



MISCARRIAGE
ASSOCIATION

The knowledge to help

Recurrent miscarriage



A single miscarriage can be very distressing; and it can be devastating if the next pregnancy fails too ... and then the next.

This leaflet looks at the known and possible causes of recurrent miscarriage and the tests and treatments that might help you¹.

What is recurrent miscarriage?

Recurrent miscarriage means having three or more miscarriages in a row. It affects about one in every hundred couples trying for a baby.

Sometimes a treatable cause can be found, and sometimes not. But in either case, most couples are more likely to have a successful pregnancy next time than to miscarry again.

“ My biggest thought with each loss is – what have I done so wrong to deserve this? ”

Your feelings

It can be heartbreaking to miscarry one baby after another. Each new pregnancy brings both hope and anxiety. And each new loss may be harder to bear, especially if you feel that time is running out.

The experience can place great strain on even the strongest relationships. You and your partner might react differently from each other and that can cause great tension.

Family and friends may find it harder to support you with each miscarriage; they may even think you're getting used to loss and able to cope.

And all the time there may be a sense that your life is on hold while you try – and try again – for a baby.

¹ We have written this leaflet for women and their partners who have been affected by recurrent miscarriage. It might also be useful for anyone who wants to know more about tests and treatments.

Testing after recurrent miscarriage

If you have had three miscarriages in a row, you should be offered tests to try to find the cause. This should happen whether or not you already have one or more children.

Testing is not usually offered after one or two early miscarriages (up to 14 weeks) because these are often due to chance. But you might be offered tests after two early miscarriages if you are in your late 30s or 40s or if it has taken you a long time to conceive.

If you had a late (second trimester) miscarriage, where your baby died after 14 weeks of pregnancy, you should be offered tests after this loss.

For more information on late miscarriage, see our leaflet *Late miscarriage: second trimester loss*.

Your hopes

It is natural to pin your hopes on testing as the answer to your problems. But there are three reasons why it may not be the answer you're looking for:

- A cause may not be found; when this happens your miscarriages are called 'unexplained' (see *page 12*);
- Even if a cause *is* found, it may not be treatable;
- Treatment may not lead to a successful pregnancy. This can happen if a pregnancy miscarries for a different reason than the one being treated.

“I’m having some tests after two miscarriages. I know it may be a step forward but it’s really hard and I’m very anxious. Tests may be a silver lining, but it’s a silver lining in a big black cloud that I didn’t want hanging over me in the first place!”

Why recurrent miscarriage happens

This section looks at things that increase your risk of recurrent miscarriage. It also looks at known and possible causes.

Risk factors

Your risk of recurrent miscarriage is higher if:

- you and your partner are older; the risk is highest if you are over 35 and your partner over 40;
- you are very overweight. Being very underweight may also increase your risk.

Each new pregnancy loss increases the risk of a further miscarriage. But even after three miscarriages, most couples will have a live baby next time.

“ They didn’t find anything wrong. But if there’s nothing wrong with me, why do I keep losing babies? ”

Known causes

Antiphospholipid syndrome (APS)

This blood clotting problem is the most important treatable cause of recurrent miscarriage.

It happens when your immune system makes abnormal antibodies that attack fats called phospholipids in your blood. This makes the blood more ‘sticky’ and likely to clot, which is why APS is sometimes called ‘sticky blood syndrome’.

It is also known as ‘Hughes syndrome’ after the expert who named it.

It is not clear why these antibodies cause miscarriage. They may stop the pregnancy embedding properly in the uterus (womb); or they may interfere with blood flow to the placenta, which supports the baby.

APS can also lead to problems in later pregnancy, including the baby not growing enough, pre-eclampsia or stillbirth.

For more detail see our leaflet *Antiphospholipid syndrome and pregnancy loss*.

Other blood clotting problems

Some inherited blood clotting disorders can cause recurrent miscarriage, particularly after 14 weeks. These include factor V Leiden, factor II (prothrombin), gene mutation and protein S deficiency.

Abnormal chromosomes

The chromosomes in every cell of your body carry hereditary information in the form of genes.

Everyone has 23 pairs of chromosomes, and 22 of these are the same in men and women. The 23rd pair are different because they determine gender. Men normally have one X and one Y chromosome and women two X chromosomes.

A baby inherits half its chromosomes from each parent.

About half of all miscarriages happen because the baby's chromosomes are abnormal. This is not usually an inherited problem: it happens when the egg and sperm meet or soon after the egg is fertilised. The older you are the more likely this is to happen.

