The Miscarriage Association

Acknowledging Pregnancy Loss

Investigations following recurrent miscarriage

If you would like general information or to talk to someone else who has experienced recurrent miscarriage and can offer understanding and support, please contact:

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Introduction

One in one hundred couples trying for a baby experiences recurrent miscarriage, usually defined as three or more miscarriages in a row. This leaflet aims to outline some of the investigations which may be carried out at that time. Although this leaflet is written for both partners, the term "you" will generally be used to mean the female partner.

Why investigate only after three miscarriages?

Many couples who have been through a miscarriage are anxious to find out why it happened, especially if that information can improve their chances of success in their next pregnancy. Most, however, will not be offered investigations after a single miscarriage, or even two. Although this can be distressing, this is because most women who have one or two miscarriages will go on to have a healthy pregnancy next time. This suggests that their miscarriages were due to chance rather than to an underlying cause.

If a couple has had three or more consecutive miscarriages, statistics show that there is more likely to be an underlying cause or causes and so tests are usually offered at this point. This does not necessarily mean that a cause or causes will be found. Although we are learning more about the causes of miscarriage, there is much that is still unknown.

If you do undergo investigations for recurrent miscarriage, it is possible, therefore, that many of the tests performed will be reported as normal and a clear cause for the miscarriages will not be found. This can be frustrating both for you and for the staff involved, although it does mean that there is a very high chance of the next pregnancy being successful. If a problem **is** identified, there is still a good chance of having a successful pregnancy.

What investigations will be offered?

This list includes tests which may be offered.

- Chromosomal analysis: (a) of blood from both parents (karyotype)
  (b) of the baby (fetal karyotype)
- Lupus anticoagulant and anticardiolipin antibodies (antiphospholipid antibodies)
- Other immunological investigations
- Hormonal blood tests
- Investigations of the anatomy of the uterus (womb) and cervix
- Tests for infection
- Research investigations

Chromosomal analysis or karyotype: parents

What are chromosomes?

Chromosomes carry the genetic information for each individual. Everyone has 23 pairs of chromosomes, making 46 in all. All but one pair are identical in men and women. The 23rd pair – the sex chromosomes – decide the individual's gender and are therefore different. Men normally have one X and one Y chromosome and women have two X chromosomes. A baby inherits half of its chromosomes from its mother and half from its father.

How can chromosomes cause a problem?

About half of all miscarriages occur as a result of a chromosomal abnormality in the baby or fetus. In most cases where this abnormality causes miscarriage, the problem is not passed on from a parent, but happens when the egg and sperm meet, or early in the development of the fertilised egg.

Between three and five percent of couples with recurrent miscarriage have a problem with a chromosomal abnormality called a **balanced translocation**. In this situation, part of the information from one chromosome is replaced by that of another chromosome. Although this doesn't cause a problem to the affected parent, it can be passed on to the baby and cause an **unbalanced** translocation, where some genetic information is present twice and some is missing. This can lead to miscarriage.
The Miscarriage Association can provide a leaflet on balanced translocation.

Testing

Chromosomal analysis involves taking a blood test from both the man and the woman and sending the samples to a genetics laboratory. The results can take between four and six weeks to obtain, as the cells have to be specially processed before they can be examined under the microscope.

Treatment

There is no treatment which can alter the chromosomes in an individual if they are already abnormal. If the analysis shows that you or your partner carry an abnormality, then you will be offered specialist genetic counselling to give you more information and help you decide about future pregnancies.

Chromosomal analysis of the baby: fetal karyotype

Your clinic may offer to carry out chromosomal analysis of fetal tissue, although this can depend on the laboratory facilities available. It involves sending tissue from the miscarriage to the genetics laboratory where it undergoes the same process as for blood. Unfortunately a result is obtained only in approximately half of cases.

It takes about six to eight weeks or more to obtain the results. If the result is abnormal, but both parents have a normal chromosome pattern, then the abnormality in the baby is unlikely to recur in a subsequent pregnancy.

Tests for lupus anticoagulant and anticardiolipin antibodies

What are these?

