Autoimmune Infertility

Causes of Infertility

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Autoimmune disease is a primary contributing factor in infertility. Learn about the different causes and how they’re treated.

What is Infertility?

Infertility is defined as the inability to become pregnant after 12 months of unprotected intercourse. Today, as many as 15 percent of all couples are reported to have problems with infertility or premature ovarian failure (POF). Men and women are equally responsible for failure to conceive. And while the reasons for infertility are sometimes difficult to determine, autoimmune diseases including oophoritis, orchitis and hypothyroidism, are well-known causes of infertility.

Causes in Males

In men, type 1 diabetes mellitus and autoimmune thyroid disease can both contribute to infertility. And the autoimmune condition of orchitis, which causes testicular inflammation, sperm antibodies or lymphocytic infiltration of spermatazoa may also cause infertility. Orchitis can be caused by prior infection, surgery affecting the testes, and genital trauma.

Causes in Women

Normally, a decline in female fertility begins in the mid-30's and becomes marked after age 40. In premature ovarian failure menstrual periods stop and levels of follicle stimulating hormone (FSH) rise similar to levels seen in menopause, before age 40. Women with POF are at increased risk for adrenal insufficiency, and some reports suggest that women with POF have a 300 percent greater risk of developing Addison's disease (primary autoimmune adrenal insufficiency) than other women. About 2-10 percent of all women with POF have adrenal insufficiency, and among these women about 70 percent have adrenal cortex antibodies.

Approximately 10 percent of all cases of POF are caused by autoimmune oophoritis, an autoimmune condition causing ovarian gland inflammation, atrophy and destruction as well as hormonal deficiencies. Oophoritis can occur in girls with polyglandular syndrome type 1 (APECED) before they begin to menstruate. Antibodies against the adrenal component P450c17 are seen in oophoritis and are good indicators of future ovarian failure. These autoantibodies react against both adrenal and ovarian components (theca cells of the ovary) and also the Leydig cells of the testis and syncytiotrophoblast cells of the placenta. Seventeen percent of women with POF are reported to have a co-existing
autoimmune disease, most commonly autoimmune hypothyroidism in 27 percent of cases, and nearly 20 percent of these patients ovulate intermittently. Besides autoimmune hypothyroidism, patients with POF may also have Addison's disease (2.5 percent of cases) and type 1 diabetes mellitus (2.5 percent of cases). About 25 percent of women with Addison's disease stop menstruating prematurely during the course of their disease and about 10 percent develop POF.

However, most women (80-90 percent) with POF have neither Addison's disease nor adrenal steroid antibodies. These patients are classified as having resistant ovary syndrome that is insensitive to ovulation induction with exogenous gonadotrophin therapy. Up to 21 percent of these women are reported to have autoantibodies to 3-beta-hydroxysteroid dehydrogenase, an enzyme necessary for ovarian function. However, there are no techniques currently available to routinely test for these antibodies.

**Autoantibodies in Infertility**

Women and men may both produce antibodies to spermatozoa. These antibodies destroy sperm or interfere with its function, contributing to infertility. Sperm antibodies in cervical mucus or on sperm are associated with a reduction in cervical mucus penetration. Sperm antibodies can occur after vasectomy and in homosexual men they can occur after unprotected receptive anal intercourse. Sperm antibodies can be detected in cervical mucus, seminal fluid, and in serum or as an antigen-antibody complex on donor sperm.

Women may also produce antibodies to ovarian components, primarily maturing ovarian follicles, in the form of steroid cell autoantibodies. These are the same antibodies found in autoimmune adrenal insufficiency. Female hormones are primarily produced by the adrenal cortex, which also produces aldosterone and cortisol.

**In Thyroid Disease**

Impaired fertility occurs in systemic sclerosis and in untreated or under-treated hypothyroidism. In Graves' disease, fertility may also be impaired, particularly in male patients. Fertility related to hyperthyroidism improves when thyroid hormone levels are corrected. Patients with autoimmune diseases such as systemic lupus erythematosus who are treated with cytotoxic agents, for instance cyclophosphamide, may experience impaired fertility that is directly related to patient age and the cumulative drug dose.

**Autoimmune Clotting Disorders**

In patients with autoimmune disorders, fertility drugs may cause hormone-associated disease flares or increase the risk of clotting. In particular, patients with antiphospholipid syndrome or lupus anticoagulant disorders are at risk for clotting, which can cause miscarriage and implantation failures.

According to recent theories, immune system changes similar to antiphospholipid syndrome may affect very early pregnancies and cause infertility. It's been suggested that
autoantibodies directed at ova, sperm or other components may interfere with fertilization. In addition, autoantibodies may be involved in endometriosis and in vitro fertilization failures. Ovarian antibodies that, as mentioned, are seen in up to 70 percent of women with POF can be classified into antibodies directed against ovarian cells, eggs, and also their surrounding tissue (zona pellucida). Some women have more than one type of ovarian antibody.

**Treatment**

When autoantibodies are implicated in infertility, treatment with intravenous immunoglobulins is sometimes used to bind and temporarily neutralize these autoantibodies. Some of the most important recent advances in infertility research have been conducted by Dr. Alan Beer and involve serotonin antibodies. For more information on Dr. Beer's research see <http://repro-med.net>.

In summary, there are many causes of infertility affecting both males and females. Because autoimmune disease is a well-known contributing factor, screening for common autoimmune disorders should be a part of any infertility evaluation.

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