormone synthesis</td>
<td>Markedly elevated</td>
</tr>
<tr>
<td>Treatment</td>
<td>Thionamides and KClO₅</td>
<td>Excessive hormone release (destructive thyrotoxic syndrome)</td>
</tr>
<tr>
<td>Subsequent hypothyroidism</td>
<td>Unlikely</td>
<td>Glucocorticoids</td>
</tr>
<tr>
<td>Color flow Doppler sonography</td>
<td>Normal or increased blood flow</td>
<td>Possible</td>
</tr>
</tbody>
</table>

RAIU, radioactive iodine uptake; IL-6, interleukin-6; KClO₅, potassium perchlorate.
Contrast Media and Thyroid Function

Another potential source of excess iodine is radiographic contrast media. As noted in the section about the management of thyroid storm, the oral cholecystographic agents, iopanoic acid and sodium ipodate, may be used short-term in thyrotoxic patients for their side effect of decreasing peripheral conversion of $T_3$ to $T_4$ and blocking hormone secretion from the thyroid. Used over a longer period of time, however, such agents will only exacerbate the underlying hyperthyroidism (14). Many other agents are available that have variable effects on the thyroid gland. Typically, patients with no underlying thyroid disease will not be affected by the use of these agents (60), but patients with Graves disease, multinodular goiter, or the elderly are at risk to develop thyrotoxicosis after their use (38). The lipid-soluble agents used for myelography, bronchoscopy, and urography are cleared slowly and release iopanoic iodine for months to years. Newer water-soluble preparations used in arteriography and computed tomography are cleared from the plasma more quickly, but the iodine they release during these procedures can still affect thyroid function. The degree of thyroid dysfunction can range from mild transient subclinical hyperthyroidism to thyroid storm (61–65). Most patients experience only transient thyrotoxicosis, and the syndrome resolves when the excess iodine is cleared. If treatment is required, thionamides and $\beta$-adrenergic blockade may be used until the thyrotoxicosis resolves (65).

Thyrotoxic Periodic Paralysis

Thyrotoxic periodic paralysis (TPP) is a complication of hyperthyroidism characterized by localized or generalized attacks of weakness or flaccid paralysis and hypokalemia (66). Although it has been reported in Western countries and in women, it is more common in Asian men, where the incidence is 1.9% in thyrotoxic patients (67). The clinical presentation is identical to familial hypokalemic periodic paralysis, but the pathophysiology is distinct. Although the mechanism of the syndrome is not clearly defined, hypokalemia alone is not enough to elicit the paralysis. Hypokalemia sufficient to create the paralysis in a hyperthyroid patient has no effect on the same patient when euthyroid (68). This finding points to the importance of thyroid hormone excess in the pathophysiology of this process. It is most commonly associated with Graves disease but may be seen with any form of thyrotoxicosis (69).

Clinical Presentation

The clinical presentation is one of flaccid weakness that is symmetrical; lower extremities are generally affected more than the upper extremities. Breathing may be impaired if the patient has a more generalized weakness. The onset of the attacks is usually sudden and may be preceded by cramping. Ingestion of alcohol or carbohydrates and strenuous physical exercise commonly precipitate the episodes of weakness. Patients have decreased or absent deep-tendon reflexes. The symptoms may last from a few hours to several days (68).

Treatment

Treatment is aimed at correction of the hyperthyroidism. If hypokalemia is present, replacement should be given. Some patients are given a potassium-sparing diuretic in addition to the potassium supplementation until euthyroidism is achieved. $\beta$-Adrenergic antagonists also decrease the frequency of attacks in these patients (67).

Preoperative Management

Adequate preparation for surgery in thyrotoxic patients is critical to the successful outcome of the procedure. Surgery in a hyperthyroid patient can precipitate thyroid storm, with high morbidity and mortality if preoperative care is inadequate. The type of treatment will depend on the amount of time before the surgery. Elective procedures should be postponed until the $T_3$ and $T_4$ levels are normalized with thionamides and $\beta$-adrenergic blockade. This can usually be achieved within approximately 2 weeks. It is important to note that a suppressed TSH may not normalize for months, and this value should not be used as the criteria to assess the thyroid status. Urgent or emergent procedures may be safely done after initiation of PTU and a $\beta$-adrenergic antagonist. Iodide, as either SSKI, Lugol solution, or an oral radiographic contrast agent—sodium iodide or iopanoic acid—should also be administered to block release of thyroid hormone and decrease peripheral conversion of $T_4$ to $T_3$ (70). Finally, a glucocorticoid, such as hydrocortisone or dexamethasone, should also be used if the patient is suspected of having concomitant adrenal insufficiency, or additional inhibition of extrathyroidal conversion of $T_4$ to $T_3$ is needed (71). Considerable lowering of $T_3$ and $T_4$ levels can be achieved within 1 to 3 days and normalization within 3 to 5 days, if the above regimen is used (71,72).

