

This leaflet covers endometriosis and fertility, including surgical, medical and fertility treatment including in-vitro fertilisation (IVF). There is a detailed reference list and suggestions for further reading at the end of the leaflet. Medical terms have been highlighted in italics.

Endometriosis and fertility

Endometriosis is a common gynaecological disease. It does not necessarily cause infertility or pain, and many with endometriosis will be able to conceive without medical intervention. Minimal to mild endometriosis is common and it is far more likely that you will have no difficulty conceiving. With increasing severity of endometriosis, scar tissue (*adhesions*) becomes more common and the chance of conception decreases. This is because, with severe disease, there is more scar tissue (*adhesions*) that can trap the egg and prevent it from getting down the Fallopian tube.

While there is an association between infertility and endometriosis, the cause has not been fully established. Even with severe endometriosis, conception is still possible without medical intervention.

The main factor that influences fertility is age. Fertility starts to rapidly decline after the age of 38 when the rate at which egg sacs (*follicles*) disappear from the ovaries accelerates. In addition, the rates of miscarriage and chromosomal abnormalities, such as Down's syndrome, increase with age. The reason for this is that, from birth, there is a lifetime supply of eggs (oocytes) within the ovaries. They undergo maturation and ovulation, but no new eggs are produced. Male reproductive organs produce new sperm every three months and can conceive a child into old age, although there is evidence emerging that the chance of miscarriage also relates to male age.

What is the likelihood of getting pregnant if I have endometriosis?

Many with endometriosis will be able to conceive without medical intervention. However, anatomical distortion and adhesions caused by endometriosis, particularly in moderate and severe disease, reduces the chance of conception. The chance of conceiving with minimal to mild endometriosis may also be different from normal. 60 - 70% of those with endometriosis will get pregnant 'spontaneously', by which doctors mean, without medical intervention.

To put this into context:

100 individuals without endometriosis, all start trying for a baby

At the end of one year, 84 will be pregnant.

100 with minimal-mild endometriosis, all start trying for a baby

At the end of one year, 75 will be pregnant.

100 with moderate endometriosis, all start trying for a baby

At the end of one year, 50 will be pregnant.

100 with severe endometriosis, all start trying for a baby



At the end of one year, 25 will be pregnant.

Grade or severity of endometriosis

There are several different classification systems for endometriosis. The American Society of Reproductive Medicine developed a system with a focus on fertility, where endometriosis is classified into minimal, mild, moderate and severe. This classification helps to predict the chance of getting pregnant and does not always align with the degree of pain. It is possible to have severe pain with minor endometriosis and minor pain with severe endometriosis.

At this current time, no other test or investigation can give the same detailed information as a laparoscopy. During a laparoscopy, the pelvic cavity is carefully inspected. A score is worked out based on the area affected by endometriosis, whether there are cysts of endometriosis on the ovaries and whether there is scar tissue or adhesions sticking tissues together. MRI and ultrasound scans can support the diagnosis of ovarian cysts caused by endometriosis (endometriomas) and deep endometriosis, but negative scan findings do not rule out the presence of endometriosis.

How and why does endometriosis affect fertility?

Endometriosis can lead to the formation of scar tissue (*adhesions*), these can look like cobwebs and can be fine, or dense. Adhesions are more common in moderate and severe endometriosis. This scar tissue can distort the pelvic anatomy. For example, if the ovary is wrapped in adhesions, the released egg gets trapped and is unable to reach the tube. The tubes and ovaries dangle down in another important area called the Pouch of Douglas. If this area is covered by adhesions, then the chance of getting pregnant is also lower. Ovarian cysts caused by endometriosis (*endometrioma*) may cause damage to the ovary and this could affect ovarian function and egg supply.

It is less clear why minimal or mild endometriosis may cause infertility. In minimal-mild endometriosis, there may be spots of endometriosis, and minimal or no scar tissue. If someone is trying to get pregnant, it is also important to consider male fertility as this could also be a contributing factor.

Theories for why minimal to mild endometriosis causes infertility include:

- Toxins in peritoneal fluid (naturally occurring fluid within the body cavity)
- Problems with egg transport down the fallopian tube
- An abnormal immune response (antibodies)
- Failure of the egg sac (follicle) to release its egg (luteinised unruptured follicle syndrome)

If endometriosis is affecting fertility, treatment of endometriosis can improve the chance of pregnancy. A recent review (Barfort, et al. 2020) concluded that laparoscopic surgery and treatment of endometriosis increases natural pregnancy rates, especially in cases where minimal-mild endometriosis was diagnosed. Exactly how the endometriosis was treated (laser, excision (cutting out) or diathermy) did not appear to affect outcomes.



Studies that have a 'no treatment arm' to compare with active treatment provide useful information about what happens to endometriosis without treatment over time. Overall, these suggest that endometriosis slowly gets worse with no treatment.

If you are trying to get pregnant, there is no treatment currently available to slow the progression of endometriosis, as all medical treatments apart from some painkillers are either contraceptives or can be harmful to the unborn child and you are advised to use barrier contraception during treatment.