An antibody is part of the body's defence mechanism. Lupus anticoagulant (LA) and anticardiolipin antibodies (aCL) are part of a larger group of antibodies called antiphospholipid antibodies. An abnormally high level of these antibodies is found in about 15% of women who experience recurrent miscarriage, and is called antiphospholipid syndrome (APS) or Hughes syndrome. (You may also hear it called "sticky blood syndrome".)

How can these antibodies cause a problem?

It may be that they affect the blood supply in the placenta or that they cause abnormal implantation of the placenta in the wall of the uterus (womb). More research is needed in order to identify exactly how these antibodies cause pregnancy problems.

Testing

Investigations involve taking a blood sample from the female partner to identify if the antibodies are present. In order to establish a clear diagnosis of antiphospholipid syndrome it is essential to have two positive tests, taken at least six weeks apart.

Treatment

Treatment is usually with low dose aspirin (75mg daily), starting before conception or early in pregnancy. Your doctor may also recommend injections of low molecular weight heparin once you are pregnant and the baby's heartbeat has been seen on scan.

You may find it helpful to read The Miscarriage Association leaflet *Antiphospholipid syndrome and pregnancy loss.*

Other immunological investigations

The following tests are less routine, but your doctor may suggest that they are appropriate for you.

Antithrombin III, protein S, protein C, activated protein C resistance (APCR), and factor V Leiden

It is still not clear whether these factors are linked to miscarriage, but some units test for these at the same time as testing for lupus anticoagulant and anticardiolipin antibodies. If you have an abnormal result, you may be advised to take low dose aspirin. More research is still needed to identify whether this treatment is helpful.

Hormonal blood tests

Luteinising Hormone (LH)

What is this?

LH is a hormone produced by the pituitary gland in the brain. It stimulates a follicle in the ovary containing the egg to burst and release the egg, which then travels from the ovary to the uterus.

How can LH cause a problem?

In the condition called **Polycystic Ovary Syndrome (PCOS)**, there are usually many small cysts in the ovaries. It is not known why some women have this condition. The incidence of polycystic ovaries is higher in women with recurrent miscarriage and approximately half of these women will produce abnormal amounts of luteinising hormone. Women with high LH levels may find it harder to conceive and are more likely to miscarry when they do conceive. They may also experience problems associated with polycystic ovaries, such as irregular periods, greasy skin and increased body weight.

Testing

LH levels can be measured in the blood, with the test usually taken between days 2 and 5 of the menstrual cycle. Polycystic ovaries can also be diagnosed by an ultrasound scan.

Treatment

Despite continuing research into high LH levels and PCOS, there is still no clear and tested treatment for either condition. However, some women may be offered treatment as part of a research trial.

Progesterone and hCG

Treatment with progesterone and hCG has been tried in an attempt to maintain pregnancy by boosting hormone levels. The scientific evidence is mixed, but your doctor may feel that this treatment is appropriate. More research is being carried out in this area.

Other hormone and endocrine tests

Some tests performed as part of hospital protocols have never been conclusively linked to miscarriage, unless the levels are very abnormal, and in these cases you would have other symptoms. However, they may still be carried out in some clinics. They include:

Thyroid Function Test

What is this?

The thyroid gland is situated in the neck and produces essential hormones.

How can the thyroid cause a problem?

It used to be thought that a thyroid hormone imbalance could cause

miscarriage, but there is no evidence for this unless the condition is very severe. In this case, however, the symptoms of the thyroid problem would almost certainly have already been investigated and the problem diagnosed.

Testing

Your doctor will take a blood test if there is any suspicion that the level of hormone produced by your thyroid gland is abnormal.

Blood sugar level

Diabetes is not in itself a risk factor for miscarriage, but women whose diabetes is poorly controlled have an increased risk of miscarriage. A routine test for diabetes is not usually performed unless there are symptoms of the condition or a strong family history.

Investigation of the uterus (womb)

It is thought that some cases of miscarriage, especially in later pregnancy, may be due to an abnormal or irregularly-shaped uterus. Sometimes the uterus has an extra wall down its centre, which makes it look as if it is divided into two **(bicornuate or septate uterus)** or it may have only developed one half **(unicornuate uterus)**. It is not clear if such problems cause recurrent miscarriage, but they can be identified in the following ways:

Hysterosalpingogram (HSG)

This investigation is performed to assess the shape of the uterine cavity and to check if the fallopian tubes are open. It is essential that you are not pregnant when this investigation is carried out, as it involves X-rays. Each individual hospital will have its own protocol for ensuring it is arranged safely for you. The test usually takes place in the X-ray department and takes about ten minutes to perform.

