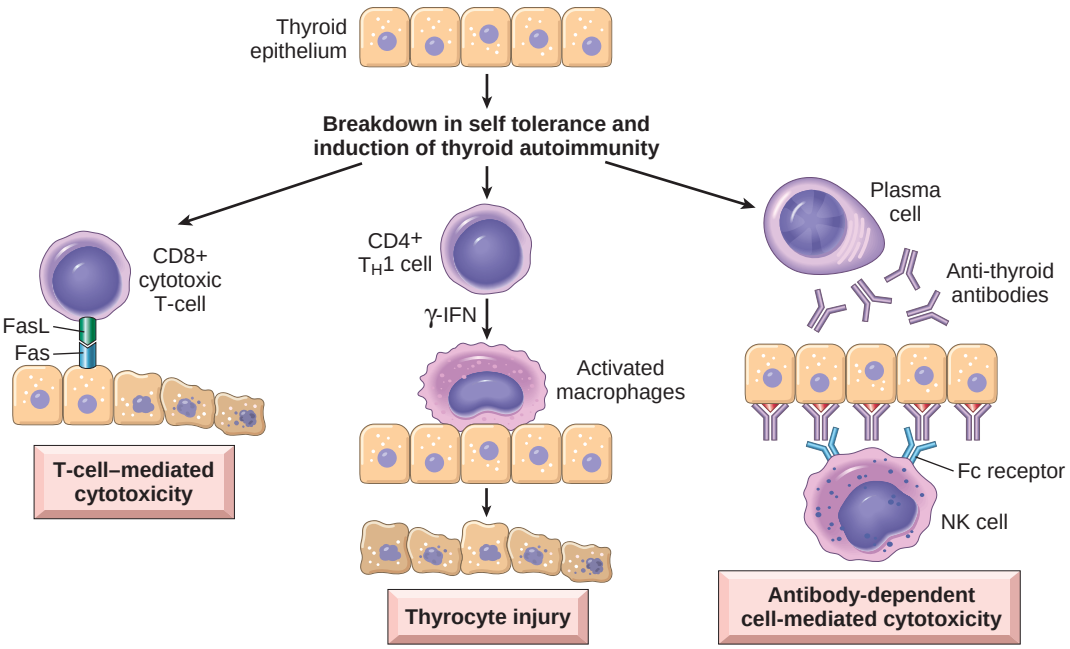

Figure 24-10 Pathogenesis of Hashimoto thyroiditis. Breakdown of peripheral tolerance to thyroid autoantigens, results in progressive autoimmune destruction of thyroid cells by infiltrating cytotoxic T cells, locally released cytokines, or by antibody-dependent cytotoxicity.

- *CD8+ cytotoxic T cell-mediated cell death:* CD8+ cytotoxic T cells may destroy thyroid follicular cells.
- *Cytokine-mediated cell death:* Activation of CD4+ T cells leads to the production of inflammatory cytokines such as interferon-γ in the thyroid gland, with resultant recruitment and activation of macrophages and damage to follicles.
- A less likely mechanism involves binding of antithyroid antibodies (antithyroglobulin, and antithyroid peroxidase antibodies) followed by antibody-dependent cell-mediated cytotoxicity (Chapter 6).

MORPHOLOGY

The thyroid is often diffusely enlarged, although more localized enlargement may be seen in some cases. The capsule is intact, and the gland is well demarcated from adjacent structures. The cut surface is pale, yellow-tan, firm, and somewhat nodular. There is extensive infiltration of the parenchyma by a **mononuclear inflammatory infiltrate** containing small lymphocytes, plasma cells, and well-developed **germinal centers** (Fig. 24-11). The thyroid follicles are atrophic and are lined in many areas by epithelial cells distinguished by the presence of abundant eosinophilic, granular cytoplasm, termed **Hürthle cells**. This is a metaplastic response of the normally low cuboidal follicular epithelium to ongoing injury. In fine-needle aspiration biopsy samples, the presence of Hürthle cells in conjunction with a heterogeneous population of lymphocytes is characteristic of Hashimoto thyroiditis. In "classic" Hashimoto thyroiditis, interstitial connective tissue is increased and may be abundant. Unlike Reidel thyroiditis (see later), the fibrosis does not extend beyond the capsule of the gland.

Clinical Course. Hashimoto thyroiditis most often comes to clinical attention as painless enlargement of the thyroid, usually associated with some degree of hypothyroidism, in a middle-aged woman. The enlargement of the gland is usually symmetric and diffuse, but in some cases it may be sufficiently localized to raise the suspicion of a neoplasm. In the usual case, hypothyroidism develops gradually. In some patients, however, it may be preceded by transient thyrotoxicosis caused by disruption of thyroid follicles, leading to release of thyroid hormones ("*hashitoxicosis*"). During this phase, free T_4 and T_3 levels are elevated, TSH is diminished, and radioactive iodine uptake is decreased. As hypothyroidism supervenes, T_4 and T_3 levels fall, accompanied by a compensatory increase in TSH.

Individuals with Hashimoto thyroiditis are at increased risk for developing other autoimmune diseases, both

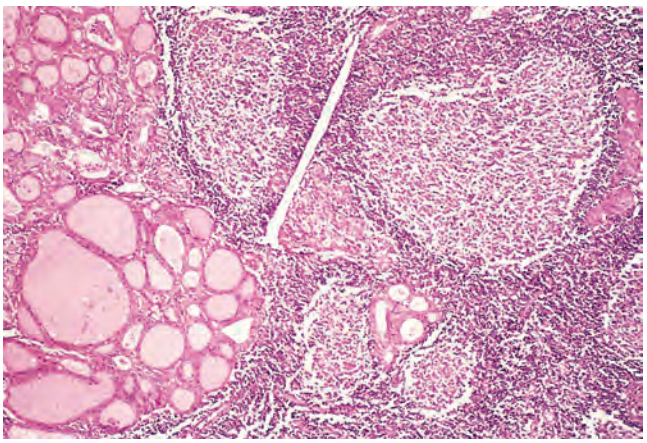

Figure 24-11 Hashimoto thyroiditis. The thyroid parenchyma contains a dense lymphocytic infiltrate with germinal centers. Residual thyroid follicles lined by deeply eosinophilic Hürthle cells are also seen.