Hypothyroidism

Hypothyroidism is a common clinical problem, affecting approximately 4.6% of the population in the United States (73). It is important to recognize the clinical features and potential complications of a patient with hypothyroidism. Nonthyroidal illness, surgery, or diagnostic testing can lead to metabolic decompensation in patients with undiagnosed or untreated hypothyroidism. Additionally, it is important to note that untreated hypothyroidism may slow the metabolism of certain drugs, thereby increasing the risk of problematic side effects. Hypothyroidism is most often caused by autoimmune thyroiditis, also known as Hashimoto thyroiditis. Other common causes of hypothyroidism are noted in Table 166.7.

The clinical manifestations of hypothyroidism are manifold. Most of the symptoms are nonspecific, which can lead to a delay in the diagnosis. In elderly patients, the diagnosis may be missed because the patient may be asymptomatic or the signs attributed to aging (74). Patients in the ICU may present with severe central nervous system (CNS) disturbances, cardiovascular derangements, hypotenremia, or respiratory failure. Table 166.8 notes the signs and symptoms of hypothyroidism.
Chapter 166: Thyroid Disease in the Intensive Care Unit

TABLE 166.7

<table>
<thead>
<tr>
<th>CAUSES OF HYPOTHYROIDISM</th>
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<tbody>
<tr>
<td>Autimmune, Hashimoto thyroiditis</td>
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<tr>
<td>Postthyroidectomy</td>
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<tr>
<td>Postradiation</td>
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<td>^131I treatment</td>
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<td>External beam radiation</td>
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<td>Iodine deficiency</td>
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<td>Drugs</td>
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<tr>
<td>Lithium</td>
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<td>Iodine-containing drugs (amiodarone, radiocontrast agents)</td>
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<tr>
<td>Secondary hyperthyroidism</td>
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<tr>
<td>Pituitary tumor, irradiation, empty sella syndrome, infiltrative disorders</td>
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<tr>
<td>Hypothalamic disease</td>
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<tr>
<td>Transient disorders</td>
<td></td>
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<tr>
<td>Silent, subacute thyroiditis</td>
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</table>

Cardiovascular Manifestations

The symptoms of cardiovascular dysfunction are much less pronounced in patients with hypothyroidism compared to their thyrotoxic counterparts. These cardiovascular changes may manifest themselves in the hypothyroid patient who is undergoing the stress of anesthesia and surgery. Cardiovascular hemodynamics are affected by hypothyroidism in several ways. In particular, patients have decreased cardiac output, mediated by reduced contractility and heart rate (75). This reduction in cardiac output contributes to the dyspnea on exertion seen in many hypothyroid patients. These patients also have increased systemic vascular resistance, predisposing them to hypertension (76). Diastolic filling and compliance are reduced, leading to diastolic dysfunction (77). Patients may have an elevation of diastolic pressure out of proportion to systolic pressure, leading to diastolic dysfunction (77). Patients with hypothyroidism may also have increased cardiac output, diastolic hypertension, and increased systemic vascular resistance suggests that hypothyroidism can cause congestive heart failure. It is rare, however, for hypothyroidism to be the sole causative agent in the development of heart failure (79).

