

Autoimmunity and the Endocrine System: thyroid, hypophysis and pregnancy.

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The endocrine system produces hormones that regulate metabolism, growth and development, sexual function, reproduction, sleep, mood, cardiovascular system, and other functions. The main endocrine glands are pituitary, thyroid, parathyroid, adrenal glands, pancreas, ovaries (in females) and testicles (in males); they secrete a range of hormones that affect the whole body. Each type of hormone is targeted toward certain organs and tissues. Significant alterations of hormone levels indicate problems of endocrine system. Endocrine diseases also occur if the body does not respond to hormones in the appropriate ways. Stress, infections and changes in the blood's composition and electrolytes balance can also influence hormone levels (1).

The hypothalamus, through the releasing factors, regulates the secretion of pituitary hormones, that are able to regulate the functions of targeted organs (for example TSH regulates thyroid function, ACTH the adrenal function, LH and FSH the reproductive system). Each target organ is able to send, through its own secretion, a regularly feedback to the hypothalamus and the hypophysis. The regulation of the hypothalamus is under the control of the Central Nervous System, that is influenced by physical and neurophysiological stress conditions. The immune system is also under the control of the immune-endocrine axis, in fact stressful events are able to modify the immune system functions, and are related also to the appearance of different autoimmune disorders. On the other side, the autoimmune reaction can develop against endocrine glands, inducing a dysfunction of the targeted endocrine organs.

The most frequent endocrine autoimmune dysfunctions are related to a reduction of the function of the endocrine glands (hypopituitarism, hypothyroidism, Type 1 diabetes, hypoadrenalism, etc.). Less frequently, hyperfunction is associated with the autoimmune process, such as in Graves' disease (GD).

Among autoimmune endocrine disorders, hypophysitis is a heterogeneous condition that leads to inflammation of the sella and/or suprasellar region, potentially resulting in hormonal deficiencies and/or mass effects. This disorder is reviewed extensively in the paper by **C. Koch et al** (2-4).

Thyroid hormones impact vital body functions, including heart rate, skin maintenance, growth, temperature regulation, fertility and digestion. The most frequent autoimmune endocrine disorder is Hashimoto's thyroiditis (HT), that is

reviewed by **F. Ragusa et al** (5-7). It is the leading cause of hypothyroidism in the iodine-sufficient areas of the world.

The versatile clinical manifestations of the HT often include psycho-neurological disorders. **L. Churilov et al** (8) describe the development of current views on the role of thyroid in ontogeny and functions of brain, as well as classical and newest ideas on the aetiology and pathogenesis of Hashimoto's encephalopathy.

Thyroid autoimmunity (together with endometriosis and celiac disease) is also a well known cause of infertility and/or subfertility, therefore when difficulties in the onset of pregnancy are reported, the association of systemic autoimmune conditions needs to be taken in consideration, as examined by **A. Tincani et al** (9). Nonsteroidal anti-inflammatory drugs can cause temporary infertility and corticosteroids are associated with a prolonged time to pregnancy during the treatment of some rheumatic diseases. Furthermore, in the second paper by **A. Tincani et al.** (10) the multidisciplinary strategy for the management of pregnancy and childbirth in patients with particular autoimmune diseases is analysed. Each disease such as rheumatoid arthritis, systemic lupus erythematosus, antiphospholipid syndrome etc. carries its own potential maternal and fetal risks that need to be clearly evaluated during the pre-pregnancy counselling.

K. Sharif et al (11) have discussed the role of autoimmunity as a primary cause of primary ovarian insufficiency, that results in amenorrhea in women aged less than 40 years old. Multiple potential immune antigens have been proposed as possible cross-reactive targets for antibody mediated autoimmune disease.

Several triggers can contribute to the development of autoimmune disorders, such as the environmental and genetic ones. In autoimmune polyglandular diseases (APD), genetic associations with HLA haplotypes and polymorphisms of genes encoding immunologically relevant gene products have been reported. **G. Kahaly et al** (12,13) have reviewed these diseases, underlining the importance to detect APD at an early stage, with the advantage of less frequent complications, effective therapy and better prognosis.

The aggregation of different autoimmune disorders, in particular that between autoimmune thyroid disorders with rheumatologic, or dermatologic autoimmune diseases, is examined by **P. Fallahi et al** (13-18).

These diseases share also a common immune-pathogenesis, underlined by a Th1 prevalent autoimmune response that is a characteristic of the organ specific autoimmune diseases (e.g. HT, GD), and/or of the systemic rheumatologic or dermatologic autoimmune disorders in their initial, and active phases, with an increased CXCL10 serum and/or tissue expressions.

The issue of prolactin with autoimmunity is a of close association. So much so that one can treat autoimmunity by prescribing Bromocriptine, which inhibits the stimulating effect of prolactin on the immune system. This issue is covered by the two papers by **V. Borba et al** (19,20). The authors even raise the possibility that some of the postpartum exacerbations of autoimmune diseases may be due to the increased levels of prolactin in those women. Especially in those who are breastfeeding. It is not

surprising that there is already one study showing the reduction in these postpartum exacerbations in patients with autoimmune diseases by avoiding breastfeeding. This subject needs a thorough evaluation.

Recently, these aspects of autoimmunity and the endocrine system were also reviewed by other papers (3,4,13,21).

Conclusion

There is an increasing incidence of autoimmune endocrine disorders worldwide (for example for type 1 diabetes and HT). The causes are not actually well known, but environmental pollution, infections and also therapeutics are implied in the increasing incidence of these diseases.

Since autoimmune endocrine disorders are affecting the health and the quality of life of hundred millions people in the world, several efforts are ongoing for the prevention and the early diagnosis of these disorders, that have been examined in the papers of this Special Issue.

Furthermore, several researches have been done to modulate the autoimmune reaction with different drugs, such as traditional immune-modulant molecules (corticosteroids), or new specific drugs directed against specific cytokines or chemokines (i.e. antibodies, or small molecules). Antigen-specific therapy for GD, by inducing T cell tolerance through an immunization with TSH-R peptides, has been published. However more researches are needed for the prevention and therapy of endocrine autoimmune diseases.

We do hope that you will enjoy reading the collection of these endocrinology papers related to autoimmunity.

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