What is Recurrent Miscarriage (RM)?

A miscarriage is when you lose a pregnancy at some point in the first 23 weeks. When this happens three or more consecutive times, doctors call this ‘recurrent miscarriage’. For women and their partners this is understandably very distressing. Around one woman in every 100 has recurrent miscarriages. This is about three times more than you would expect to happen just by chance, so it seems that for some women there must be a specific reason for their losses.

For others, however, no underlying problem can be identified; their repeated miscarriages may be due to chance alone.

Why does RM happen?

Often, despite careful investigations, the reasons for RM cannot be found. However, if you and your partner feel able to keep trying, you still have a good chance of a successful birth in the future. A number of factors may play a part in RM:

- **Your age and past pregnancies**
  The older you are, the greater your risk of having a miscarriage. The more miscarriages you have had already, the more likely you will be to have another one.

- **Abnormalities in the embryo**
  An embryo is the fertilised human egg that leads to a baby. An abnormality in the embryo is the most common reason for single miscarriages. However, the more miscarriages you have, the less likely this is to be the cause.

- **Abnormal immunity**
  Antibodies are substances produced by our immune systems to help fight off infections. Around 15 in every 100 women who have RM have antibodies called antiphospholipid antibodies (APA), in their blood compared to fewer than 2 in every 100 women with normal pregnancies. These APA react against the woman’s own tissues (autoimmune response) and in so doing can harm her pregnancies. Women with APA and a history of recurrent miscarriage have only a one in ten chance of successful pregnancy. Some people have
suggested that some women miscarry because their immune system does not respond to the baby in the usual way. This is known as an alloimmune reaction.

• **Womb structure**

It is not clear how far abnormalities of the womb affect the risk of RM. These have been found in anything from 2 to 37 out of every 100 women with RM. Women with severe untreated abnormalities seem to be more likely to miscarry or give birth early. Minor variations in the structure of the womb do not cause miscarriage.

• **Weak cervix**

The entrance to the womb (the cervix) opens too early during pregnancy in some women, leading to miscarriage in the third to sixth month. This is known as having a weak (or incompetent) cervix. Unfortunately there is no really reliable test for this outside of pregnancy.

• **Polycystic ovaries**

Polycystic ovaries are slightly larger than normal ovaries and produce many more small follicles (the eggs that develop in the ovaries) than normal. This may be linked to an imbalance of hormones that control the menstrual cycle in women. Nearly one half of women with RM at early gestation have polycystic ovaries; this is about twice the number of women in the general population.

Having polycystic ovaries is not a direct cause of RM and does not mean you are at greater risk of further miscarriages. Many women with polycystic ovaries and RM have high levels of male type hormones (free androgen index) in their blood and studies have shown that reducing these high androgen levels might lead to fewer miscarriages.

• **Infections**

If a serious infection gets into the bloodstream it may lead to miscarriage. If a woman gets a vaginal infection called bacterial vaginosis early in pregnancy, it may increase the risk of having a miscarriage around the fourth to sixth month, or of giving birth early. It is unclear whether other vaginal infections cause RM.

• **Blood conditions**

Certain inherited conditions mean that your blood may be more likely to clot than is usual. These conditions are known as thrombophilias. The presence of thrombophilia in a woman does not mean that she will inevitably develop a serious blood clot.

• **Diabetes and thyroid problems**

Diabetes or thyroid disorders that are not well controlled can be factors in single miscarriages. There is some developing evidence that subclinical hypothyroidism (underactive thyroid that shows up in blood tests without showing symptoms in you) may be associated with RM.

• **Genetic factors**

Genetic abnormalities occur in about 1-3 out of every 100 couples/women with RM. These affect one of the chromosomes (the genetic structures within our cells that contain our
DNA which we inherit from our parents). Such abnormalities may cause no problem for you or your partner, but can cause problems if passed on to your baby.

**How does the recurrent miscarriage clinic work?**

Women are referred to the clinic by their GP, early pregnancy assessment unit or from other hospitals in the region. In order to be referred to the clinic a woman must satisfy at least one of the following criteria:

- Be under 35 years old and have had 3 consecutive miscarriages.
- Be over 35 years old and have had 2 consecutive miscarriages.
- Become pregnant as a result of IVF and have had 2 consecutive miscarriages.

Couples are first seen to arrange initial investigations. The results of these investigations may take up to 10 weeks to come back. At the follow-up appointment, an individualised care plan will then be made for all couples.

**What can be done?**

- **Supportive antenatal care**
  Women who get supportive care from the beginning of a pregnancy have a better chance of successful birth. You will be offered fortnightly scans from 6 weeks to 10 weeks to closely monitor your pregnancy. Follow-up will be arranged in the dedicated RM antenatal clinic at Saint Mary's Hospital or at the antenatal clinic in your local hospital if this is more convenient for you.