Much less commonly (in less than five in one hundred couples with recurrent

miscarriage), one partner carries a chromosomal defect called a 'balanced translocation'. This doesn't cause a problem for the parent, but it can be passed on to the baby as an 'unbalanced translocation'. This means that some genetic information is duplicated and some is missing.

There's a very helpful explanation of balanced translocation, produced by University College Dublin. (See page 13)

Cervical weakness (also known as 'incompetent cervix')

Your cervix is a kind of 'gateway' between the uterus and vagina, which normally dilates (widens) during labour to allow the baby to be born.

Some women – probably less than one in a hundred – have a weakness in the cervix that allows it to dilate too early. This is a known cause of late (second trimester) miscarriage.

“ All the tests came back as normal. My husband was relieved as it showed that there was no obvious problem. But I was disappointed as I really wanted an answer: ‘Here’s what’s wrong. Take this magic tablet.’ ”

Possible causes

The problems listed on this page may play a part in causing recurrent miscarriage, which is why we've included them here. But the scientific evidence isn't strong enough to say this for sure.

Abnormally-shaped uterus

Some miscarriages, particularly late ones, are thought to happen because the uterus (womb) has an abnormal shape.

It may be divided down the centre – known as 'bicornuate' or 'septate' uterus; or just one half of the uterus may have developed – known as 'unicornuate' uterus.

It is not clear from research how many women with recurrent miscarriage have these abnormalities. Also we don't know how common these problems are in women who *don't* miscarry.

This makes it impossible to be sure that they cause miscarriage.

“ I can't face the thought of another miscarriage, but I'm even more frightened of not trying again. ”

Polycystic ovary syndrome (PCOS)

Women with this condition have many small cysts in their ovaries. They also tend to have hormonal problems, including high levels of insulin and male hormone in the blood.

It is these problems that are thought to play a part in recurrent miscarriage, but it is not clear how.

Infection

Some serious infections can cause or increase the risk of single miscarriages. These include toxoplasmosis, rubella, listeria and genital infection. But it is not clear whether infection plays a role in recurrent miscarriage.

Immune problems

Raised levels of uterine NK (uNK) cells may increase the risk of recurrent miscarriage, but more research is needed to prove this.

It's important to know that these uNK cells are different from the NK cells found in general circulating blood (e.g. from your arm).

Diabetes and thyroid problems

Uncontrolled diabetes and untreated thyroid problems can cause miscarriage. But well-controlled diabetes and treated thyroid problems do not cause recurrent miscarriage.

Recommended tests and treatments

The tests and treatments below are recommended by the Royal College of Obstetricians and Gynaecologists (RCOG). Their guidance¹ is based on the latest research evidence.

You and your partner should be seen by expert health professionals, ideally at a special recurrent miscarriage clinic. Your doctor should know whether there is one in your area.

Antiphospholipid syndrome (APS)

Testing

You should be offered blood tests for APS after three or more early miscarriages or one or more late ones.

To get a clear diagnosis you have to test positive on two separate occasions for one of the antiphospholipid antibodies. These are known as ‘lupus anticoagulant’ and ‘anticardiolipin’ antibodies.

Experts recommend that the two tests are done six to twelve weeks apart. You might find this hard to cope with if you want to try to conceive again sooner than that.

Treatment

If you do have APS you will probably be treated with low dose aspirin and heparin injections. This combination has been shown to improve your chance of having a live baby.

The aspirin treatment (75 mg daily) will start early in pregnancy, when you have a positive pregnancy test. The heparin injections are usually started once the baby’s heartbeat has been seen on a scan.

If you have this treatment, you will be monitored carefully throughout your next pregnancy. That’s because APS can cause other problems for you and your baby.

For more information see our leaflet *Antiphospholipid syndrome and pregnancy loss*.

Other blood clotting problems

Testing

You may be offered blood tests for inherited clotting disorders called ‘thrombophilias’. These include factor V Leiden, factor II (prothrombin), gene mutation and protein S. These disorders tend to cause late miscarriage so you probably won’t be tested if you miscarried early.

Treatment

If tests show you have one of these disorders you may be offered heparin injections in your next pregnancy. If you had a late miscarriage this may improve your chance of having a live baby. There isn’t enough evidence to judge whether it helps women with recurrent early miscarriage.

¹ See reference 1 on page 14.

Genetic problems

Testing

If possible your clinic should test tissue from the miscarriage for abnormalities in the baby's chromosomes. But this may be difficult to arrange if you didn't miscarry in hospital.

It can take up to eight weeks to get a result and about half of all tests don't give clear answers.

If tests on the miscarriage tissue show chromosomal abnormalities, that usually means that this is a 'one-off' problem and you have a good chance that you will have a healthy pregnancy next time.

