Thyroid Disorders
Sarah Stewart de Ramirez and Frederick Korley

KEY POINTS

- Hypothyroidism secondary to iodine deficiency is the most common endocrine disorder worldwide.
- Primary hypothyroidism results from dysfunction of thyroid tissue. Secondary hypothyroidism is a component of panhypopituitarism that results from pituitary disease.
- Severe hypothyroidism is a rare condition characterized by altered mental status, hypothermia, and primary thyroid dysfunction. Myxedema is seen in most cases; true coma is not.
- Patients with suspected severe hypothyroidism should receive empiric, low-dose intravenous levothyroxine.
- Thyroid storm, the most extreme form of thyrotoxicosis, is a rapidly fatal condition.
- Antithyroid medication should be given at least 1 hour before the administration of iodine for the treatment of thyroid storm.
- Emergency department testing for thyroid disease includes serum thyrotropin, or thyroid-stimulating hormone, and free thyroxine measurements.

PERSPECTIVE

Hypothyroidism is a deficiency of thyroid hormones resulting in a hypometabolic state. Iodine deficiency accounts for most cases of hypothyroidism and goiter in underdeveloped countries; Hashimoto thyroiditis is a more commonly recognized cause in westernized societies.

Thyrotoxicosis describes any condition characterized by an excess of free thyroid hormones in the circulation. The term is frequently used interchangeably with hyperthyroidism; however, hyperthyroidism refers only to disease states in which the thyroid gland produces an excess of thyroid hormones.

EPIDEMIOLOGY

Abnormal thyroid function is by far the most common endocrine disorder worldwide and is second only to diabetes mellitus in the United States. Thyrotoxicosis is a rare condition that is 10 times more prevalent in women than in men (2% versus 0.2%). It is uncommon before the age of 15 years. Although most manifestations of thyrotoxicosis do not represent a true emergency, the extreme case of so-called thyroid storm does. Early detection and treatment of this condition may prevent progression to shock and death.

ANATOMY

The thyroid gland derives its name from the shape of the nearby thyroid cartilage (from the Greek, meaning “shield”). Although it varies, the isthmus is usually centered over the third tracheal ring. Normal adult thyroid dimensions are a height of 5 cm, thickness of 1.5 cm, isthmus thickness of 0.5 cm, volume of 10 cm, and weight of 12 to 20 g. Thyroid thickness greater than 2 cm is considered abnormal.

The thyroid gland is palpable on physical examination in nonobese patients; thyroid nodules and some cancers are sometimes noted on palpation. Rarely, ectopic thyroid gland tissue is found at the base of the tongue.

PHYSIOLOGY

Thyrotropin-releasing hormone (TRH) is synthesized in the hypothalamus and regulates the production of thyroid-stimulating hormone (TSH), or thyrotropin, in the anterior pituitary gland. Principal cells in the thyroid bind TSH, which activates the production and release of thyroid hormones.

The thyroid is highly efficient in its absorption and extraction of iodine. Iodine is added to tyrosine to make up diiodotyrosine (DIT); two molecules of DIT combine to form thyroxine (T4), much of which is stored in the thyroid gland. T4 is released into the circulation largely bound by thyroid-binding globulin (TBG). Even though levels of TBG vary widely, this protein is seldom involved in a disease process.

Triiodothyronine (T3) is formed by peripheral conversion of T4 in tissues. When compared with T4, T3 is four to six times more active, exhibits less affinity for TBG, and has a much shorter half-life (12 hours versus 6 days). T3 and T4 exert feedback on the hypothalamus and TRH levels, thereby completing a regulatory loop.

T3 and T4 stimulate metabolic activity in tissues throughout the body. Both hormones are associated with growth and development early in life.
Thyroid disorders

Goiter refers to a visible enlargement of the thyroid gland that may result from euthyroid, hyperthyroid, or hypothyroid states. The presence of a goiter mandates a detailed review of systems and appropriate thyroid testing to determine the functional status of the tissue. The most common cause of goiter is iodine deficiency. Other causes include Hashimoto thyroiditis, Graves disease, nodules, cancer, and lithium therapy.

Goiters are usually benign, but thyroid malignancy must be considered in each case. Three rare but potentially life-threatening emergencies can result from continued enlargement of a malignant goiter. First, partial or complete obstruction of the jugular veins may occur, especially in hypercoagulable patients. Clot extension from a partially obstructed jugular vein can impede venous drainage from the brain. Second, invasive or extremely large goiters have been reported to cause airway compromise. Third, malignant involvement of the carotid sheath structures can result in devastating morbidity.

Hypothyroidism is a deficiency of thyroid hormones that results in decreased metabolic activity. It mimics many conditions commonly encountered in the emergency department (ED) and is accompanied by a myriad of indolent symptoms (Boxes 167.1 and 167.2).

In a recent study of the incidence of newly diagnosed primary overt hypothyroidism in adults seen in a Taiwanese ED, the most common symptoms were fatigue (50%), dyspnea (45%), chest tightness (20%), constipation (14%), and cold intolerance (9%). The majority of these patients were seen during winter months. In only 21% was hypothyroidism diagnosed by the emergency physician. Clinicians should maintain a high index of suspicion for hypothyroidism in patients with new-onset depression.

