IMMUNOLOGICAL ASPECTS OF ENDOCRINE DISORDERS

AN ESSAY

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BY

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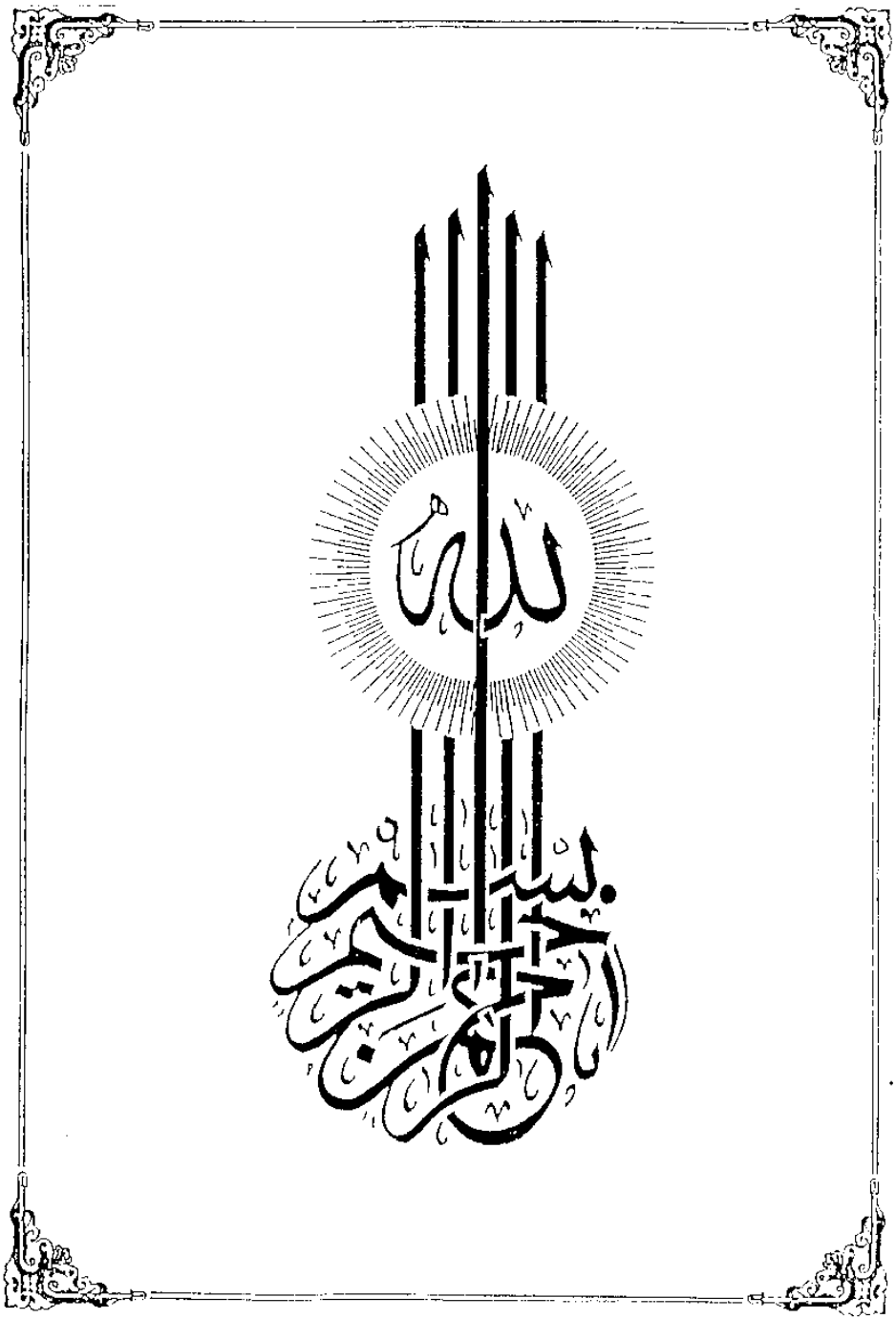
بسم الله الرحمن الرحيم



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TO MY BELOVED

FAMILY

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I. INTRODUCTION

INTRODUCTION

Some of the best studied examples of organ specific autoimmune diseases are found among the endocrine disorders (Rose et al., 1983).

The criteria for establishing the autoimmune etiology of an organ-specific human disease are: association with other autoimmune diseases, histologic findings suggestive of immune destruction, presence of autoantibodies, evidence of cell-mediated immunity and experimental production of the disease in animal models (Kahn and Flier, 1980).

This essay will include recent data about endocrine autoimmunity, the factors involved in the causation of these diseases as well as investigation and treatment of these diseases.

Immune mediated endocrine diseases considered in this essay will include, disorders of the thyroid gland and other immune mediated disorders of the parathyroid gland, pancreas, adrenal gland, pituitary gland and the gonads.

II. DISORDERS OF THE THYROID GLAND

THYROID AUTOIMMUNE DISEASE

This is the classic example of specific autoimmunity and has been studied in the laboratory more than any other autoimmune entity. Of 95 pediatric patients seen sequentially in 2 endocrine clinics for goiter, 33 had CLT (chronic lymphocytic thyroiditis) and 38 had thyrotoxicosis. Consequently, approximately 75% of children presenting with goiter have autoimmune disease as the cause of that goiter (Blizzard, 1981).