If the result shows that the baby has an 'unbalanced translocation' (see page 5), you and your partner will be offered blood tests to show whether one of you carries the chromosome problem called a 'balanced translocation'.

It can take up to six weeks to get a result.

Treatment

If you or your partner are found to carry a balanced translocation there is no treatment. You should be offered special genetic counselling to help you to decide about future pregnancies.

“ It's scary to get a positive pregnancy test result now because I might have to go through the loss and grief all over again. It's very different from the happiness and excitement I felt when I got a positive test result in my first pregnancy. ”

Abnormally-shaped uterus

Testing

You should be offered tests to check the shape of your uterus. The first step is a pelvic ultrasound scan. If your uterus looks abnormal on the scan the diagnosis can be confirmed by one of these further tests:

- **hysteroscopy**, where the uterus is examined through the vagina using a special viewing tube called a hysteroscope;
- **laparoscopy**, where the uterus is examined through a small cut in the abdomen, using a laparoscope;
- **a three-dimensional pelvic ultrasound scan**, which is more detailed than the first scan.

Treatment

Surgeons can correct some abnormalities of the uterus. But there is no evidence that this improves a woman's chance of having a baby.

Open surgery on the uterus may harm fertility. And the scar could rupture during pregnancy, at great risk to mother and baby.

Surgery carried out through the cervix looks more promising; but doctors need to know more about its safety and effectiveness before they can recommend it.

Cervical weakness

Testing

Cervical weakness can be hard to diagnose and there is no reliable test outside of pregnancy.

Treatment

If you have had a late miscarriage and your doctor thinks it might be due to cervical weakness, you may be offered regular scans of your cervix in your next pregnancy.

Some women are treated with a 'cervical stitch'. This is an operation to keep the cervix closed during pregnancy. The stitch is normally inserted under general or epidural anaesthetic at 13 or 14 weeks, then removed towards the end of the pregnancy.

It is not clear that this treatment reduces the risk of miscarriage and it does carry some risks. For these reasons it is recommended only for some women.

For more information, see our leaflet *About the cervical stitch*.

Other tests and treatment

In this section, we look at tests and treatments that are sometimes offered to couples with recurrent miscarriage, but are **not** currently recommended.

This guidance comes from experts who have searched all the research evidence for these tests and treatments and found that:

- there is no proof that they make you less likely to miscarry **and/or**
- they might be harmful **or**
- they have been shown to be harmful

We have included them in this leaflet because you might read about them, or be offered them, and want to know more.

Of course, recommendations can change as new research comes to light. This can be confusing and you may want to talk to your doctor and/or contact us at the Miscarriage Association to find out more.

hCG supplements

Human chorionic gonadotrophin (hCG) is a hormone produced only during pregnancy and is vital for keeping the pregnancy going. There is no clear evidence that taking hCG supplements prevents miscarriage.

Progesterone supplements

The hormone progesterone plays an important role in normal pregnancy; and supplements have often been suggested as a treatment for recurrent miscarriage.

New research¹ however, shows that progesterone **isn't** the answer for women with recurrent miscarriage. A high-quality study of 826 women with previously unexplained recurrent miscarriage showed that those who received progesterone treatment in early pregnancy had just the same chance of miscarrying as those who received a placebo (or dummy treatment).

The research **did** show that the women taking the progesterone treatment suffered no harm, nor did their babies. That is very important information for women taking progesterone for other reasons, such as fertility treatment, or for those taking part in other research trials.

Metformin treatment

Metformin is a drug that stops high levels of insulin building up in the blood. Small studies have suggested that it *might* help women with recurrent miscarriage and PCOS. But more research is needed to prove that this is true.

¹ The PROMISE trial. Coomarasamy A *et al.* *A Randomized Trial of Progesterone in Women with Recurrent Miscarriages.* N Eng J Med 2015 Nov 26;373(22):2141-8. DOI: 10.1056/NEJMoa1504927. http://www.nejm.org/doi/full/10.1056/NEJMoa1504927?query=featured_home

Pre-implantation genetic diagnosis

This is sometimes offered to couples with a translocation problem who are planning to use in-vitro fertilisation (IVF). It involves screening embryos for abnormalities before implanting them in the uterus.

This treatment is not recommended if you don't have fertility problems. That's because you are more likely to have a successful pregnancy without IVF, which has a success rate of only about 30 per cent.

Immunotherapy

There is a range of immune treatments that don't help women with recurrent miscarriage and can actually be harmful. These include:

- paternal cell immunisation
- third party donor leucocytes
- intravenous immunoglobulin.

Experts advise against immunotherapy treatment.