Ultrasound

It is sometimes possible to see abnormalities inside the uterus at the time of a scan, especially a vaginal scan. A scan will also enable the ovaries to be examined at the same time. Occasionally **polycystic ovaries** are diagnosed by ultrasound scan (see above).

Some units will offer a scan and an examination of the inside of the uterus at the same time – **saline installation sonography (SIS)**. A small plastic tube is passed through the cervix and a water-like solution injected through it. The scan can determine whether there is any abnormality inside the uterus.

Hysteroscopy

This investigation allows the doctor to see the shape of the uterus and to examine its lining. A very thin telescope is inserted into the womb through the cervix under local or general anaesthetic.

MRI scan
Some units assess the shape of the uterus by MRI (Magnetic Resonance Imaging) scan rather than the above investigations.

Investigation of the cervix

Cervical Resistance Test

This test is sometimes performed if the doctor thinks that there is a weakness of the cervix. There has usually been a history of losing a pregnancy after the first 14 weeks, with a rapid labour and rupture of the membranes. This condition may be called **cervical incompetence** or **cervical weakness**.

Treatment
If the test indicates cervical weakness, a cervical stitch may be advised. This procedure is usually carried out under general anaesthetic when a woman reaches 13 or 14 weeks of pregnancy.
The Miscarriage Association publishes a leaflet on the cervical stitch.

Tests for infection

How can infection cause a problem?

In general, infection is not thought to be a cause of recurrent miscarriage, but severe infection at the time of miscarriage may be the cause of the loss.

There is some evidence that a condition called **bacterial vaginosis (BV)** may cause later miscarriage. In BV, the normal vaginal bacteria are replaced by other bacteria and this causes a vaginal discharge with a 'fishy' smell. Bacterial vaginosis has more recently been associated with early pregnancy loss.

Testing
Your doctor may take a vaginal swab to check for infection and a specific swab for BV. S/he may also suggest blood tests which can indicate if there is an infection.

Treatment
BV is treated with antibiotics.

Research investigations

There are many hospitals and clinics carrying out research to try to identify why miscarriage occurs. Research may focus on male as well as female factors. If you are asked to take part in a research study, you will be given full information before deciding. Any decision must be yours, but if you feel that you wish to help in the study, then it may benefit you or others who have also suffered from miscarriage.

Summary

There are many different causes of miscarriage and a number of investigations which can be carried out. In some cases, there may be a combination of causes leading to miscarriage, rather than a single underlying one. Investigations for recurrent miscarriage are usually carried out in a specialised clinic and you may wish to ask your doctor if you can be referred to such a centre.

Different clinics will give greater priority to certain investigations. Most centres, however, will test your and your partner's chromosomes and will also test for antiphospholipid antibodies. The rest of the tests outlined in this leaflet may or may not be required, depending on your medical history.

Don't be afraid to ask questions. The medical and nursing staff will be able to tell you more about the tests they plan to perform, when results will be available and what they mean.

The internet is a source of a great deal of information, though it can be difficult to judge how accurate this information is. It is important to remember that you may read about investigations and treatments for recurrent miscarriage which have not been properly studied or assessed. You may want to discuss what you have read at your recurrent miscarriage clinic.

Finally, it is important to remember that for most couples with a history of recurrent miscarriage, investigations do not identify any specific cause or causes. While this can be very frustrating, it is equally important to remember that for most of you reading this leaflet, you are more likely to have a successful pregnancy next time than to miscarry again.

If you would like to talk to someone else who has been through the experience of recurrent miscarriage, please contact us at The Miscarriage Association and we will put you in touch with one of our support volunteers.

We hope that this information has been helpful to you.

Our sincere thanks to Dr Marjory MacLean, Gynaecologist, Early Pregnancy Unit, Hairmyres Hospital, East Kilbride, for her help in writing this leaflet.

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