genea
WORLD LEADING FERTILITY

Miscarriage Fact Sheet

What is miscarriage?

Miscarriage is the spontaneous loss of a pregnancy before 20 weeks. The majority of miscarriages cannot be prevented. While the causes of many miscarriages are unexplained, more than half will occur because of a chromosomal issue affecting the developing fetus. Nothing can stop a miscarriage from occurring in these cases.

The loss of a pregnancy through miscarriage can be heartbreaking for women and couples.

While it may be of little comfort to learn, miscarriage is sadly very common, with one-in-five pregnancies ending in miscarriage before 20 weeks. The vast majority of these occur in the first 12 weeks, known as the first trimester.

It is thought this rate could be even higher as some women miscarry before they know for certain they are pregnant.

There is evidence that the rate of miscarriage increases with age.

Most women who miscarry will go on to conceive again and deliver a healthy baby.

As devastating as any miscarriage is, if it is an isolated incident, a miscarriage can provide some hope that a person or couple can become pregnant, even if it follows a period of infertility.

However, in some cases women will experience more than one miscarriage. This is called recurrent miscarriage and sadly is also quite common. In fact, about one in 20 women will experience two miscarriages in a row.

It is recommended that if a woman has two or more miscarriages, further investigation is warranted, preferably with a Fertility Specialist who has expertise in miscarriage management.

What causes a miscarriage?

Most women and couples who suffer a miscarriage, desperately want to know the cause. Unfortunately, there are a number of reasons why a miscarriage may have occurred, and the reason is not always straightforward.

While it's worthwhile investigating to see if there is an underlying cause, a medical explanation will not be found in 50 per cent of cases. For those women who have an unexplained miscarriage, the likelihood of a successful pregnancy, resulting in the birth of a healthy baby, is not that different to the overall chance of success based on the woman's age.

Common causes of miscarriage

Among the most common causes of miscarriage are:

- chromosomal issues
- abnormalities of the uterus or cervix
- blood clotting disorders (thrombophilias)
- autoimmune conditions
- hormonal disorders
- certain severe infections
- certain medical conditions, such as diabetes or thyroid conditions
- genetic abnormalities
- age
- lifestyle factors, such as smoking and excessive alcohol consumption
- recreational drug use.

Chromosomal changes (aneuploidy)

Chromosomes are tiny threadlike structures found inside the nucleus of cells. Normal human cells contain 46 chromosomes, of which half are inherited from each parent. Each chromosome carries genes that define a person's physical characteristics, such as eye colour.

Aneuploidy is when there are missing or extra chromosomes, or segments of chromosomes in each cell.

Aneuploidy can occur randomly in the early stages of embryo development, which may result in a baby born with developmental and health problems. This is the most common reason for embryos to either not implant, or to miscarry. A common chromosomal condition is trisomy 21, also known as Down syndrome, which occurs when there is an extra copy of chromosome 21 in all cells.

It is estimated that 50 per cent of first trimester miscarriages are linked to aneuploidy.[1] Nine out of 10 of these pregnancies will not survive past 12 weeks.

The chance of a pregnancy being aneuploid increases based on:

- Maternal age
- A parental chromosome rearrangement called a balanced translocation.
- A previous pregnancy with a chromosome issue.

Most of the time it is a result of a one-off, random occurrence and will not happen again with subsequent pregnancies.

Occasionally though, it is the result of rearrangements in the mother or father's chromosomes. This is called a balanced translocation.

Balanced translocations

Some individuals have part of one chromosome swapped over with part of another chromosome. This is called a balanced translocation. People with a balanced translocation are healthy as they have all the necessary genetic information, just in a slightly different arrangement. However, when we pass on our chromosomes into our eggs or sperm, a balanced translocation carrier has a higher chance of passing on an unbalanced amount of chromosomes. This can lead to miscarriage, or a pregnancy with a health issue.

If a translocation is suspected as the cause for recurrent pregnancy loss, both parents can be tested via a test called a karyotype. If confirmed that a translocation is causing an increased chance for miscarriage, there are several options available.

You can continue to try to get pregnant naturally, knowing the risk of miscarriage is greater.

There is also the option of getting pregnant naturally and having prenatal diagnosis (CVS or amniocentesis) or non-invasive prenatal screening (NIPT) from around 12 weeks of pregnancy.

These are accurate options but may need you to make decisions as to whether you would continue the pregnancy if the chromosomes are reported as unbalanced (aneuploid).

