

## Short Communication

# The role of fetal microchimerism in autoimmune disease

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**Abstract:** Fetal microchimerism occurs in normal human reproduction and is a relatively new discovery in biology. Recent data in the scientific and medical literature indicates that some of the autoimmune diseases that show a predilection for women in their child-bearing years and beyond are linked to fetal microchimerism from previous pregnancies. The pathological role of fetal microchimeric progenitor immature T cells in autoimmune disease in women is explored. Fetal microchimerism is increased in women who had a termination of pregnancy and may be associated with the development of autoimmune disease later on in life. Furthermore, the consistently rising incidence of autoimmune diseases in women over the past four decades may be attributed to the increase in the utilization of abortion.

**Keywords:** Microchimerism, autoimmune disease, abortion, pathophysiology

## Introduction

Fetal microchimerism, which can be thought of as a form of trans-placental stem cell transplant, is becoming a plausible and unifying biological entity that helps to explain the etiology, the large diversity of tissue pathology, the predilection for females and the yearly increase in the incidence of autoimmune diseases in women. During their reproductive and post-reproductive years, women have a greater propensity than men to develop any one of a large variety of chronic autoimmune diseases. Autoimmune diseases are characterized by: (1) being the third most common category of chronic diseases after cancer and heart disease, (2) affecting 5% to 8% of the population, (3) having had for decades an unexplainable increasing incidence, (4) having the potential of affecting virtually any tissue in the body, (5) comprising over 80 different autoimmune diseases and (6) being predominately thyroid diseases and rheumatoid arthritis, which together comprise over 65 percent of the total incidence of all autoimmune diseases [1-6].

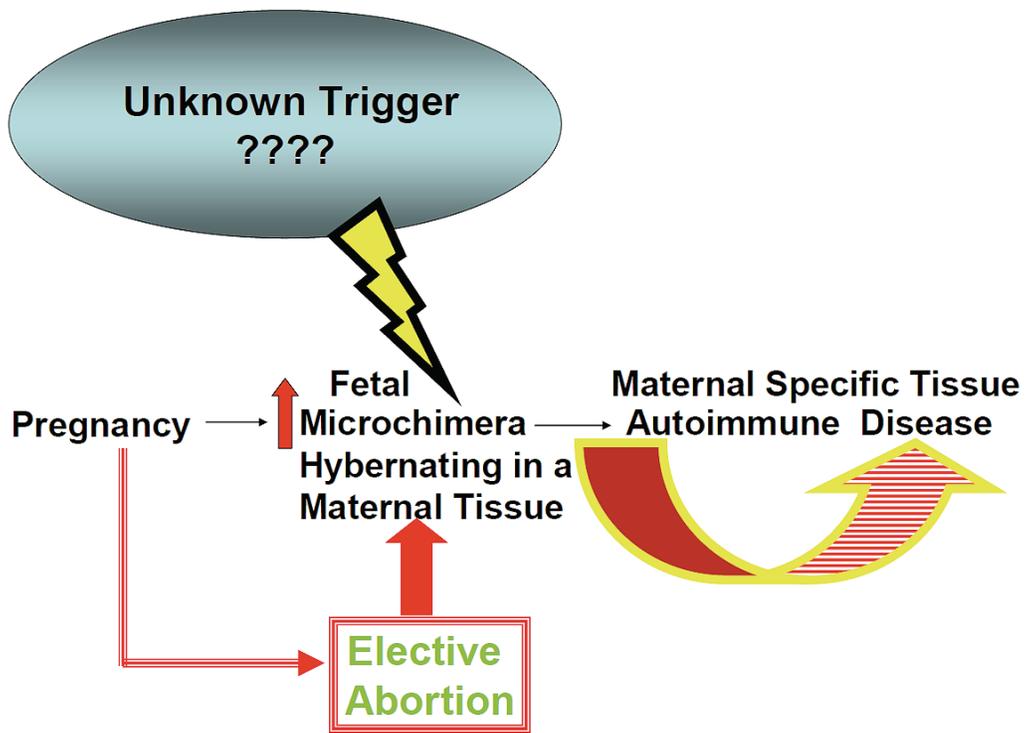
## Materials and method

The following databases were searched for

articles related to microchimerism, autoimmune disease, abortion and pathophysiology: Web of Science, PubMed, Google.

