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Auto-immune disorders and fertility

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Auto-immune disease occurs when the immune system attacks self-molecules as a result of a breakdown of immunologic tolerance to auto-reactive immune cells. Auto-immune disorders are largely of unknown etiology and affect approximately 3% of the North American and European populations, mainly women (75% of the patients).

There seems to be a bidirectional relationship between auto-immunity and reproduction: auto-immunity may impair female fertility and reproductive outcome and pregnancy can be detrimental for patients with auto-immune disorders. Except for drug-induced (e.g.cyclophosphamide) ovarian failure, primary infertility is not prominent among patients with systemic auto-immune diseases, such as SLE. In males, auto-immunity to sperm antigens can be related to infertility by 2 main pathogenic mechanisms: the adverse effects of antibodies directly on spermatozoa and the association with disordered spermatogenesis resulting in oligospermia and azoospermia. Although some studies support the conclusion that some auto-antibodies are present more often in infertile patients compared with control women it is unclear which antibodies, if any, are associated with an altered prognosis for the infertile women. Another important issue concerning auto-immunity and infertility is the role of auto-antibodies directed against ovary, adrenal and thyroid glands in the development of premature ovarian failure, a primary ovarian defect affecting about 1% of women less than 40 years old.

There is also controversy about the role of several auto-antibodies that have been described in women with unexplained infertility, either with or without a known underlying autoimmune disease. Organ- specific auto-immune diseases producing ovary, adrenal and thyroid failure (endocrine auto-immune diseases) may cause female infertility due to premature ovarian failure (POF).

One of the reasons to suspect the auto-immune etiology of POF is its frequent association with some endocrine auto-immune diseases, mainly thyroid diseases. The frequency of POF in other endocrine auto-immune diseases is unknown but it often occurs as part of an auto-immune polyglandular syndrome with high frequencies of hypothyroidism, insulin-dependent diabetes mellitus and adrenal abnormalities. However, against the auto-immune origin of POF in these patients is the fact that it is very uncommon to find oophoritis. Therefore, evidence indicates that auto-immunity is primarily responsible for POF, mainly in cases associated with auto-immune thyroid diseases, Addison´s disease and with other polyendocrine auto-immune diseases, but in patients with isolated POF the evidence favoring an immune origin is not so strong.

The auto-immune thyroid diseases are also frequently associated with endometriosis and the polycystic ovarian syndrome, two conditions where infertility is common.

Recurrent pregnancy loss (RPL), usually defined as two or more consecutive spontaneous abortions, affects 2-5% of women during reproductive age. The antiphospholipid syndrome (APS) – either primary or associated to systhemic lupus erythematosus (SLE) is the auto-immune disease most commonly associated with RPL in affected pregnant patients. The antibodies that may be predictive of pregnancy losses in patients with known auto-immune diseases (SLE) remain unknown as well as those that should be evaluated in women with unexplained RPL.

SLE is the auto-immune disease that most commonly can be compromised by pregnancy because of its fluctuant nature that alternates periods of clinical activity with others of remission, with hormonal changes being some possible triggers of reactivation. The influence of pregnancy in other auto-immune disease is less notorious, either because they rarely appear in young women (Sjogren´s syndrome, systemic vasculitis) or because their outcome is scarcely influenced by hormonal changes. The

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use of prophylactic steroids during pregnancy also remains a matter of controversy. Some authors recommend the use of prednisone throughout pregnancy for all pregnancy lupus patients, others not.

Pregnancy does not cause SLE to worsen, provided that the disease is clinically inactive at conception and patients are managed according to a careful multi-disciplinary monitoring and treatment schedule. SLE patients should be advised to become pregnant when the disease is inactive, strict obstetrical/medical care should be performed during pregnancy and, although prophylactic steroids are not required, several drugs, such as hydroxychloroquine, prednisone and azathioprine, can be safely used in case of an SLE flare.

However, pregnancy may adversely affect auto-immune conditions, mainly SLE. This stresses the need for well-coordinated, multi-disciplinary teams, including obstetricians/gynecologists, internists/rheumatologists and hematologists/immunologists, to manage reproductive issues in females affected by auto-immune diseases.

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