Lymphocytic Thyroiditis, Rat

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Synonyms. Autoimmune thyroiditis, immune complex thyroiditis, Hashimoto’s thyroiditis, lymphadenoid goiter.

Gross Appearance

The gross appearance varies with the stage of the disease. The thyroid glands may not appear abnormal when only minimally involved. However, if there is considerable lymphocytic infiltration, the glands are symmetrically enlarged and the cut surfaces are pale. The thyroids may weigh up to ten times their normal weight. The capsule is intact and usually smooth, but can be lobulated.

Microscopic Features

The thyroid glands have a multifocal to diffuse infiltration of lymphocytes, plasma cells, and macrophages (Fig. 322). The degree of cellular infiltration varies, but eventually becomes diffuse with secondary lymphoid follicle formation. The thyroid follicles become compressed, with reduced size and depletion of colloid. The epithelial cells are large and appear hyperplastic. Some follicles may be atrophic, while others may have degenerative changes and infiltration of the epithelium with lymphocytes (Fig. 323). Fibrosis in uncommon.

Ultrastructure

Ultrastructural investigations confirm the findings described under microscopic features. Moderate electron-dense deposits in the basement membrane region, assumed to represent immune complexes, have been identified by immuno-fluorescence (Bigazzi and Rose 1975; Clagett et al. 1974; Kalderon et al. 1977; Kitchen et al. 1979). Plasma cells are present in the regions of these deposits.

Differential Diagnosis

The histopathologic diagnosis of lymphocytic thyroiditis is not difficult because of the characteristic infiltration of lymphoid cells. The morphologic appearance of spontaneous or experimentally induced lymphocytic thyroiditis is similar. The demonstration of circulating thyroid antibodies is confirmatory evidence. Autoantibodies to thyroglobulin are present, and immune complexes can be identified in the affected glands by immunofluorescence and immuno-cytochemistry. These studies strongly indicate that the disease process is autoimmune (Allison 1976; Gosselin et al. 1980; Kalderon and Bogaars 1977; Kitchen et al. 1979).

Biologic Features

Natural History. Most rats with spontaneous or experimentally induced lymphocytic thyroiditis have no clinical evidence of thyroid disease. However, thyroid function decreases slowly, and the decrease is often not recognized until the thyroiditis has been present for a considerable time. It is a slowly progressive disease with minimal effect on survival.

Pathogenesis and Etiology. Lymphocytic thyroiditis has been produced experimentally in guinea pigs, rats, hamsters, rabbits, monkeys, dogs, and baboons by immunization with thyroid antigens, usually thyroglobulin mixed with adjuvants (Volpe 1978). This disease has been produced in
rats by administration of chemicals (Kitchen et al. 1979; Reuber and Glover 1976; Silverman and Rose 1971, 1975) and by thymectomy and irradiation (Penhale and Ahmed 1982). Spontaneous lymphocytic thyroiditis has been reported in chickens, rats, beagle dogs, monkeys, *Mastomys*, and man (Bigazzi and Rose 1975; Gosselin et al. 1981; Solleveld 1981).

Considerable evidence has been accumulated which indicates that lymphocytic thyroiditis is the prototype of autoimmune disease. However, there are several factors which can influence the development of the disease, such as heredity, active thymus, age, and sex. The role of genetic factors has been identified in chickens (Rose et al. 1973), rats (Bigazzi and Rose 1975), mice (Kojima...