TABLE 166.8

<table>
<thead>
<tr>
<th>CLINICAL MANIFESTATIONS OF HYPOTHYROIDISM</th>
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<tbody>
<tr>
<td>Symptoms</td>
<td>Signs</td>
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<tr>
<td>Fatigue and weakness</td>
<td>Delayed relaxation of tendon reflexes</td>
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<tr>
<td>Cold intolerance</td>
<td>Bradycardia</td>
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<tr>
<td>Weight gain</td>
<td>Hypereventilation</td>
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<tr>
<td>Constipation</td>
<td>Reduced pulse pressure</td>
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<tr>
<td>Dyspnea on exertion</td>
<td>Generalized and periorbital edema</td>
</tr>
<tr>
<td>Depression</td>
<td>Myalgia</td>
</tr>
<tr>
<td>Myalgia</td>
<td>Dry skin and hair</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Loss of hair</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Cerebral and pleural effusions</td>
</tr>
<tr>
<td>Thyroid swelling</td>
<td>Generalized and periorbital edema</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Myalgia</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Dry skin and hair</td>
</tr>
</tbody>
</table>

Pulmonary Manifestations

Dyspnea on exertion is a common presenting complaint in patients with hypothyroidism, in part due to the impaired cardiac function and reduced pulmonary function. Respiratory muscle weakness also appears to play a role in this dyspnea (82–84). There is a reduction in central pulmonary drive in response to hypoxia and hypercapnia, leading to hypoventilation (34,85). Upper airway obstruction may occur as a result of gusset (see below: Acute Airway Obstruction) (86). Sleep apnea may occur as a result of macroGLOSSIA (87). Patients may thus require continuous positive airway pressure in addition to replacement of the thyroid hormone. Finally, a restrictive pattern of disease may be seen in the presence of a pulmonary effusion (34).

Gastrointestinal Manifestations

Peristalsis is slowed in patients with hypothyroidism. Most patients have normal bowel motility, but a small proportion with hypothyroidism requires laxative use. Patients may report vague abdominal pain and distention. Rarely, severe cases may present with ileus (88–90). Severely hypothyroid patients may also have malabsorption. The mechanism of this abnormal absorption is not clearly defined; theories include myxedematous infiltration of the mucosa, associated autoimmunity (91), and decreased intestinal motility (92).

Metabolic Manifestations

Hypothyroidism may lead to decreased free water clearance and subsequent hyponatremia. The magnitude of sodium derangement is directly related to the severity of hypothyroidism; most patients with hyponatremia have myxedema coma (93). The mechanism of the development of hyponatremia in these patients is unclear (94–96). Hyperlipidemia is a more common side effect of hypothyroidism than hyponatremia. Lipid clearance is decreased in patients with hypothyroidism, resulting in elevated levels of free fatty acids, low-density lipoprotein (LDL), and total cholesterol (97). Treatment of the hypothyroidism results in improvement of the lipid panel (98,99).

Treatment

Thyroid hormone is preferentially replaced with T4. Levothyroxine is then converted to T3 intracellularly, and thus, it is unnecessary to administer T3 in most situations. In adults, the starting dose of T4 is typically 1.7 μg/kg/day (based on ideal body weight). Elderly patients or those with coronary disease...
Myxedema Coma

Myxedema coma is a rare but life-threatening complication of hypothyroidism. It may occur after severe long-standing hypothyroidism or after an acute precipitating event such as surgery or infection. It is more likely to occur in elderly women during the winter months (100). Any of the usual causes of hypothyroidism (Table 166.6) may induce myxedema coma. Prompt recognition and treatment are essential, even before laboratory results are available. Mortality rates are improving due to early diagnosis and treatment, but mortality remains at 30% to 40%. Patients with cardiac complications and the elderly are at greatest risk (101,102).

Clinical Presentation. Most patients with myxedema coma have had symptoms of hypothyroidism for many months. There is a gradual onset of lethargy, progressing to stupor, which is precipitated by cold exposure, infection, or medica-
tions. Other precipitating events are stroke, congestive heart failure, trauma, or gastrointestinal bleeding. The patient is typ-
ically an obese elderly woman with yellow discoloration of the skin. The principal features of myxedema are hypothermia, bradycardia, and decreased mental status or coma (40). Pa-
tients also characteristically have a decreased respiratory rate as a result of reduced hypoxic ventilatory drive (103). The resultant carbon dioxide retention can exacerbate the altered mental status. Similar to the patient with profound hypothy-
roidism, the respiratory muscle weakness and pleural effusions, if present, can make ventilating these patients difficult (83,103).

Hypothermia is present in nearly all patients with myxedema coma (100). Temperature may be quite low (less than 80°F [20°C]); values below 90°F [32°C] predict a poorer prognosis (102). The hypothermia may go unrecognized if the proper thermometer is not used; many thermometers may not be able to measure below 93°F [34°C]. The diagnosis of myxedema coma should be considered in any unconscious pa-
tient with infection who does not have a fever. Warming should be gradual, using ordinary hospital blankets. Electric heating blankets should not be used, as they may cause peripheral va-
sodilation and subsequent hypotension.