Pre-implantation genetic testing

One option to reduce the chance of miscarriages caused by a translocation is Pre-implantation Genetic Testing for Structural Rearrangements (PGT-SR).

This involves undergoing IVF and having the resulting embryos tested in the laboratory. This will allow you to avoid using embryos with unbalanced chromosomes, therefore significantly increasing the chances of an ongoing pregnancy and birth of a healthy baby.

PGT is also an option for anyone (those without a balanced translocation) who are having IVF and would like to screen the chromosomes of embryos before transferring, to reduce the chance of miscarriage caused by random chromosome changes that can occur by chance. This is called Pre-implantation Genetic Testing - Aneuploidy (PGT-A).

Uterine abnormalities

There are several physical abnormalities of the uterus that are linked to pregnancy loss. Most can be treated with surgery and fall under two categories:

- Congenital abnormalities – These are defects that have been present in the uterus since birth. An example of this is septate uterus, which occurs when the uterus is divided into two parts by a membrane.
- Uterine fibroids (leiomyomata) – These are benign (non-cancerous) growths made up of muscle and tissue.

Hormonal disorders

There are a number of hormonal disorders that are commonly associated with recurrent pregnancy loss.

- **Progesterone** – Women who suffer recurrent miscarriage are often found to have low levels of the hormone progesterone. Low progesterone levels in early pregnancy reflect that the pregnancy has not implanted successfully in the uterine lining, rather than that the developing placenta is not producing enough progesterone to maintain the pregnancy. Because it is thought low progesterone is the effect, not the cause of miscarriage, this explains why giving women progesterone and/or hCG hormone injections in early pregnancy won't help avoid a miscarriage. However, there may be some benefit in giving progesterone to women suspected of having immune problems.
- **Follicle Stimulating Hormone** – Follicle stimulating hormone (FSH) drives the ovaries to start growing follicles. Some women with a history of pregnancy loss are found to have high FSH levels because their ovaries have become prematurely menopausal, resulting in lower egg quality. Very low levels of another hormone, AMH, also reflect that a woman is not producing enough eggs.
- **Thin uterine lining (the endometrium)** – The lining of the uterus plays a very important role, and some women will have thinner than normal endometrium lining, which makes it difficult for an embryo to implant. A thin lining represents a hormone issue and can be the result of scarring (e.g. from a previous curette). Currently, the only way to determine how an endometrium will respond to implantation is to take a sample and look at the tissue under a microscope. An endometrial biopsy is no more uncomfortable than a cervical screening test. Low oestrogen levels are one cause of a thin uterine lining and might be treatable with hormone therapy.
- **Polycystic Ovarian Syndrome (PCOS)** – Women with a history of recurrent miscarriage are sometimes found to be suffering from PCOS. This common condition affects about one-in-10 women in Australia and can be diagnosed with a pelvic ultrasound. It causes a range of symptoms, including multiple small cysts on the ovary or ovaries. PCOS is sometimes associated with hormonal imbalances such as increased production of luteinising hormone (LH) and testosterone, which may increase the risk of miscarriage.

Immune disorders

The immune system is designed to recognise and attack foreign substances within the body. Immune disorders in relation to implantation and miscarriage are the subject of much speculation and active research.

One of the most common autoimmune disorders that affect pregnancy is antiphospholipid antibodies (ANA).

Blood clotting disorders (thrombophilias)

There are several blood clotting disorders (thrombophilias) that can cause miscarriage.

Such disorders can be genetic (inherited from parents) or acquired (developed).

Antiphospholipid antibodies cause the blood to clot more easily and effectively, causing a blockage in the forming placental blood vessels. The two most important types of antiphospholipid antibodies are lupus anticoagulant and anticardiolipin antibodies.

Antiphospholipid syndrome is a blood clotting disorder associated with repeated miscarriage.

Environment and lifestyle factors

Research has uncovered a number of risk factors for miscarriage. Miscarriage is more common in older women because chromosomal abnormalities become more likely as women age. The risk of miscarriage may be increased in pregnant women who:

- Smoke
- Use illegal drugs
- Are exposed to high levels of radiation or other toxic agents
- Drink alcohol
- Consume more than 500mg of caffeine a day.

Miscarriages in early pregnancy are NOT caused by:

- Exercising
- Travelling
- Sex
- Birth control
- Morning sickness
- Stress or worry
- A fall or fright

Please speak to your Fertility Specialist about your individual circumstances.

Support is also available through The Pink Elephants support network; pinkelephants.org.au

[1]Simpson JL. Clin Obstet Gynecol 2007;50(1):10–30