Treatment with steroids

Steroid treatment may reduce the risk of miscarriage in some women. A small pilot trial suggested that steroids might benefit women who have raised uterine NK cells. However, a larger trial is needed to see if those results are confirmed or not.

It is always important to consider risks and benefits of any medication in pregnancy, and steroids should be used only under medical supervision.

Suppression of high levels of luteinising hormone (LH)

Using drugs to suppress high blood levels of LH in women with PCOS does not improve their chances of having a live birth.

“ I've found lots of information on the Internet, but different sites say different things. It's really hard to know what to believe. ”

Unexplained recurrent miscarriage

More than half of the couples who have investigations for recurrent miscarriage don't come out with an answer as to why they have miscarried.

If this happens to you, you might be very disappointed. You may have hoped that finding the cause of your miscarriages would mean that you could be treated and the problem solved.

You might find it very hard to cope with not knowing why you have had repeated miscarriages. And it might be very scary to think about trying again.

On the other hand, you may feel relieved that you don't have any major problems. You can also be reassured that this is actually good news. There is no obvious reason why you can't have a baby; and even after three miscarriages you have a good chance that things will work out next time.

“ Being told all was normal was frustrating, but it did give me some hope and now we have our beautiful healthy daughter. ”

Looking ahead

Some research¹ has shown that women with unexplained recurrent miscarriage are more likely to have a healthy pregnancy next time if they have supportive care at a specialist unit. This includes being able to have regular scans or to talk to the specialist staff.

No one knows how or why it might make a difference, but it may reduce stress.

You might also find it helpful to get non-medical support – from family, friends, colleagues or organisations like the Miscarriage Association (see *page 13*).

Even though there is no proof that it will make you less likely to miscarry, it can be a relief to be able to talk to people who understand what you are going through and are willing to listen.

It can be very painful to go through repeated miscarriages. You might be determined to keep on trying. But there may come a time when it gets too much and you begin to think about other options.

Deciding to stop trying can be difficult – and it's a decision you might make and 'un-make' several times.

You may find it helpful to read our leaflet *When the trying stops*.

¹ See references 2 and 3 on page 14

Finding help and support

If you are struggling to cope with your feelings, you may need some support – perhaps especially from someone who understands the special circumstances of repeated miscarriage.

Sometimes just reading about how other people have felt after recurrent miscarriage can make a difference.

The Miscarriage Association has a telephone helpline, a volunteer support service, an online support forum and a range of helpful leaflets on all aspects of miscarriage.

The online support forum has a special area for recurrent miscarriage.
Tel: 01924 200799;
www.miscarriageassociation.org.uk
17 Wentworth Terrace, Wakefield
WF1 3QW

The British Association for Counselling and Psychotherapy

can help you find a counsellor or psychotherapist.

Tel: 0870 443 5252;
www.counselling.co.uk
BACP House, 15 St John's Business
Park, Lutterworth LE17 4HB

Relate can help with relationship problems.

Tel: 0300 100 1234;
www.relate.org.uk
Premier House, Carolina Court,
Lakeside, Doncaster DN4 5RA

The Samaritans can help people in serious emotional distress, 24 hours a day.

Tel: 08457 909090;
www.samaritans.org.uk

Useful reading

Leaflets from the Miscarriage Association:

Your feelings after miscarriage

Late miscarriage: second trimester loss

Antiphospholipid syndrome and pregnancy loss

About the cervical stitch

When the trying stops

Useful animation

www.youtube.com/watch?v=MLDCJ2gUC84&app=desktop

Need to talk to someone who understands?

Call our support line on 01924 200799. Monday to Friday, 9am-4pm

Or email info@miscarriageassociation.org.uk

References

¹ *Recurrent Miscarriage, Investigation and Treatment of Couples (Green-top 17)*, Royal College of Obstetricians and Gynaecologists, May 2011 (available online at <http://www.rcog.org.uk>)

² Stray-Pederson & Stray-Pederson. *Aetiologic factors and subsequent reproductive performance in 195 couples with a prior history of habitual abortion*. *American Journal of Obstetrics & Gynaecology*. 1984; **148**: **2**: 140-146.

³ Liddle, Pattinson & Zanderigo. *Recurrent miscarriage – outcome after supportive care in early pregnancy*. *Australian Journal of Obstetrics & Gynaecology*. 1991; **31**: **4**: 320-322.

“ Each loss is as devastating as the first, if not more so. But somehow you find the strength and hope to keep going and keep trying. Maybe it’s a need to fill the void that has been left by the baby you’ve lost. Or maybe it’s the eternal hope that you will one day hold your baby in your arms. ”





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Rec/04/15