- **Screening for abnormalities in the structure of your womb**
  We will offer you a pelvic ultrasound scan to check for and assess any abnormalities in the structure of your womb. In Saint Mary's Hospital, we have a dedicated out-patient hysteroscopy clinic where we review all women where an abnormality in the womb is suspected on scan and also those women who have had more than four first trimester miscarriages. This involves looking inside the womb with a camera. This is usually done under local anaesthetic or no anaesthetic, but can be arranged under general anaesthetic as a day case procedure if necessary.

  In some cases a magnetic resonance (MR) scan may be used to confirm the abnormality and determine the most appropriate treatment.

  Depending on the findings, in some cases specialist uterine surgery may be appropriate (for example for intrauterine adhesions (Ashermann's syndrome)/uterine septum/uterine fibroid.)
• **Endometrial Scratch**

For some women we might suggest a procedure called an endometrial scratch. This is where thin plastic tubing is passed through the cervix to gently 'scratch' the endometrium (lining of the womb). The procedure is carried out in the second half of the menstrual cycle (known as the luteal phase – the time after ovulation (when the ovaries release an egg) and before your period starts). Endometrial scratch is thought to make it more likely that an embryo will implant.

• **Hormone treatment**

The luteal phase is usually about 12 to 14 days long. During this time, your ovaries produce a hormone called progesterone. This hormone tells lining of the womb (the endometrium) to grow. If you become pregnant, the developing baby attaches to this thickened lining. If you do not become pregnant, the lining eventually sheds, and you have a period.

Sometimes your ovaries do not release enough progesterone (luteal phase hormone insufficiency). If this is the case, you will be offered progesterone supplements from day 21 of your cycle (day 1 = first day of your period). If your pregnancy test is positive during that cycle, the progesterone supplements should be continued until 12 weeks. If your pregnancy test is negative, the progesterone supplements can be stopped and the process should be repeated for the next few cycles.

• **Screening for abnormalities in the baby and placenta**

If you have had three consecutive miscarriages and lose your next baby, we may suggest checking for abnormalities in the baby or the placenta afterwards. We will do this by checking the genes of the baby through a test known as karyotyping. We will also ask your permission to examine the placenta through a microscope. The results of these tests can take up to eight weeks to come back and around half of all tests do not give clear answers but they may help identify possible causes and enable us to discuss further options and treatment available to you. If you have had a successful pregnancy in between miscarriages, this test will not be offered to you.

• **Screening for vaginal infections**

You will be offered swab tests (and treatment if necessary) for an infection known as bacterial vaginosis (BV). If you have BV, treatment with antibiotics may help to reduce the risks of miscarriage after 12 weeks, and premature birth.

• **Treatment for Antiphospholipid antibodies (APA)**

There is good evidence that treating women with APA and RM with low-dose aspirin tablets and low-dose heparin injections in future pregnancies improves their chances of live birth. This treatment increases the chances of live birth from just 1 in 10 if they have no treatment, up to about 7 in 10. Despite this treatment, women with APA are still at risk of other problems in pregnancy such as:

• Pre-eclampsia, which is a condition affecting the placenta that can cause high blood pressure, liver and kidney problems in pregnancy and lead to a risk of seizures (eclampsia).
• Restriction in the baby’s growth.
• Premature birth.

This is why we will offer to carefully monitor your pregnancy so that you can be offered appropriate treatment for any problems that arise.

Depending on the level of the antibodies, we offer low dose heparin injections when you have a positive pregnancy test. Patients with positive antibodies will be advised to contact the specialist haematology midwife when your pregnancy test is positive so we can arrange starting this treatment.

Aspirin in pregnancy

If you need to be on aspirin, it should not be started before 8 weeks of pregnancy. There is evidence that taking aspirin whilst trying to conceive and before 8 weeks of pregnancy will have an adverse effect on implantation. For this reason we recommend that you do not take aspirin unless a recurrent miscarriage practitioner has advised you to do so.

• Treatment for thrombophilies

Although women have a higher risk of miscarriage if they also have an inherited tendency to blood clotting (thrombophilia), they may still have a healthy and successful pregnancy. At present there is no test available to identify which women with thrombophilies are more likely to miscarry. This is why we choose to treat all women with certain types of thrombophilies and RM with low-dose heparin injections to reduce the risk of blood clots and hopefully improve the chances of live birth.

• Tests and treatment for a weak cervix

For women with a weak cervix, you may be offered an operation to put a stitch in your cervix (cervical cerclage) to make it stay closed. The indication for this would be if you had three or more miscarriages in the second trimester or preterm births before 27 weeks. This would normally be carried out at around 14 weeks in your next pregnancy.

For women who are not offered this ‘history indicated’ cervical cerclage but who have a history of second trimester miscarriage, you will be offered surveillance scans in our Preterm Labour Clinic where the length of the cervix is measured using a transvaginal scan. If these scans show that the length of the cervix is less than 25mm before 24 weeks of pregnancy, you will be offered a ‘scan indicated’ cervical cerclage.