The most readily accepted thesis explaining the etiology of these thyroid autoimmune disease is that there is an immunologic defect in the T-cell population that is divided into at least two subtypes: helper cells that assist B cells to produce circulating antibodies and suppressor cells that inhibit B cells from producing circulating antibodies (Blizzard, 1981).

With a defect in normal suppressor activity, B cells can interact with normal antigens and produce circulating antibodies. The antibodies may vary according to the antigen to which they are exposed i.e they may be antibodies directed against thyroglobulin, microsomal components of thyroid cells, or membrane antigens

such as the receptors for thyrotropin stimulating hormone (TSH). Antibodies against the latter include the thyroid-stimulating immunoglobulins (TSI) such as long acting thyroid stimulator (LATS) and LATS-protector (LATS-P). Killer (K) cells, whcih are probably another subgroup of T cells, may contribute to the lymphocytic infiltration which is characteristic of CLT, by reacting with an antigen-antibody complex or in the thyroid cell (Volpe, 1977).

Since thyrotoxicosis, CLT and exophthalmos are all autoimmune diseases, they may occur singly or in association. Thyrotoxicosis and exophthalmos particularly occur in association. Occasionally , patients with CLT have associated exophthalmos without any element of thyrotoxicosis. Patients with CLT will occasionally have associated thyrotoxicosis, this probably accounts for most of the patients with "hashitoxicosis". All three entities may occur in the same patient. (Khangure and Dingle, 1977).

HASHIMOTO'S THYROIDITIS

Hashimoto's or autoimmune thyroiditis is the most cause of thyroid disease in children and adolescents and accounts for many of the enlarged thyroids formerly designated "adolescent" goiter. It is also the most common cause of juvenile hypothyroidism, with or without goiter. Its incidence may be high as 1 % in school-children. (Behrman and Vaughan 1983).

Hashimoto's thyroiditis is a form of chronic thyroiditis characterized by a goiter exhibiting epithelial cell abnormalities and lymphocytic infiltration and by course which progresses toward thyroidal hypofunction. There are many synonyms for this disorder including: chronic lymphocytic thyroiditis: lymphadenoid goiter and recently autoimmune thyroiditis (Ingbar and Woeber, 1981).

The exact etiology of Hashimoto's disease in human is uncertain. However, the disease is now believed to be immunologically mediated in genetically predisposed persons (Volpê, 1977).

There is a significant family aggregation of cases with Hashimoto's thyroiditis (Bode et al., 1973). The disease may be found in 15 to 25 % of first-degree relatives of patients and has been reported in paris

of identical twins. A close relationship of this disease and Graves' disease has been suggested by the fact that in identical twins, cases have been described in which one twin has Hashimoto's thyroiditis and the other has Graves' disease (Chertow et al., 1973).

A significant association also exists between Hashimoto's disease and the human leukocyte antigen HLA-DR3 in patients with atrophic thyroiditis (Moens and Farid, 1978) and between Hashimoto's disease and HLA-DR5 in those with goitrous thyroiditis (Farid et al., 1981). Both are also associated with HLA-B8 haplotype (Ingbar 1986).

Thyroiditis and thyroid antibodies have been observed more often than expected in several genetic syndromes (Doniach, 1975).

An increased prevalence of thyroiditis has been noted in patients with ovarian dysgenesis (especially with "X" isochromosome defects),e.g.in Turner's syndrome (with "XO" karyotype). The biologic implications of these associations are unclear but suggest a role for other genetic factors in the development of thyroid autoantibodies (Kahn and Flier, 1980).

The coexistance of Hashimoto's disease and other diseases of autoimmune etiology has been seen. These include diabetes mellitus, idiopathic adrenal atrophy, rheumatoid arthritis, chronic active hepatitis, vitiligo, early graying of hair, biliary cirrhosis, Sjogren's syndrome, lupus erythematosus, idiopathic thrombocytopenic purpura and pernicious anemia (Ingbar, 1986). As many as 6 % of patients with Hashimoto's have been reported to have pernicious anemia (Larsen, 1985).

An association between Hashimoto's disease and angioimmunoblastic lymphadenopathy has also been noted (Ingbar, 1986).

Idiopathic Addison's disease and Hashimoto's disease may appear in the same patients. This combination is called Schmidt's syndrome (Larsen, 1985).

Occasionally patients with Hashimoto's present with hyperthyroidism in association with a thyroid gland that is unusually firm and with high titers of circulating antithyroid antibodies, a combination which suggests probably correctly, the co-occurrence of Graves' disease and Hashimoto's thyroiditis (Hashitoxicosis). In others hyperthyroidism may supervene in patients known to have Hashimoto's thyroiditis, presumably due

to the emergence of clones of lymphocytes that produce anti-TSH receptor antibodies (Ingbar, 1987).

The presence of lymphocytic infiltration of the thyroid, of circulating antithyroid antibodies and of a clinical or immunological overlap with other diseases with autoimmune components provides compelling evidence that immunologicl factors are involved in the pathogenesis of Hashimoto's disease (Ingbar, 1986).

A humorally mediated autoimmune mechanism has been suggested by the observation that antimicrosomal antibodies are cytotoxic to thyroid tissue in vitro (Ingbar, 1986).

The exact mechanism by which these various anti-thyroid antibodies develops is not clear. The early concept was that thyroglobulin was a sequestered antigen and thyroiditis was produced by release of this antigen into the circulation by some injury to the thyroid. This theory was disproved by demonstration of thyro-globulin in blood and lymph of normal persons (Beall, 1978).

It has also been suggested that the autoimmune response in Hashimoto's disease occurs as a result