

FNA requires adequate tissue samples and interpretation by an experienced cytologist.

## HYPERTHYROIDISM

Thyrotoxicosis is the clinical syndrome that results from elevated levels of circulating thyroid hormones. Clinical manifestations of thyrotoxicosis result from the direct physiologic effects of the thyroid hormones as well as the increased sensitivity to catecholamines. Tachycardia, tremor, stare, sweating, and lid lag are all caused by catecholamine hypersensitivity.

## Signs and Symptoms

Table 63-3 lists the signs and symptoms of hyperthyroidism. Thyrotoxic crisis, or *thyroid storm*, is a life-threatening complication of hyperthyroidism that can be precipitated by surgery, radioactive iodine therapy, or severe stress (e.g., uncontrolled diabetes mellitus, myocardial infarction, acute infection). Patients develop fever, flushing, sweating, significant tachycardia, atrial fibrillation, and cardiac failure. Significant agitation, restlessness, delirium, and coma frequently occur. Gastrointestinal manifestations may include nausea, vomiting, and diarrhea. Hyperpyrexia out of proportion to other clinical findings is the hallmark of thyroid storm.

## Differential Diagnosis

Thyrotoxicosis usually reflects excess secretion of thyroid hormones resulting from Graves' disease, toxic adenoma, multinodular goiter, or thyroiditis (Table 63-4 and Fig. 63-2). However, it may be the result of excessive ingestion of thyroid hormone or, rarely, thyroid hormone production from an ectopic site (as in struma ovarii).

## Graves' Disease

Graves' disease, the most common cause of thyrotoxicosis, is an autoimmune disease that is more common in women, with a peak incidence between 20 and 40 years of age. One or more of the following features are present: (1) goiter; (2) thyrotoxicosis; (3) eye disease ranging from tearing to proptosis, extraocular muscle paralysis, and loss of sight as a result of optic nerve involvement; and (4) thyroid dermopathy, usually observed as significant skin thickening without pitting in a pretibial distribution (pretibial myxedema).

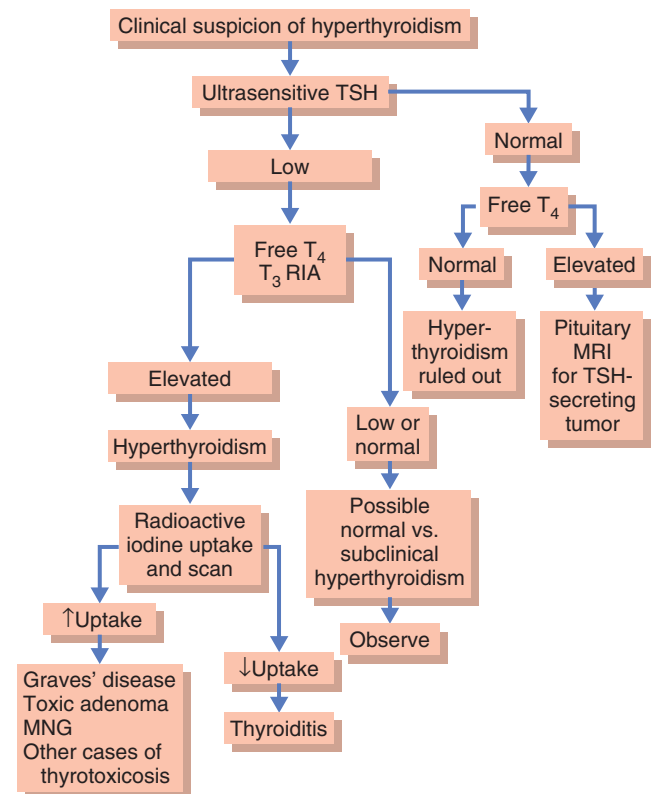
## Pathogenesis

Thyrotoxicosis in Graves' disease is caused by overproduction of an antibody that binds to the TSH receptor. These thyroid-stimulating immunoglobulins increase thyroid cell growth and

thyroid hormone secretion. Ophthalmopathy results from inflammatory infiltration of the extraocular eye muscles by lymphocytes with mucopolysaccharide deposition. The inflammatory reaction that contributes to the eye signs in Graves' disease may be caused by sensitization of lymphocytes to antigens that are common to the orbital muscles and the thyroid.

## Clinical Presentation

The common manifestations of thyrotoxicosis (see Table 63-3) are characteristic features of younger patients with Graves' disease. In addition, patients may exhibit a diffuse goiter or the eye signs characteristic of Graves' disease. Older patients often do not have the florid clinical features of thyrotoxicosis, and the condition termed *apathetic hyperthyroidism* is exhibited as flat affect, emotional lability, weight loss, muscle weakness,



**FIGURE 63-2** Algorithm for differential diagnosis of hyperthyroidism. MNG, Multinodular goiter; MRI, magnetic resonance imaging; RIA, radioimmunoassay; T<sub>3</sub>, triiodothyronine; T<sub>4</sub>, thyroxine; TSH, thyroid-stimulating hormone.

**TABLE 63-3** SIGNS AND SYMPTOMS OF HYPERTHYROIDISM

SYMPTOMS	SIGNS
Palpitations	Tachycardia
Nervousness	Atrial fibrillation
Shortness of breath	Wide pulse pressure
Heat intolerance	Brisk reflexes
Fatigue and weakness	Fine tremor
Increased appetite	Proximal limb-girdle myopathy
Weight loss	Chemosis (swelling of conjunctiva)
Oligomenorrhea	Thyroid bruit (Graves' disease)

**TABLE 63-4** CAUSES OF THYROTOXICOSIS

COMMON CAUSES	THYROTOXICOSIS FACTITIA Postpartum thyroiditis (probably variant of silent thyroiditis)
Graves' disease	
Toxic adenoma (solitary)	
Toxic multinodular goiter	
LESS COMMON CAUSES	RARE CAUSES
Subacute thyroiditis (de Quervain's or granulomatous thyroiditis)	Struma ovarii
Hashimoto's thyroiditis with transient hyperthyroid phase	Metastatic thyroid carcinoma
	Hydatidiform mole
	TSH-secreting pituitary tumor

TSH, Thyroid-stimulating hormone.