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The Connection Between Chronic Endometritis and Recurrent Miscarriage

How a "silent" inflammatory condition is disrupting healthy pregnancies.

Chronic Endometritis - a "Silent" Inflammatory Condition

Chronic endometritis is a unique gynecologic disease characterized by inflammation involving the endometrium.

This issue is largely caused by an inciting factor - such as endometriosis, or a pelvic infection - that results in a chronic, inflammatory insult to the endometrial tissue.

The endometrium is the functional lining of the uterus and is necessary for pregnancy. A healthy endometrial environment is a prerequisite for reproductive success. Accordingly, any disruption within the endometrial environment could potentially impact human fertility.

It has been postulated that chronic endometritis may lead to infertility, miscarriage, and other reproductive issues by interfering with endometrial receptivity given the disease is characterized by disruption of the uterine microenvironment.

Unfortunately, chronic endometritis is often a "silent" reproductive factor given it can not be identified via conventional infertility investigations - such as ultrasound and hysterosalpingography - resulting in a potential blindspot for couples experiencing fertility problems.

There is currently no standardized definition for chronic endometritis, but the condition is often described as the presence of plasma cells (a type of immune-related white blood cell) detected on an endometrial biopsy.

But this condition can also be visualized with the aid of hysteroscopy - a procedure in which a small camera is inserted into the uterine cavity and the endometrium directly evaluated.

Specific signs of endometrial inflammation seen at the time of a hysteroscopic evaluation include micro-polyps, edema, and hyperemia. Studies have shown that this type of visual evaluation of the endometrial tissue is reliable in diagnosing chronic endometritis.

In addition, recent literature has described a visual-scoring system that can be calculated at the time of a hysteroscopic evaluation. This scoring framework can then be used to

accurately characterize the extent of the disease, and also evaluate a woman's response to treatment.

Symptoms of chronic endometritis include brown bleeding with menstrual flow, intermenstrual bleeding, infertility, miscarriage, endometrial polyps, and artificial reproductive technology failure.

For example, one study revealed 30% of couples experiencing repeat implantation failure, often defined as three failed in vitro fertilization treatments, were diagnosed with chronic endometritis.

Given its potential impact on human fertility, one must have a high index of suspicion for the presence of chronic endometritis in women presenting with reproductive and gynecologic issues.

Chronic Endometritis, Recurrent Miscarriage, and Endometrial Infection

Recurrent miscarriage is defined as having 3 or more miscarriages before 20 weeks' of pregnancy, and this important reproductive issue has been shown to affect up to 3% of all couples.

A conventional evaluation for recurrent miscarriage often includes the evaluation of genetic issues, antiphospholipid syndrome, endocrine disorders, and uterine abnormalities.

Unfortunately, 50% of couples are eventually diagnosed with "unexplained" recurrent miscarriage - meaning after such a conventional reproductive evaluation there remains no obvious reason for their repetitive pregnancy losses.

Yet, chronic endometritis is a known inflammatory condition impacting the endometrium and is related to reproductive issues making it an important factor to consider when evaluating couples with fertility concerns.

For example, research reveals chronic endometritis can impact up to 57% and 67% of couples experiencing infertility and recurrent implantation failure; respectively.

Most recently, an important study performed by Cicenelli et al. found approximately 58% of women with recurrent miscarriage had chronic endometritis on hysteroscopic evaluation. Of these women, 68% had positive endometrial cultures - highlighting the direct association between chronic endometritis, endometrial infection, and recurrent miscarriage.

Potential Benefit of Chronic Endometritis Treatment

Given an endometrial infection is a known cause of chronic endometritis, several studies have evaluated the benefit of treating these infections with an appropriate course of antibiotics.

McQueen et al., in a 2014, first-of-its-kind study, assessed the prevalence of chronic endometritis and subsequent live birth rates in women with recurrent miscarriage and fetal demise. The study found a 9% incidence of chronic endometritis on endometrial biopsy. These results, the authors advocated, suggest an endometrial biopsy should be included as an essential part of the evaluation of couples struggling with these reproductive issues. In addition, the authors found encouraging live birth rates following treatment of chronic endometritis.

Gay et al., in a 2021 study further evaluated live birth rates in women with chronic endometritis and recurrent miscarriage following a course of antibiotic treatment. The authors

found a significant improvement in the live birth rates among those women treated for chronic endometritis.

Finally, Cicinelli et al. evaluated women with chronic endometritis and a history of recurrent miscarriage treated with antibiotics. They found women achieving complete resolution of chronic endometritis - as determined by repeat hysteroscopic evaluation, biopsy and culture - had significantly higher pregnancy rates. This study confirmed an improvement in reproductive outcomes following appropriate chronic endometritis treatment and confirmed resolution.

True Health Matters **Summary**

Chronic endometritis is an inflammatory condition related to various reproductive and gynecologic issues. Unfortunately, chronic endometritis is often a “silent” reproductive factor given it can not be identified via a conventional infertility investigation. Research shows chronic endometritis is directly related to infection within the endometrial tissue, and is associated with recurrent miscarriage at a high rate. Given appropriate antibiotic treatment can improve reproductive success - evaluating chronic endometritis is important when supporting couples experiencing fertility-related issues including recurrent miscarriage.

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