The cardiovascular abnormalities seen in myxedema coma are similar to those associated with severe hypothyroidism. Patients can present with bradycardia, reduced cardiac output, and decreased cardiac contractility, which may lead to hypotension. Signs of congestive heart failure may be found. In patients with diminished heart sounds, low-voltage ECGs, or cardiomegaly on chest radiograph, an investigation for pericar-
dial effusion should be performed (104).

This profound level of hypothyroidism may lead to impaired free water excretion. As a result, over half of patients can have hyponatremia (100,103). Severely reduced sodium levels can also exacerbate the altered mental status. The impaired free water clearance may be manifested by generalized nonpitting edema and periorbital swelling. Patients should be managed by free water restriction; the condition will improve with thyroid hormone replacement.

Complications

Myxedema Coma

Because of the high mortality rate of this endocrine disease, patients with myxedema coma should be treated ag-
gressively (106). Patients should be presumed to have adrenal insufficiency and treated with stress-dose steroids (hydrocorti-
sone, 100 mg IV every 8 hours) until laboratory data exclude the diagnosis. The administration of levotheroxine prior to glu-
corticoids in such patients can provoke an adrenal crisis.

The optimal replacement strategy for levothyroxine is un-
known because of the rarity of the condition. Clinical judg-
ment must be used to weigh the risk of rapid administration of thyroid hormone—with the possibility of precipitation of myocardial infarction—against the risk of not replacing the thyroid hormone fast enough in light of the high mortality of undetected myxedema coma. Whether to administer T4 or T3 alone or in combination and the dose of these agents is a subject of much debate among endocrinologists. It is preferable to administer thyroid hormone intravenously in patients with myxedema because of the possibility of impaired gastrointestinal absorption. One regimen is to begin 200 to 300 μg of T4 intravenously (4 μg/kg ideal body weight), followed by 100 μg 24 hours later. The patient can then be maintained on 50 μg IV or orally (PO) daily. T3 is also given at an initial dose of 10 μg and can be given every 8 to 12 hours until the patient can take oral medications (100).

Supportive care should be directed to the coexisting medi-
cal conditions. Hyponatremia can usually be managed with free water restriction, but 3% saline may be given in extreme cir-
cumstances. Hypotension will usually improve with initiation of levotheroxine. Refractory hypotension should be treated with vasopressor agents until the thyroid hormone has had time to act. Patients may require mechanical ventilation be-
cause of respiratory muscle weakness, depressed mental status, or decreased hypoxic ventilatory drive. Warming should be ac-
complished as noted above. Finally, it is important to address the underlying medical illness that precipitated the myxedema coma.

Preoperative Management of Hypothyroidism

Patients with mild to moderate hypothyroidism may proceed to surgery, as no convincing evidence exists to show that there is an adverse effect on outcomes (107–110); if the procedure is elective, it is optimal to begin replacement with thyroid
hormone and delay the surgery until the patient is euthyroid. The exception to this rule is a patient with coronary artery disease who presents with angina, palpitations, or syncope. Such patients should have their coronary vasculature addressed first, and then have their thyroid hormone replaced postoperatively. Evidence suggests that replacement of thyroid hormone before restoring coronary blood flow could tax an already ischemic myocardium (111). A patient with severe hypothyroidism—for example, very low levels of thyroid hormone, or myxedema coma, or clinical symptoms of chronic thyroid hormone deficiency such as altered mentation, pericardial effusion, or heart failure—who requires urgent surgery should be given a loading dose of intravenous T₄ and possibly T₃. In addition, stress-dose glucocorticoids should be given if adrenal or pituitary function is uncertain, as replacement of thyroxine in a patient with adrenal insufficiency can precipitate adrenal crisis. The patient may be given an initial dose of T₄ at 200 to 300 μg IV, followed by 50 μg daily. Depending on the patient’s age and cardiac risk factors, T₃ may be given simultaneously at 10 μg every 8 to 12 hours (112).