SEVERE HYPOTHYROIDISM
(MYXEDEMA COMA)

Patients with severe hypothyroidism may have mild to moderate hypothermia, depression, lack of energy, and altered mental status. Myxedema coma is a misnomer often used for severe hypothyroidism; not all patients with severe hypothyroidism are truly comatose, whereas most (but not all) patients with hypothyroid coma have myxedema. Myxedema coma best describes a patient in extremis secondary to a severe hypothyroid state (Box 167.3).

**BOX 167.1 Symptoms of Hypothyroidism**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Sign</th>
</tr>
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<tbody>
<tr>
<td>Fatigue</td>
<td>Irritability</td>
</tr>
<tr>
<td>Cold intolerance</td>
<td>Coarse hair</td>
</tr>
<tr>
<td>Weakness</td>
<td>Dry skin</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Myalgias</td>
</tr>
<tr>
<td>Depression</td>
<td>Arthralgias</td>
</tr>
<tr>
<td>Decreased mental</td>
<td>Brittle fingernails</td>
</tr>
<tr>
<td>function</td>
<td>Myxedema</td>
</tr>
<tr>
<td>Constipation</td>
<td>Menstrual irregularity</td>
</tr>
<tr>
<td>Decreased libido</td>
<td>Peripheral neuropathy</td>
</tr>
</tbody>
</table>

**BOX 167.2 Signs of Hypothyroidism**

<table>
<thead>
<tr>
<th>Sign</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged reflexes</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Facial edema</td>
</tr>
<tr>
<td>Narrow eyebrows</td>
<td>Periorbital edema</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>Pale, dry skin</td>
</tr>
<tr>
<td>Hoarse voice</td>
<td>Sparse axillary and pubic hair</td>
</tr>
</tbody>
</table>

**BOX 167.3 Findings in Patients with Severe Hypothyroidism (Myxedema Coma)**

<table>
<thead>
<tr>
<th>Finding</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased mentation</td>
<td>Nonpitting edema</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Delayed or absent deep tendon reflexes</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Hyponatremia</td>
</tr>
</tbody>
</table>
DIAGNOSIS

Historical symptoms and physical signs suggestive of hypothyroidism justify testing. The incidence of this disease is so high in elderly women that screening of these patients, even though they are asymptomatic, is performed by many primary care physicians.

Markers of primary hypothyroidism include a high serum TSH level and a low unbound free $T_4$ (FT$_4$) level in the presence of classic signs and symptoms. Symptomatic patients with even minimally elevated TSH may benefit from low-dose thyroxine supplementation.

There is disagreement about the level of TSH and FT$_4$ required to begin treatment in asymptomatic individuals. Several sources recommend thyroxine supplementation for asymptomatic patients with a serum TSH level that is three times the upper limit of normal, regardless of a low or low-normal FT$_4$ level.

Secondary hypothyroidism, generally a component of panhypopituitarism, is marked by low TSH, low FT$_4$, and low serum cortisol levels. Both thyroid and steroid replacement is required, and further diagnostic evaluation (e.g., pituitary imaging, endocrine testing) is indicated.

Hypothyroid patients may also have low serum sodium levels and elevated total cholesterol, both of which may resolve with thyroxine therapy.

TREATMENT

MILD HYPOTHYROIDISM

Treatment is initiated with levothyroxine, 1.6 mcg/day. In patients with primary thyroid disease, TSH should be monitored every 30 days. Those being treated with levothyroxine do not require monitoring of FT$_4$. Although mild hypothyroidism is not an emergency per se, initiating treatment for symptomatic patients (in consultation with an endocrinologist) is appropriate if the diagnosis is established in the ED. Routine follow-up is necessary.

SEVERE HYPOTHYROIDISM (MYXEDEMA COMA)

Management of severe hypothyroidism consists of standard ED resuscitation measures, including consideration and empiric treatment of potential sepsis. The only treatment step specific for severe hypothyroidism is intravenous (IV) administration of levothyroxine. Empiric administration of low-dose levothyroxine is appropriate in patients in whom a serum TSH level cannot be obtained in timely fashion. ED treatment of myxedema coma is summarized in Box 167.4.

Note that previous studies have deemed $T_3$ supplementation to be unsafe; however, because of the low incidence of myxedema coma, large clinical trials of $T_3$ have not been performed.

DISPOSITION

Patients with mild hypothyroidism may be managed as outpatients with referral to a primary care physician and an endocrinologist. Patients with severe hypothyroidism should be admitted to the hospital for further management.

