## Diffuse Nontoxic (Simple) Goiter

**Diffuse nontoxic (simple) goiter causes enlargement of the entire gland without producing nodularity.** Because the enlarged follicles are filled with colloid, the term *colloid goiter* has been applied to this condition. This disorder occurs in both an endemic and a sporadic distribution.

- *Endemic goiter* occurs in geographic areas where the soil, water, and food supply contain low levels of iodine. The term endemic is used when goiters are present in more than 10% of the population in a given region. Such conditions are particularly common in mountainous areas of the world, including the Andes and Himalayas, where iodine deficiency is widespread. The lack of iodine leads to decreased synthesis of thyroid hormone and a compensatory increase in TSH, leading to follicular cell hypertrophy and hyperplasia and goitrous enlargement. With increasing dietary iodine supplementation, the frequency and severity of endemic goiter have declined significantly, although as many as 200 million people worldwide continue to be at risk for severe iodine deficiency.

  Variations in the prevalence of endemic goiter in regions with similar levels of iodine deficiency point to the existence of other causative influences, particularly dietary substances, referred to as *goitrogens*. The ingestion of substances that interfere with thyroid hormone synthesis at some level, such as vegetables belonging to the Brassicaceae (Cruciferae) family (e.g., cabbage, cauliflower, Brussels sprouts, turnips, and cassava), has been documented to be goitrogenic. Native populations subsisting on cassava root are particularly at risk. Cassava contains a thiocyanate that inhibits iodide transport within the thyroid, worsening any possible concurrent iodine deficiency.
- *Sporadic goiter* occurs less frequently than does endemic goiter. There is a striking female preponderance and a peak incidence at puberty or in young adult life. Sporadic goiter can be caused by several conditions, including the ingestion of substances that interfere with thyroid hormone synthesis. In other instances, goiter may result from hereditary enzymatic defects that interfere with thyroid hormone synthesis, all transmitted as autosomal-recessive conditions (dyshormonogenetic goiter; see earlier). In most cases, however, the cause of sporadic goiter is not apparent.

### MORPHOLOGY

Two phases can be identified in the evolution of diffuse nontoxic goiter: the **hyperplastic phase** and the phase of **colloid involution.** In the hyperplastic phase, the thyroid gland is diffusely and symmetrically enlarged, although the increase is usually modest, and the gland rarely exceeds 100 to 150 gm. The follicles are lined by crowded columnar cells, which may pile up and form projections similar to those seen in Graves disease. The accumulation is not uniform throughout the gland, and some follicles are hugely distended, whereas others remain small. If dietary iodine subsequently increases or if the demand for thyroid hormone decreases, the stimulated follicular epithelium involutes to form an enlarged, colloid-rich gland **(colloid goiter).** In these cases the cut surface of the thyroid is usually brown, somewhat glassy, and translucent. Histologically the follicular epithelium is flattened and cuboidal, and colloid is abundant during periods of involution.

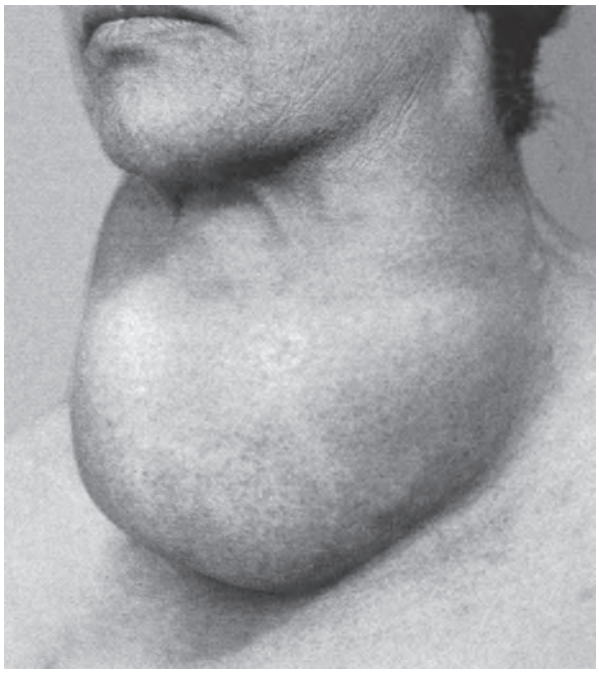

**Figure 24-14** A 52-year-old woman with a huge colloid goiter who developed compressive symptoms. (Reproduced with permission from Lloyd RV, et al (eds): Atlas of Nontumor Pathology: Endocrine Diseases. Washington, DC, American Registry of Pathology, 2002.)

***Clinical Course.*** As stated earlier, the vast majority of persons with simple goiters are clinically euthyroid. Therefore, the clinical manifestations are primarily related to *mass effects* from the enlarged thyroid gland (Fig. 24-14). Although serum $T_3$ and $T_4$ levels are normal, the serum TSH is usually elevated or at the upper range of normal, as is expected in marginally euthyroid individuals. In children, dyshormonogenetic goiter, caused by a congenital biosynthetic defect, may induce cretinism.

## Multinodular Goiter

With time, recurrent episodes of hyperplasia and involution combine to produce a more irregular enlargement of the thyroid, termed *multinodular goiter*. Virtually all long-standing simple goiters convert into multinodular goiters. **Multinodular goiters produce the most extreme thyroid enlargements and are more frequently mistaken for neoplasms than any other form of thyroid disease**. Because they derive from simple goiter, they occur in both sporadic and endemic forms, having the same female-to-male distribution and presumably the same origins but affecting older individuals because they are late complications.

It is believed that multinodular goiters arise because of variations among follicular cells in their response to external stimuli, such as trophic hormones. If some cells in a follicle have a growth advantage, perhaps because of intrinsic genetic abnormalities similar to those that give