**THYROID FUNCTION IN NONTHYROIDAL ILLNESS**

Aberrations in thyroid function during illness occur along a continuum, with wider deviations from the mean as the patient becomes more severely ill. Several names have been ascribed to the condition, including euthyroid sick syndrome, low T₄ syndrome, low T₃ syndrome, and nonthyroidal illness. Considerable debate exists as to whether this syndrome represents a pathologic process marked by hypothyroidism or an adaptive response to systemic illness that allows the body to lower its tissue energy requirements. In light of this controversy, it is understandable that no consensus exists on whether or how to treat this entity.

Interpretation of thyroid function tests in critically ill patients is complex. For this reason, thyroid function should not be measured in this setting unless a thyroid disorder is strongly suspected. When it is deemed appropriate to evaluate the hypothalamic-pituitary-thyroid axis, the clinician should check a TSH, total T₄, free T₄, and total T₃.

The most commonly seen change in thyroid hormone function tests in hospitalized patients is a low serum T₄ concentration (113). Most T₄ in the serum is produced by deiodination of T₃ to T₄ in the peripheral tissues. The levels of the enzyme responsible for this conversion, 5'-monodeiodinase, are decreased with even mild illness (114). As described in the above section about drugs and thyroid function, many commonly used medications in the ICU may also decrease the peripheral conversion of T₃ to T₄, further lowering the circulating T₄ levels. Glucocorticoids and β-adrenergic antagonists are the most common offending agents. In addition, free fatty acids inhibit the deiodinase activity (115). Cytokines have also been shown to have a role in the development of the sick euthyroid syndrome by their role in decreasing the conversion of T₄ to T₃ (116).

Concomitant with the decline in T₄ levels is a rise in rT₃ (reverse T₃) in nonthyroidal illness. Fasting may produce this clinical picture within 24 to 36 hours and is reversed as quickly with refeeding (117). This pattern of low T₄, high rT₃, is found in many patients with various acute and chronic illnesses, whether due to infection, surgery, cancer, cardiovascular diseases, pulmonary processes, burns, or trauma. The metabolic rate in this setting is unchanged in the setting of illness. The increase in this value is, instead, a reflection of the attenuated rates of clearance of rT₃ (118). The complicating factor with routinely measuring the rT₃ levels in patients suspected of having nonthyroidal illness is that it may take up to a week to process the test in the laboratory.

Thyroxine (T₃) levels may also be reduced in up to 20% of hospitalized patients and 50% of critically ill patients (119). These low T₃ levels are correlated with a higher mortality rate (120). The reduction in T₃ can, in part, be attributed to decreased concentrations of one of the three thyroid hormone-binding proteins: thyroid-binding globulin (TBG), transthyretin, and albumin. Agents that inhibit the TBG binding protein interaction have also been identified as responsible for the lowering of T₃ levels in the serum of critically ill patients. Some data point to high levels of free fatty acids as a causative agent in this process (121).

Serum TSH levels are typically normal in most patients with nonthyroidal illness, although during the recovery phase of the illness, thyrotropin concentrations may rise (122). In more critically ill patients, the TSH may simultaneously fall with the decline in T₄ levels. Such findings have led some to suggest that some patients may have an acquired transient central hypothyroidism during the nonthyroidal illness. Thyroid hormone replacement, however, has not been shown to improve outcomes in critically ill patients (123). Medications may also alter TSH levels (Table 166.2). Dopamine infusions are frequently associated with a reduction in serum TSH concentration.

When measuring TSH levels in the ICU, it is important to use a high-sensitivity assay with a lower detection limit of at least 0.01 mIU/L. The vast majority of hospitalized patients with low, but detectable, TSH by this assay have sick euthyroid syndrome. In contrast, patients with undetectable thyrotropin are more likely to be hyperthyroid. Finally, those patients with high TSH (up to 20 mIU/L) are likely recovering from a nonthyroidal illness and should be reassessed 6 weeks after the hospitalization.

