Fertility & Cryogenics Lab

# Tests Explained

## Recurrent Pregnancy Loss

- **Anti-Phospholipid Antibodies (APA)**

  Phospholipids are a main component of the cell membrane. Antibodies against phospholipids in the blood attach to the cell membrane. Positive APA is an autoimmune disorder that results in an increased blood clotting tendency that can cut off blood flow to the fetus. These antibodies can also cause the placenta to have a weak attachment to the uterine lining and may cause recurrent miscarriages.

  Cardiolipin is a phospholipid, a main component of cell membranes. It is essential for proper cell functions necessary for embryo development. Elevated levels of antibodies to cardiolipin are an autoimmune disorder that may interfere with the ability of cells to function normally, and have been associated with venous and/or arterial thrombosis (clotting), lower counts of blood platelets, and fetal loss.

  We test for 2 different forms of antibodies (IgM, and IgG) against the most common APA: anti-phosphatidylserine, anti-cardiolipin, and anti-$\beta_2$ glucoprotein antibodies. Next in significance are anti- phosphatidylethanolamine, anti-phosphatidylinositol, anti-prothombin, and anti-annexin antibodies followed by other less common antibodies such as anti-phosphatidic acid and anti-phosphatidylglycerol antibodies.

  - Anti-phosphatidylserine Antibodies (IgG & IgM)
  - Anti-phosphatidic Acid Antibodies (IgG & IgM)
  - Anti-phosphatidylglycerol Antibodies (IgG & IgM)
  - Anti-phosphatidylinositol Antibodies (IgG, IgM)
  - Anti-phosphatidylethanolamine Antibodies (IgG, IgM)
  - Anti-phosphatidylcholine Antibodies (IgG, IgM)
  - Anti-prothombin Antibodies (IgG, IgM)
  - Anti-annexin Antibodies (IgG, IgM)
  - Anti- $\beta_2$ glucoprotein Antibodies (IgG, IgM)
  - Anti-cardiolipin Antibodies (IgG, IgM)

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- **Anti-Nuclear Antibody Panel (ANA) (IgG & IgM)**

    - Anti-Histone antibodies
    - Anti-dsDNA antibodies
    - Anti-Jo-1 antibodies
    - Anti-La (SS-B) antibodies
    - Anti-Ro(SS-A) antibodies
    - Anti-Scl-70 antibodies
    - Anti-Sm antibodies
    - Anti-Sm/RNP antibodies

  Some autoimmune disorders result from the body forming antibodies that attack the different components of the nuclei of normal cells. These antibodies can destroy cells leading to disorders like lupus and rheumatoid arthritis, and cause recurrent pregnancy loss or infertility. The ANA antibodies cause inflammation in the body or in the uterus during implantation. Many women with high levels of these antibodies are unable to become pregnant or carry a pregnancy to term as a result.

  The anti-double stranded DNA (dsDNA) antibodies and the anti-histone antibodies measure the woman's immunological reaction to damaged DNA. When these are present in the blood, the woman's body may recognize her own embryos as foreign organisms and mistakenly trigger an immunological attack to eliminate the embryo.

- **Anti-thyroid peroxidase (TPO) Antibodies**

  Thyroid peroxidase is an enzyme present in the thyroid gland that is important to the production of thyroid hormones.

  Autoantibodies to thyroid peroxidase are produced by the body itself as an autoimmune disorder. TPO antibodies can attack the thyroid and damage thyroid function. The anti-thyroid peroxidase antibodies test (TPO) detects autoantibodies directed against the thyroid peroxidase (TPO) enzyme. A positive test for these antibodies indicates an increased risk for miscarriage.

- **Anti-thyroglobulin (Tg) Antibodies**

  Thyroglobulin is a protein found in the thyroid gland. Anti-thyroglobulin antibodies sometimes found in the bloodstream may attack the protein thyroglobulin. These antibodies can ultimately lead to the destruction of the thyroid gland. Anti-thyroglobulin antibodies can be found in women with infertility and recurrent miscarriages. The toxins released due to destruction of thyroglobulin during embryo implantation and gestation may cause failure of implantation and miscarriage.

