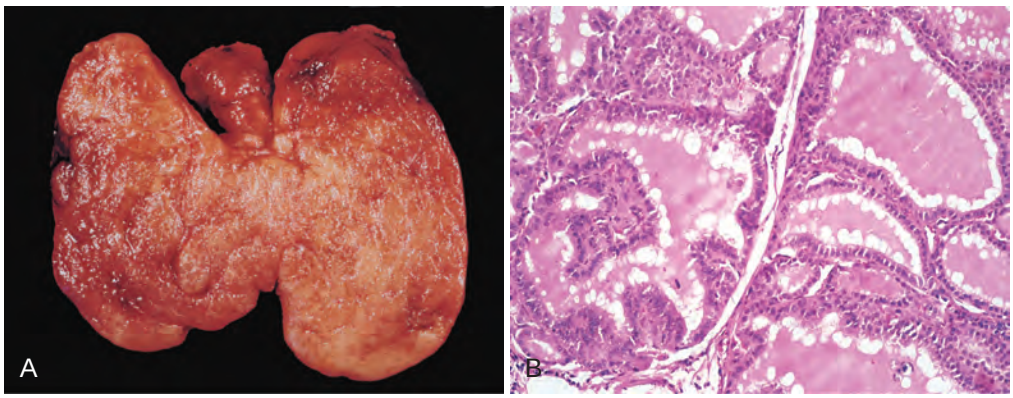

Figure 24-13 Graves disease. **A,** There is diffuse symmetric enlargement of the gland and a beefy deep red parenchyma. Compare with gross photograph of multinodular goiter in Figure 24-15. **B,** Diffusely hyperplastic thyroid in a case of Graves disease. The follicles are lined by tall, columnar epithelium. The crowded, enlarged epithelial cells project into the lumens of the follicles. These cells actively resorb the colloid in the centers of the follicles, resulting in the scalloped appearance of the edges of the colloid. (**A,** Reproduced with permission from Lloyd RV, et al (eds): Atlas of Nontumor Pathology: Endocrine Diseases. Washington, DC, American Registry of Pathology, 2002.)

mucopolysaccharides. In addition, there is infiltration by lymphocytes and fibrosis. Orbital muscles are edematous initially but may undergo fibrosis late in the course of the disease. The dermopathy, if present, is characterized by thickening of the dermis due to deposition of glycosaminoglycans and lymphocyte infiltration.

Clinical Course. The clinical findings in Graves disease include some changes associated with *thyrotoxicosis* and others associated uniquely with Graves disease, such as *diffuse hyperplasia of the thyroid, ophthalmopathy,* and *dermopathy*. The degree of thyrotoxicosis varies from case to case and is sometimes less conspicuous than other manifestations of the disease. Diffuse enlargement of the thyroid is present in all cases. The *thyroid enlargement* may be accompanied by increased flow of blood through the hyperactive gland, often producing an audible "bruit." *Sympathetic overactivity* produces a characteristic wide, staring gaze and lid lag. The ophthalmopathy of Graves disease results in abnormal protrusion of the eyeball (*exophthalmos*). The extraocular muscles are often weak. The exophthalmos may persist or progress despite successful treatment of the thyrotoxicosis, sometimes resulting in corneal injury. The infiltrative dermopathy, or *pretibial myxedema*, is most common in the skin overlying the shins, where it presents as scaly thickening and induration. The basis of such localization is not clear, and it is present only in a minority of patients. Sometimes individuals spontaneously develop thyroid hypofunction. Patients are at increased risk for other autoimmune diseases, such as systemic lupus erythematosus, pernicious anemia, type 1 diabetes, and Addison disease.

Laboratory findings in Graves disease include *elevated free T_4 and T_3* levels and *depressed TSH* levels. Because of ongoing stimulation of the thyroid follicles by thyroid-stimulating immunoglobulins, radioiodine scans show a diffusely increased uptake of iodine.

Graves disease is treated with β-blockers, which address symptoms related to the increased β-adrenergic tone (e.g., tachycardia, palpitations, tremulousness, and anxiety), and by measures aimed at decreasing thyroid hormone synthesis, such as the administration of thionamides (e.g., propylthiouracil), radioiodine ablation, and thyroidectomy. Surgery is used mostly in patients who have large goiters that are compressing surrounding structures.

KEY CONCEPTS

Graves Disease

- Graves disease, the most common cause of endogenous hyperthyroidism, is characterized by the triad of thyrotoxicosis, ophthalmopathy, and dermopathy.
- Graves disease is an autoimmune disorder caused by activation of thyroid epithelial cells by autoantibodies to the TSH receptor that mimic TSH action (*thyroid-stimulating immunoglobulins*).
- The thyroid in Graves disease is characterized by diffuse hypertrophy and hyperplasia of follicles and lymphoid infiltrates; glycosaminoglycan deposition and lymphoid infiltrates are responsible for the ophthalmopathy and dermopathy.
- Laboratory features include elevations in serum free T_3 and T_4 and decreased serum TSH.

Diffuse and Multinodular Goiters

Enlargement of the thyroid, or *goiter* is caused by impaired synthesis of thyroid hormone, which is most often the result of dietary iodine deficiency. Impairment of thyroid hormone synthesis leads to a compensatory rise in the serum TSH level, which, in turn, causes hypertrophy and hyperplasia of thyroid follicular cells and, ultimately, gross enlargement of the thyroid gland. The compensatory increase in functional mass of the gland overcomes the hormone deficiency, ensuring a *euthyroid* metabolic state in most individuals. If the underlying disorder is sufficiently severe (e.g., a congenital biosynthetic defect or endemic iodine deficiency, discussed later), the compensatory responses may be inadequate, resulting in *goitrous hypothyroidism*. The degree of thyroid enlargement is proportional to the level and duration of thyroid hormone deficiency. Goiters can broadly be divided into two types: *diffuse nontoxic* and *multinodular*.