Cervical cerclage is usually done through the vagina (transvaginal cerclage). At Saint Mary’s Hospital we now offer abdominal cerclage in cases where it is thought that this is likely to be more successful than cervical cerclage, for example:

• Failure of previous transvaginal cerclage.
• Very short cervix.
• Scarred cervix.
This is done through keyhole surgery or occasionally a ‘bikini line’ abdominal cut. All operations involve some risk so we would only recommend this procedure to you if we believe that you and your baby are likely to benefit.

- **Screening for underactive thyroid**
  You will be offered a blood test to check your thyroid function. If this shows that your thyroid is underactive, you will be offered treatment for this even if you are not showing any symptoms.

- **Screening for Coeliac disease**
  Coeliac disease is an autoimmune condition caused by intolerance to gluten in the diet. It affects 1 in 100 people and the common symptoms are bloating, diarrhoea and weight loss. There is some evidence to suggest a link with Coeliac disease and RM so you will be offered screening for this. If the test is positive you will be referred to a gastroenterologist who may undertake further tests such as biopsy for confirmation and a gluten-free diet will be recommended if necessary.

- **Treatment with Vitamin D**
  There is a link between vitamin D deficiency and RM. You will be screened for vitamin D deficiency and treated with high dose vitamin D supplements if necessary.

- **Other Tests and Treatment**
  Natural Killer (NK) cells are found in the lining of the womb and form part of the body’s immune system. There is some new evidence to suggest that they may play an important part in unexplained RM but testing for them and treatment is not currently available on the NHS. At Saint Mary’s Hospital we can direct you for NK cells testing if it is felt by your consultant that this may provide some answers or additional treatment options for you, but this option is currently only available on a private basis and would involve you paying a fee of around £400.

  If the test indicates high levels of NK cells you will be offered treatment with prednisolone in the first 12 weeks of pregnancy as this has been shown to increase your chance of a healthy pregnancy. This is a safe drug to take in pregnancy. There is a small risk of growth restriction in your baby. All women who are taking prednisolone in early pregnancy are therefore offered growth scans at 28 and 32 weeks.

**Tests and treatments that have not been proven to be useful**

The following tests/treatments are often asked about because of either press reports or internet publications. We do not offer them in this Unit as the currently available evidence does not suggest that they are beneficial to the woman with RM or her pregnancy.

**Unnecessary tests:**

- Partner compatibility testing.
- Immunity testing.
• Paternal cell immunisation, third-party donor leucocytes, trophoblast membranes and intravenous immunoglobulin in women with previous unexplained recurrent miscarriage do not improve the live birth rate and so is not offered.

• Peripheral blood Karyotyping of the couple in the absence of any indication to do so, either from history or genetic analysis of miscarriage products.

• Low dose aspirin (on its own).

Although low dose aspirin (LDA) is a useful treatment for antiphospholipid syndrome when used in combination with low-dose heparin, the current evidence suggests that LDA on its own is not beneficial for women with unexplained RM and so we do not recommend it. Aspirin should not be taken around the time of conception as it interferes with implantation of the pregnancy. If aspirin is thought to be helpful for you, it should only be started once you are 8 weeks pregnant.

The Multi-disciplinary links

The RM clinic has links with other clinics both at Saint Mary’s Hospital and Manchester Royal Infirmary, meaning that couples have access to the best possible care. These include:

• Preterm Labour Clinic. You may be referred here if your history suggests you have a weakness in your cervix.

• Haematology Antenatal Clinic. All women who are found to have thrombophilias or APA will have continued management throughout their pregnancy in the specialist antenatal clinic or the Recurrent Miscarriage Antenatal Clinic.

• Genetics Clinic. You may be referred here if karyotyping shows any abnormalities in the miscarried baby or placenta.

• Endocrine Clinic. Women with diabetes or thyroid problems may be jointly managed by this clinic.

• Gastroenterology Clinic. Women with positive test for Coeliac disease will be referred here.

The Multi-disciplinary team members

The RM service comprises a multi-disciplinary team of individuals who provide differing elements of input into your care, including:

• A Consultant Gynaecologist who leads the RM Service
• Consultant Obstetricians
• Consultant Haematologist
• Consultant Endocrinologist
• Consultant Immunologist
• Consultant Geneticist
• Consultant Gastroenterologist
• Specialist nurses from the RM Clinic and the Emergency Gynaecology Unit
• Specialist Midwife from the Haematology clinic
• Counsellor
• Bereavement nurse

**What does the future hold for you?**

Unfortunately we will not be able to tell you for sure what will happen if you become pregnant again. However, even if we have not found a cause for your miscarriages, you still have a good chance (3 in 4) of a healthy birth.

**Is there anything else you should know?**

• You have the right to be fully informed about your health care and to share in making decisions about it. We will respect and take your wishes into account.
• No treatment can be guaranteed to work all the time for everyone.

**Please use this space to write down any questions or concerns you may have.**

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