



FERTILITY CENTER

*Pathway to Parenthood*

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## A GUIDE TO THE INTERPRETATION OF THE REPRODUCTIVE IMMUNOPHENOTYPE BLOOD TEST

### Introduction ▲

The reproductive immunophenotype is a specialized blood test done in the flow cytometer where eight of the most important white blood cell types are counted. Everyone has 30 different types of white blood cells (lymphocytes); however, disorders in the percentages of these eight cell types predict a future pregnancy loss, whether the person is an infertility patient preparing for assisted reproductive technologies or a patient who becomes pregnant and loses her pregnancy through miscarriage or does not become pregnant at all. This test was developed by me and you will find little reference material in the literature regarding this test.

**CD-3 (Pan T-Cells) 63-86% ▲** system is weak (suppressed) and normal when the immune system is healthy. Infertile patients and patients with recurrent pregnancy losses have values in the high normal range. These individuals have immune systems that are strong - even overactive. A strong overactive immune system is associated with a 5% incidence of autoimmune diseases for example, thyroiditis, lupus, rheumatoid arthritis.

### **CD-4 (T-Helper Cells) 31-53% ▲**

These cells are CD-3 lymphocytes and are essential for all lymphocytes to know what to do. They cannot function without the road map provided by the CD-4 T Helper cells. CD-4 cells are killed by the HIV virus and as a result the immune system falls into disarray. In women with infertility or miscarriage these cells are also high normal because they are helping the many CD3 Pan T cells. They are rarely low in number. If they are low, the patient needs a further immunological evaluation to study the etiology of this deficiency.

### **CD-8 (T-Cytotoxic-Suppressors) 17-35% ▲**

These cells are the referees of the Pan T and the T Helper interactions. They coordinate how strongly or how weakly the immune system reacts. In women with miscarriage and or infertility these cells are often on the low side. "They get tired arbitrating the hyperactive Pan T cells and the T Helpers." They are rarely high.

These three cell types comprise the 'engine' of the immune system. AIDS and immunological deficiencies affect these cell populations and as a result they are low in number. In patients with infertility and recurrent pregnancy losses, the CD3 and CD4 cells are usually high with the T- cytotoxic suppressors a little low from overwork.

### **CD-19 (B Cells) Normal Range 3-8% ▲**

These lymphocytes are plasma cells that produce antibody of all classes. What does this mean? IgM is the first antibody produced to anything that enters our body. This antibody stays in the blood and then as the immunity progresses it produces IgG (gamma globulin G) that resides in the lymph system. One IgM molecule has the immune capacity of 5 IgG molecules. IgG (Gamma globulin G) lives and repopulates itself in the lymph gland system. IgA (Gamma globulin A) is the last antibody made in an immune response and it resides in and protects the organs, skin and GI tract. When this antibody appears, it means that the immune response is completed and cannot go any further. When IgA responses (organ immunity) are present in any test for reproductive failure it usually means that the patient has an autoimmune process such as lupus, rheumatoid arthritis or other disorders.

CD-19 B cells are almost always high normal or very elevated in women with an immune cause for their infertility or recurrent pregnancy losses. There is often a greater than 12% elevation. This is one of the most important indicators of an immune problem and that the immune system is working overtime. Endometriosis also primes this system into greater hyper-reactivity.

### **CD56+ CD16+ Natural Killer Cells 3-12% ▲**

Natural Killer cells of this type are produced in the bone marrow and these cells produce a chemotherapy molecule called TNF (Tumor Necrosis Factor). This molecule is involved in eliminating cancer cells that may develop in normal individuals. Tumor Necrosis Factor also causes joint damage in women with rheumatoid arthritis. These Natural Killer cells are often elevated in women with infertility and recurrent miscarriage. The Tumor Necrosis Factor produced by these cells kills the rapidly dividing cells of the embryo and placenta often resulting in IVF or GIFT failure, blighted ovum or a chemical pregnancy where the BhCG elevates slightly and then quickly returns to non-pregnant levels. Normal levels for this cell population are 3-12%. The CD 56 and the CD16 molecules on the surface of these cells are special glue (adhesion) molecules that allow the Natural Killer Cells to attach to cancer, placental and embryonic cells. Once glued to the placental cell, it sprays Tumor Necrosis Factor on the cell and kills it.

### **CD 56+ Natural Killer Cells 3-12% ▲**

These Natural Killer (NK) Cells include CD56+/16+ Natural Killer Cells and CD56+ Natural Killer cells with lack of a CD16 molecule. Natural Killer Cells are activated by a pregnancy that fails or a fertilized embryo that degenerates. CD56+/16+ Natural Killer Cells are produced in the decidua and they are even more geared up to kill than those from the bone marrow. They produce large quantities of Tumor Necrosis Factor locally that kills the placental cells and the fetal cells. The normal range of CD56+ Natural Killer cells is 3-12%. Levels of 18% or greater correlate with a poor reproductive outcome.

## **Natural Killer Cell Assay** ▲

The Natural Killer research test simply separates NK cells from the patient and asks them to perform their aggressive roles in the test tube. Varying concentrations of IVIg are added to the test tube to determine how much is necessary to prevent killing.

## **CD3/IL-2R+ Cells Normal Range 0-5%** ▲

These are pan T (CD3) cells that become aggressive in women with an autoimmunity disease. They may rarely elevate in women with miscarriage and infertility. If they elevate over 5%, then the T cell recognition process is activated. These cells are always elevated in patients rejecting a kidney or a bone marrow graft. We have found that some women who may be developing an autoimmune disease or who have an autoimmune disease show elevations in these cells.

## **CD 19+/5+ (B-1 Cells) Normal Range 2-10%** ▲

When this population of cells is activated, they produce polyclonal antibodies to hormones, hormone receptors and neurotransmitters. The hormones most usually attacked by these antibodies are thyroid hormones, estrogens, progesterone, gonadotropins and growth hormone. Women with elevations of these cells may be at risk for thyroiditis and the premature menopause. Patients whose levels are 80-90% often stimulate poorly with gonadotropins. Women with high levels often complain of immunological symptoms when stimulated with gonadotropins. These symptoms include joint pain, finger stiffness, headache, lethargy, malaise, fever, depression and occasionally urticaria and hives. These cells like the CD 3/IL-2R+ cells are elevated in autoimmune disorders and in situations where a person is rejecting a bone marrow transplant from a compatible donor. There is no question that they are involved in early embryonic loss or damage.

## **Summary** ▲

These comments about the reproductive immunophenotype test should serve as a guide for nurses and other health care professionals to educate patients about abnormal and normal results. If further reading material is desired, this material can be provided by calling me at Acacio Fertility Center, (949) 249 9200.

The information contained in this article is not intended to be a medical diagnosis, treatment or medical advice in any way, as it is general information and cannot be relied on without consultation with your physician. It is not intended nor is it implied to be a substitute for professional medical advice. As medical information can change rapidly, we strongly encourage you to discuss all health matters and concerns with your physician before embarking on new diagnostic or treatment strategies.

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*This handout is intended as an aid to provide patients with general information. As science is rapidly evolving, some new information may not be presented here. It is not intended to replace or define evaluation and treatment by a physician.*