THYROTOXICOSIS

Thyrotoxicosis is caused by at least one of four potential mechanisms:

1. Overproduction of thyroid hormones by the thyroid gland
2. Unregulated release of thyroid hormones secondary to destruction of thyroid cells (thyroiditis)
3. Ingestion of thyroid hormones
4. Production of thyroid hormones from ectopic foci (Fig. 167.1)

CAUSES

GRAVES DISEASE

Graves disease, the most common cause of hyperthyroidism, accounts for approximately 60% to 80% of cases of hyperthyroidism in the United States. It is the most common autoimmune disorder in North America. In this disease, thyroid-stimulating immunoglobulins (an IgG antibody) bind to and activate thyrotropin receptors on thyroid cells, thereby mimicking the action of TSH. Continued binding of the antibody to the TSH receptor leads to excessive production of $T_3$ and thyroid enlargement.4

THYROIDITIS

Thyroiditis describes conditions in which inflammatory changes lead to the destruction of thyroid cells, which results in the excess release of thyroid hormones. This is followed by depletion of circulating thyroid hormones and subsequent euthyroid and, eventually, hypothyroid states.

Autoimmune destruction of thyroid cells is seen in patients with Hashimoto thyroiditis, painless sporadic thyroiditis, and painless postpartum thyroiditis. Hashimoto thyroiditis is characterized by high levels of serum antithyroid antibodies. This
Thyrotoxicosis can be asymptomatic (subclinical hyperthyroidism) or feature mild, moderate, or severe symptoms that result from a surge in catecholamines. Patients with classic thyrotoxicosis may appear nervous, irritable, and tremulous. They may complain of unintentional weight loss, palpitations, exertional dyspnea, heat intolerance, thinning of their hair, irregular menses, increased frequency of bowel movements, and sleep disturbance. On physical examination, patients may have a palpable goiter, warm moist skin, sinus tachycardia out of proportion to fever, or atrial fibrillation on electrocardiography.

**CLINICAL PRESENTATION**

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**OTHER CAUSES**

Increased secretion of thyrotropin by a pituitary adenoma can also cause thyrotoxicosis. Alternatively, thyroid hormones may be produced from sites outside the thyroid gland. This occurs in cases of metastatic follicular thyroid carcinoma and struma ovarii (an ovarian teratoma that contains thyroid tissue).

Human chorionic gonadotropin can also stimulate TSH receptors to produce excess thyroid hormones in patients with gestational trophoblastic disease and hyperemesis gravidarum.

**NON–THYROID-STIMULATING HORMONE–MEDIATED HYPERTHYROIDISM**

Hyperthyroidism is sometimes caused by a benign, monoclonal, autonomously secreting thyroid nodule known as toxic adenoma (Plummer disease). When more than one nodule is present, it is referred to as toxic multinodular goiter. This condition is the second most common cause of thyrotoxicosis and accounts for 5% to 15% of all cases of thyrotoxicosis. In the United States, toxic multinodular goiter is primarily seen in persons older than 50 years and accounts for more than 40% of all cases of thyrotoxicosis in this age group. Similarly, thyroid follicular cell cancer can likewise lead to excessive production of thyroid hormones.
Patients with painful subacute thyroiditis will have an elevated serum erythrocyte sedimentation rate and C-reactive protein levels. Box 167.7 lists the tests that should be obtained in the ED for patients in thyroid storm. If thyrotoxicosis is suspected, an endocrinologist may schedule further testing to confirm the diagnosis and determine the cause. Such tests may include measurement of total T3, thyroid autoantibodies, and radioactive iodine uptake; ultrasonography; and fine-needle biopsy.

**TREATMENT**

A beta-blocker should be started in patients with mild symptoms to provide symptomatic relief from tremors, palpitations, tachycardia, sweating, and anxiety (Fig. 167.3). It is important to withhold other treatment until the cause of the thyrotoxicosis is confirmed. Treatment options include antithyroid medications, radioactive iodine ablation, and surgery. The risks and benefits of these treatments must be weighed by the patient and the endocrinologist.

Treatment of most forms of thyroiditis is supportive. Patients with persistent tachycardia should be given beta-blockers. Patients with painful subacute thyroiditis should be treated with nonsteroidal antiinflammatory drugs, IV fluids, and beta-blockers.

**THYROID STORM**

Medications are administered to stop the synthesis, release, and peripheral effects of thyroid hormones. The order in which antithyroid medications and iodide are given is very important. First, the synthesis of new thyroid hormone is blocked by the oral administration of 200 mg of propylthiouracil (PTU) every 4 hours or 25 mg of methimazole every 6 hours. (PTU and methimazole should not be given together.) In addition to

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**DIAGNOSIS**

The most useful ED tests for diagnosing thyrotoxicosis are TSH and FT4 measurements. The algorithm in Figure 167.2 provides an interpretation of variable TSH, FT4, and free triiodothyronine (FT3) levels. Box 167.6 lists conditions that should be considered in the differential diagnosis.
Patients with mild symptoms of thyroid disease may be discharged with beta-blocker therapy and primary care follow-up instructions. Those with moderate symptoms should be admitted to the hospital for supportive care and endocrinology consultation. Patients with severe symptoms or thyroid storm should be admitted to the intensive care unit.

**SUGGESTED READINGS**


**REFERENCES**

References can be found on Expert Consult @ www.expertconsult.com.
REFERENCES