

Table 24-3 Disorders Associated with Thyrotoxicosis

Associated with Hyperthyroidism
Primary
Diffuse hyperplasia (Graves disease)
Hyperfunctioning (“toxic”) multinodular goiter
Hyperfunctioning (“toxic”) adenoma
Iodine-induced hyperthyroidism
Neonatal thyrotoxicosis associated with maternal Graves disease
Secondary
TSH-secreting pituitary adenoma (rare)*
Not Associated with Hyperthyroidism
Granulomatous (de Quervain) thyroiditis (<i>painful</i>)
Subacute lymphocytic thyroiditis (<i>painless</i>)
Struma ovarii (ovarian teratoma with ectopic thyroid)
Factitious thyrotoxicosis (exogenous thyroxine intake)

*Associated with increased thyroid-stimulating hormone (TSH); all other causes of thyrotoxicosis associated with decreased TSH.

hypermetabolic state induced by excess thyroid hormone and to overactivity of the *sympathetic nervous system* (i.e., an increase in the β -adrenergic “tone”).

- Excessive levels of thyroid hormone result in an *increase in the basal metabolic rate*. The *skin* of thyrotoxic patients tends to be soft, warm, and flushed because of increased blood flow and peripheral vasodilation, adaptations that serve to increase heat loss. *Heat intolerance* is common. Sweating is increased because of higher levels of calorogenesis. Heightened catabolic metabolism results in *weight loss despite increased appetite*.
- *Cardiac manifestations are among the earliest and most consistent features*. Individuals with hyperthyroidism can have elevated cardiac contractility and cardiac output, in response to increased peripheral oxygen requirements. Tachycardia, palpitations, and cardiomegaly are common. Arrhythmias, particularly atrial fibrillation, occur frequently and are more common in older patients. Congestive heart failure may develop, especially in older patients with preexisting cardiac disease. Myocardial changes, such as focal lymphocytic and eosinophilic infiltrates, mild fibrosis, myofibril fatty change, and an increase in size and number of mitochondria, have been described. Some individuals with thyrotoxicosis develop reversible *left ventricular dysfunction* and “low-output” heart failure, so-called *thyrotoxic or hyperthyroid cardiomyopathy*.
- *Overactivity of the sympathetic nervous system* produces tremor, hyperactivity, emotional lability, anxiety, inability to concentrate, and insomnia. Proximal muscle weakness and decreased muscle mass are common (*thyroid myopathy*). In the *gastrointestinal system*, sympathetic hyperstimulation of the gut results in hypermotility, diarrhea, and malabsorption.
- *Ocular changes* often call attention to hyperthyroidism. A wide, staring gaze and lid lag are present because of sympathetic overstimulation of the superior tarsal muscle (also known as *Müller’s muscle*), which functions alongside the levator palpebrae superioris muscle to raise the upper eyelid (Fig. 24-9). However, true *thyroid ophthalmopathy* associated with proptosis occurs only in Graves disease (see later).

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- The *skeletal system* is also affected. Thyroid hormone stimulates bone resorption, increasing porosity of cortical bone and reducing the volume of trabecular bone. The net effect is osteoporosis and an increased risk of fractures in patients with chronic hyperthyroidism. Other findings include atrophy of skeletal muscle, with fatty infiltration and focal interstitial lymphocytic infiltrates; minimal liver enlargement due to fatty changes in the hepatocytes; and generalized lymphoid hyperplasia and lymphadenopathy in patients with Graves disease.
- *Thyroid storm* refers to the abrupt onset of severe hyperthyroidism. This condition occurs most commonly in patients with underlying Graves disease and probably results from an acute elevation in catecholamine levels, as might be encountered during infection, surgery, cessation of antithyroid medication, or any form of stress. Patients are often febrile and present with tachycardia out of proportion to the fever. Thyroid storm is a medical emergency. A significant number of untreated patients die of cardiac arrhythmias.
- *Apathetic hyperthyroidism* refers to thyrotoxicosis occurring in older adults, in whom advanced age and various co-morbidities may blunt the features of thyroid hormone excess that typically bring younger patients to attention. The diagnosis of thyrotoxicosis in these individuals is often made during laboratory work-up for unexplained weight loss or worsening cardiovascular disease.

A diagnosis of hyperthyroidism is made using both clinical and laboratory findings. The measurement of serum TSH concentration is the most useful single screening test for hyperthyroidism, because its levels are decreased even at the earliest stages, when the disease may still be subclinical. A low TSH value is usually confirmed with measurement of free T_4 , which is predictably increased. In occasional patients, hyperthyroidism results



Figure 24-9 A person with hyperthyroidism. A wide-eyed, staring gaze, caused by overactivity of the sympathetic nervous system, is one of the features of this disorder. In Graves disease, one of the most important causes of hyperthyroidism, accumulation of loose connective tissue behind the eyeballs, also adds to the protuberant appearance of the eyes.