**Acute Airway Obstruction and Goiter**

Acute airway obstruction is a life-threatening complication of an enlarged thyroid gland. Typically, development of a goiter is a gradual process, but rapid growth of the gland may occur in certain circumstances. Fortunately quite rare, but important to consider, is anaplastic thyroid cancer. Patients with this disease may present with considerable growth of the thyroid within a few weeks (124). Thyroid lymphoma can also show a rapid growth pattern but will quickly respond to appropriate chemotherapy and/or radiation therapy. Riedel thyroiditis, also rare, with a prevalence of 0.06% to 0.3%, may present with a rapidly enlarging, hard neck mass that must be differentiated from thyroid cancer or lymphoma. The fibrous tissue may invade soft tissue and muscle and lead to tracheal compression (125). The more common scenario is a patient who presents with a nodule that rapidly increases in size over several minutes to hours. In these cases, the patient has underlying nodular disease that has encroached on a nearby blood vessel and bled...
into a cystic compartment of the nodule. Typically, patients have regression of such a nodule over the ensuing weeks.

The clinical presentation of a compressive goiter is varied. Patients may present with complaints of a pressure sensation in the neck, particularly with movement of the head. Difficulty swallowing and vocal cord paralysis also may be encountered. The Pemberton sign, facial flushing and jugular venous distention on raising the arms over the head, is an indication of obstruction of venous outflow from the head. Many patients with a goiter have a mild degree of airway obstruction when screened with pulmonary function tests. Additionally, although chest radiographs accurately indicate retrosternal extension of goiters, they cannot predict airway obstruction as reliably as flow-volume loops (86). It is critical to recognize that a patient presenting with new-onset wheezing or stridor may have a substernal goiter (127).

The management of acute airway compromise is primarily surgical (128). If airway collapse is imminent, it is critical to protect the airway with intubation (129). The type of surgery necessary depends on the size of the goiter and whether there is an associated malignancy. Radiosiodine treatment can take months to years to shrink the goiter (130).

### Postthyroidectomy Hypocalcemia

**Hypoparathyroidism**

The most common cause of hypoparathyroidism is surgery on the thyroid gland. This is typically seen after cancer surgery, total thyroidectomy, or parathyroidectomy. It is most often a transient condition with symptoms occurring 3 to 2 days postoperatively. Symptoms may vary from subtle perioral numbness and tingling to profound fatigue to tetany. Table 166.9 lists the symptoms and signs that may be seen in patients with hypocalcemia. Risk of hypocalcemia is dependent on the extent of sympotms and signs that may be seen in patients with hypocalcemia. Risk of hypocalcemia is dependent on the extent of surgery, localization and preservation of the parathyroids, and skill of the surgeon. Incidence rates of postoperative, transient hypocalcemia range from 1.6% up to greater than 50%, but most of these patients will regain parathyroid function over the ensuing months. The risk of permanent hypoparathyroidism is variable, between zero and 10% (131). During nonparathyroid neck surgery, it is critical for the surgeon to recognize a compromised parathyroid gland and autotransplant the gland into the adjacent neck muscle to ensure the gland will regain function.

### Treatment

Treatment is aimed at normalization of the serum calcium. Many surgeons begin thrice-daily prophylactic oral calcium supplementation at the night of the surgery (132). If the patient develops progressive symptoms, tetany, or seizures, the use of IV calcium gluconate is warranted. In life-threatening situations, 10 mL of calcium gluconate may be administered intravenously over a 5- to 10-minute period and repeated as necessary. In less acute situations, a continuous calcium infusion may be used by mixing ten ampules of calcium gluconate in 500 mL of 5% dextrose in water. The infusion rate may vary between 0.3 mg/kg/hour to 2 mg/kg/hour, depending on the clinical setting. The goal of therapy is to reverse hypocalcemic symptoms and restore calcium levels to the low-normal range. Chronic management of permanent hypoparathyroidism is beyond the scope of this chapter.

#### Hungry Bone Syndrome

Hungry bone syndrome, HBS, is a well recognized complication of surgical correction of severe hyperparathyroidism. Patients with very high levels of parathyroid hormone (PTH) may develop significant hypocalcemia after surgical removal of the offending parathyroid adenoma(s). The mechanism of this metabolic derangement is rapid skeletal mineralization. Less commonly seen is HBS after thyroidectomy for thyrotoxicosis. Patients with hyperthyroidism may develop secondary osteoporosis and resultant hypercalcemia from the increased bone resorption. After surgical removal of the thyroid gland, patients may have a reversal of the thyrotoxic osteodystrophy and, instead, have a net flux of calcium and phosphorous deposition into the bone. In extreme thyrotoxicosis, the patient may develop hypocalcemia. This condition typically resolves within a few days to weeks with treatment of the hypocalcemia (133).

### References


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