



PATIENT'S FACT SHEET

Recurrent Pregnancy Loss

Recurrent pregnancy loss is a disease* distinct from infertility, defined by two or more failed pregnancies. When the cause is unknown, each pregnancy loss merits careful review to determine whether specific evaluation may be appropriate. After three or more losses, a thorough evaluation is warranted. Although approximately 25% of all recognized pregnancies result in miscarriage, less than 5% of women will experience two consecutive miscarriages, and only 1% experience three or more. Couples who experience recurrent pregnancy loss may benefit from a medical evaluation and psychological support.

Genetic/Chromosomal Causes. A chromosome analysis performed from the parents' blood identifies an inherited genetic cause in less than 5% of couples. Translocation (when part of one chromosome is attached to another chromosome) is the most common inherited chromosome abnormality. Although a parent who carries a translocation is frequently normal, their embryo may receive too much or too little genetic material. When this occurs, a miscarriage usually occurs. Couples with translocations or other specific chromosome defects may benefit from pre-implantation genetic diagnosis in conjunction with in vitro fertilization.

In contrast to the uncommon finding of an inherited genetic cause, many early miscarriages are due to the random (by chance) occurrence of a chromosomal abnormality in the embryo. In fact, 60% or more of early miscarriages may be caused by a random chromosomal abnormality, usually a missing or duplicated chromosome.

Age. The chance of a miscarriage increases as a woman ages. After age 40, more than one-third of all pregnancies end in miscarriage. Most of these embryos have an abnormal number of chromosomes.

Hormonal Abnormalities. Progesterone, a hormone produced by the ovary after ovulation, is necessary for a healthy pregnancy. There is controversy about whether low progesterone levels, often called luteal phase deficiency, may cause repeated miscarriages. Treatments may include ovulation induction, progesterone supplementation or injections of human chorionic gonadotropin (hCG), but there is no evidence to support the effectiveness of these treatments.

Metabolic Abnormalities. Poorly controlled diabetes increases the risk of miscarriage. Women with diabetes improve pregnancy outcomes if blood sugars are controlled before conception. Women who have insulin resistance, such as obese women and many who have polycystic ovarian syndrome (PCOS), also have higher rates of miscarriage. There is still not enough evidence to know if medications that improve insulin sensitivity lower miscarriage risks in women with PCOS (see Fact Sheet "Insulin Sensitizing Agents").

Uterine Abnormalities. Distortion of the uterine cavity may be found in approximately 10% to 15% of women with recurrent pregnancy losses. Diagnostic screening tests include hysterosalpingogram, sonohysterog-

raphy (See Fact Sheets "Hysterosalpingogram," and "Saline Infusion Sonohysterography"), ultrasound, or hysteroscopy. Congenital uterine abnormalities include a double uterus, uterine septum, and a uterus in which only one side has formed. Asherman's syndrome (scar tissue in the uterine cavity), uterine fibroids, and possibly uterine polyps are acquired abnormalities that may also cause recurrent miscarriages. Some of these conditions may be surgically corrected.

Antiphospholipid Syndrome. Blood tests for anticardiolipin antibodies and lupus anticoagulant may identify women with antiphospholipid syndrome, a cause for 3% to 15% of recurrent miscarriages. A second blood test performed at least 6 weeks later confirms the diagnosis. In women who have high levels of antiphospholipid antibodies, pregnancy outcomes are improved by the use of aspirin and heparin.

Thrombophilias. Inherited disorders that raise a woman's risk of serious blood clots (thrombosis) may also increase the risk of fetal death in the second half of pregnancy. However, there is no proven benefit for testing or treatment of women with thrombophilias and recurrent miscarriage in the first half of pregnancy.

Male factor. Increasing evidence suggests that abnormal integrity (intactness) of sperm DNA may affect embryo development and possibly increase miscarriage risk. However, these data are still very preliminary, and it is not known how often sperm defects contribute to recurrent miscarriage.

Unexplained. No explanation is found in 50% to 75% of couples with recurrent pregnancy losses.

Tests with no proven benefit for recurrent miscarriage include cultures for bacteria or viruses, tests for insulin resistance, antinuclear antibodies, antithyroid antibodies, maternal antipaternal antibodies, antibodies to infectious agents, and embryotoxic factors.

Treatments with no proven benefit include leukocyte (white blood cell) immunization and intravenous immunoglobulin (IVIG) therapy.

Conclusion. A couple may be comforted to know that the next pregnancy is successful in 60% to 70% of those with unexplained recurrent pregnancy losses. A healthy lifestyle and folic acid supplementation is recommended before attempting another pregnancy. Smoking cessation, reduced alcohol and caffeine consumption, moderate exercise, and weight control may all be of benefit. Counseling may provide comfort and help cope with the grief, anger, isolation, fear, and helplessness that many individuals experience after repeated miscarriages.

* Disease is "any deviation from or interruption of the normal structure or function of any part, organ, or system of the body as manifested by characteristic symptoms and signs; the etiology, pathology, and prognosis may be known or unknown." From: *Dorland's Illustrated Medical Dictionary*, 31st edition, 2007:535.

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