## Fetal microchimerism

Initial publications of the relatively recent discovery of fetal microchimerism occurred in the late 1970's [7]. Fetal microchimerism is the transfer of intact living fetal cells from the fetal circulation into the maternal circulation and occurs in all pregnancies and increases with gestational age [8-10]. Microchimerism can be portrayed as a legacy of pregnancy that persists for decades via fetal cell engraftment in maternal bone marrow or other tissues [11-14]. The process of microchimerism is bidirectional and the transfer of maternal cells into the fetal circulation is known as maternal microchimerism [15,16]. Transfer of fetal hematopoietic pluripotent progenitor cells begins in the fourth or fifth week after fertilization and continues throughout the pregnancy [17-22]. The presence of fetal microchimeric cells can be detected for up to 30 days in the maternal postpartum blood stream [23]. Fetal microchimeric cells of male embryos/fetuses can be selectively detected and magnified by assaying for the presence of the Y-chromosome-containing cells among a



**Figure 1.** Elective abortion increases the degree of fetal microchimerism which favors the development of autoimmune disease in post-abortion women.

large number of maternal cells marked by XX chromosomes [24,25]. More microchimeric cells are transferred after surgical abortions than after spontaneous abortions [23]. Male fetal cells have been demonstrated in both maternal synovial tissue and skin of patients with rheumatoid arthritis and in the skin and blood of women with systemic sclerosis [26-28]. Fetal cells were also shown to proliferate in consecutive cell cultures and were detected in maternal tissues as long as 27 years postpartum [29]. Fetal microchimerism occurs with either male and female embryos and fetuses but because of the uniqueness of the Y chromosome, detection of male microchimerism in maternal tissue is easier to detect. The extremely small number (5 to 10 embryo/fetal microchimeric cells) in pregnancies bearing male embryos/fetuses among millions of maternal cells can be detected [26,30]. The techniques of either polymerase chain reaction or fluorescent in situ hybridization passages demonstrated stem-cell-like properties of microchimeric cells from male embryos/fetuses [26,30,31].

**Fetal microchimerism and the increased incidence of auto-immune disease**

In the late 1990's the discovery of fetal microchimeric cells in maternal tissues led to the finding of a positive association between fetal microchimerism and autoimmune diseases in women [27,32-43]. Progenitor cells of the fetal immune system, such as immature T cells, along with T and B lymphocytes, monocytes, macrophages and NK cells, are among the different fetal cell types that ultimately can be transferred to maternal tissues. Within maternal tissues the fetal microchimeric progenitor immature T cells, also known as CD4 cells, are capable of self-renewal, proliferation, differentiation and activation. Activation of progenitor cells can result in the production of paracrine and autocrine inflammatory cytokines and chemokines that are involved in autoimmune diseases. Clones of these types of hibernating cells are involved in a form of graft-vs-host reactions seen in some autoimmune diseases [44,24,45]. The role of fetal microchimerism in transplant tolerance has remained an enigma

[46,47].

Activation of hibernating fetal microchimeric cells have been postulated to result in the initiation of an autoimmune disease. Unknown triggering agents that activate these fetal microchimeric immune cells to attack the maternal host cells resulting in an autoimmune disease, have not yet been definitely identified [48]. Viral, bacterial agents, drugs or abnormal local tissue proteins that can serve as an antigen are among the suspected triggers. Microchimerism may also contribute to the risk of an autoimmune disease by providing HLA susceptibility alleles [49]. Microchimerism in affected tissues is more likely to be demonstrable in women with autoimmune disease than in women with non-autoimmune diseases [50]. Fetal microchimerism has been demonstrated in Hashimoto's thyroiditis and Graves's Disease but found to be absent in normal thyroids [51-53].

#### Post-abortion and the incidence of fetal microchimerism

There is an increased fetal-to-maternal transfer of fetal undifferentiated progenitor cells during an abortion procedure as the placenta is being destroyed [54-56]. The amount of fetal DNA found in maternal circulation following a first-trimester abortion was found to be higher in women who underwent a surgical abortion than in women who had a chemical abortion [23]. The phenomenon of increased fetal cell trafficking following a medical abortion was also confirmed in a murine model [57]. Since the embryonic circulatory system is established in the first trimester of pregnancy, there is a greater probability for the transfer of a larger number of hematopoietic progenitor T cells during a first trimester termination of pregnancy [58,24]. Furthermore, fetal loss in elective abortions is accompanied with the loss of suppression of the maternal immune system by Early Pregnancy Factor, which may be another factor in the setting the stage for the future development of autoimmune disease [50]. Thus, women who had an elective abortion in either the first or second trimester have a greater risk for fetal microchimerism and the risk of developing an auto-immune disease for the rest of their lives (**Figure 1**). Animal experimentation and collection of human data will be necessary to sort out the underlying relationship between fetal microchimerism and specific autoimmune

diseases in women.

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