- **Prothrombin Time (PT), activated Partial Thromboplastin Time (aPTT)**
  Prothrombin Time (PT) measures the extrinsic pathway of coagulation following damage to blood vessels. Activated Partial Thromboplastin Time (aPTT) measures the intrinsic pathway of coagulation.
  Both these tests are done in tandem and help determine the variety of factors involved in the normal blood clotting process and the pathway involved. Clotting factor disorders result either in longer clotting time and hemorrhage, or excessive clotting with thrombosis and micro emboli. Deficiencies have been associated with failed embryo implantations and recurrent pregnancy loss.

- **Clotting Factors (proteins essential for normal blood clotting)**

  - **Lupus Anticoagulant**

  Lupus is a systemic autoimmune disease that mainly affects women of non-European descent, where the body attacks its own cells. One component of the disease is a specific type of anti-phospholipid antibody in the bloodstream that can cause abnormal blood clotting. Lupus anticoagulant testing is used to help determine the cause of unexplained blood clotting and/ or recurrent pregnancy loss.

- **Reproductive Immuno Phenotype**

  This test looks at a broad range of immune cells that, when abnormally elevated, increase the risk of recurrent pregnancy loss (RPL). When elevated these cells may directly or indirectly mount an immune response against a developing embryo.

- **Natural Killer Cells functional activity**

  Natural Killer (NK) Cells are part of the immune system. 80% of white blood cells in the placenta are NK cells. Natural Killer cells are essential for implantation of the embryo. If activated, they have the ability to kill the trophoblast cells (the invading outermost layer of cells of the blastocyst that attaches the embryo to the endometrium). Raised numbers and excessive activity of NK cells in the blood and uterus may cause pregnancy loss and reduced IVF success rates due to interference with implantation and embryo survival during pregnancy.

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- **T Helper cells 1 T Helper cells 2**

  T helper cells are immune regulatory cells that secrete cytokines to mediate immune response. It has been established that TNFα and IFN γ (TH1) immunity is associated with reproductive failure at different stages of pregnancy.

  IL 4 and IL 10 (TH2) successful murine pregnancy occurs with TH2 dominance.

## T Helper Cells 1

### Tumor Necrosis Factor Alpha (TNFα)

Tumor Necrosis Factor alpha (TNFα), is an inflammatory cytokine produced by macrophages/monocytes, T cytotoxic and NK cell during acute inflammation and is responsible for a diverse range of signaling events within cells, leading to necrosis or apoptosis. The protein is also important for resistance to infection and cancers.

### Interferon Gamma (IFN-γ)

A primary role for IFN-γ is the activation of macrophages to increase phagocytosis, tumoricidal properties, and intracellular killing of pathogens. IFN-γ induces macrophage production of a variety of inflammatory mediators and reactive oxygen and nitrogen intermediates.

Interferon-γ (IFN-γ) plays a key role in activation of cellular immunity and subsequently, stimulation of antitumor immune-response. Based on its cytostatic, pro-apoptotic and antiproliferative functions, IFN-γ is considered potentially useful for adjuvant immunotherapy for different types of cancer

### Interleukin 2 (IL 2)

IL 2 Trigger cloning of CD 3+8+ (T Cytotoxic cells)

## T Helper Cells 2

**Interleukin 4 (IL 4)**
IL 4 is anti-inflammatory cytokines that function mainly by suppressing the pro-inflammatory milieu

**Interleukin 6 (IL 6)**
IL-6 is an anti-inflammatory cytokine required for controlling local or systemic acute inflammatory responses. IL-6 dictates the transition from acute to chronic inflammation by changing the nature of leucocyte infiltrate (from polymorphonuclear neutrophils to monocyte/macrophages).

**Interleukin 10 (IL 10)**
IL 10 downgrade inflammatory responses, dampens TH1 cytokines expression, and enhance CD 19 (B cells) activity enhancing antibody production. It maintains balanced immune response

- **Karyotyping (Chromosome Analysis)**

  Cells from the peripheral blood are cultured from both prospective parents for the purpose of checking the chromosome makeup. Abnormal karyotypes are a significant cause of recurrent miscarriage, or infertility. Abnormalities may be extra or missing chromosomes, translocations, deletions and inversions. Karyotyping can identify the abnormalities and determine the anatomical, physical and physiological manifestations associated with them.