If you are not currently trying to get pregnant, the Combined Oral Contraceptive Pill (COCP) and progestogens such as the 'mini pill' may help to slow the progression of endometriosis. The aim of medical treatment options is to reduce pain and help manage the symptoms of endometriosis. If treatment is tolerated well and something you are comfortable with, this can be continued long-term. If you are healthy and non-smoking, the COCP can be continued until the menopause.

The COCP has never been fully assessed with laparoscopy before and after treatment. However, in comparative studies, it has proved as effective as the gonadotrophin releasing hormone agonist (GnRHa) in the treatment of pain associated with endometriosis, and doesn't carry the side effects GnRHa can have.

Does drug (medical) treatment improve fertility?

In general, medical treatment is based on hormones or "anti-hormones" and is contraceptive. The aim of medical treatment is to shrink the hormone-dependent endometriotic tissues. Most prevent pregnancy, but contraception is advised throughout treatment because the drugs can harm an unborn baby (*teratogenic*) and the contraceptive effect of the treatment should not be relied on.

Research has shown that drug treatment (medical treatment) for endometriosis does not improve fertility, either during or after treatment. It is only recommended for treatment of pain associated with endometriosis or as a preparation for surgery. When researched, the comparison in pregnancy rates was not shown to be any higher in those who opted for medical treatment (for example, danazol, burserelin, medroxyprogesterone acetate or gestrinone) when compared to those who didn't have medical treatment.

It has also been shown that completely eliminating endometriosis by medical treatment does not return fertility to normal.

Does surgical treatment improve fertility?

Surgical treatment of endometriosis improves fertility and helps pain.

The aim of surgical treatment is to destroy or cut out (*excise*) endometriotic nodules and release adhesions. Ovarian cysts (*endometrioma*) generally recur after drainage alone and need to be surgically removed by removing the cyst, or draining the cyst and destroying the lining. Surgical treatment of endometriosis helps increase the chance of getting pregnant. Research has shown that surgical treatment of minimal to mild endometriosis improves the chance of pregnancy compared to just having a diagnostic laparoscopy without treatment, Barfort, et al., 2020)



Similar findings were found in a recent research study, which identified that pregnancy rates significantly increased following surgical laparoscopic treatment when compared with placebo (Hodgson, et al., 2020).

Unfortunately, there is no compelling evidence that suggests that laparoscopic treatment of deep endometriosis improves fertility, but surgery should still remain an option for treatment to help with symptom management for those wishing to conceive.

Medical (hormonal drug) treatment after surgical treatment may delay the return of pain symptoms, if conceiving immediately is not a concern, as they are contraceptive. Medical treatment after endometriosis surgery has been shown to delay the return of symptoms. Different types of medical treatment all produced the same result. Research has shown the combined contraceptive pill taken after surgery provides pain relief and may reduce the risk of recurrence.

What types of fertility treatment are available?

There are several types of fertility treatment. The type of fertility treatment chosen can depend on the severity of endometriosis, age, how you have been trying to conceive, whether you have conceived in the past and whether there are any other fertility factors, like blocked tubes or sperm problems. The main drawbacks of fertility treatment include over-stimulation of the ovaries (*ovarian hyperstimulation*). This is a rare complication of fertility treatment where the ovaries over-respond to treatment and develop too many follicles, this causes fluid to leak from blood vessels into the abdomen causing swelling, discomfort and dehydration. Multiple pregnancy (twins, triplets, quadruplets) is also a risk when more than one embryo is replaced into the womb (uterus) and can lead to further complications within pregnancy. Careful monitoring of the treatment cycle and limiting the number of embryos replaced can reduce these drawbacks.

OI (Ovulation induction)

The aim of ovulation induction is to regulate periods, stimulating the ovaries to release an egg (*oocyte*) each month. It is suitable for young patients with healthy fallopian tubes, who do not ovulate regularly, have minimal or mild endometriosis and if there are good numbers of healthy sperm.

IUI (Intrauterine insemination)

Intrauterine insemination (IUI) of partner or donor sperm is suitable for those who are young and with healthy fallopian tubes, who ovulate regularly, have minimal or mild endometriosis and where there are good numbers of healthy sperm. IUI boosts male fertility by preparing and sorting the sperm so that only the healthiest are used. Sperm are inserted into the womb through the cervix timed with ovulation, so that they are as close as possible to the released egg.

Ovarian stimulation with IUI

Ovarian stimulation and IUI or super-ovulation and IUI boosts fertility so that several eggs are produced in one month (usually 2 or 3). It is more effective than either no treatment or IUI alone in those who have not conceived naturally and who have minimal or mild endometriosis (Hughes 1997).



A live birth rate of 10-15% per treatment cycle can be expected. IUI is less expensive and less invasive than IVF or GIFT and should be considered initially in suitable patients. About 80% of couples who will conceive with IUI, do so in the first 4-6 cycles. After 3 or 4 unsuccessful IUI treatments, IVF should be considered.

IVF (In Vitro Fertilisation) and Embryo Transfer

IVF and embryo transfer is an established and successful treatment for endometriosis-related infertility. IVF is suitable for those with damaged or blocked tubes; moderate or severe endometriosis; minimal or mild endometriosis, where there is limited sperm supply; and those who have not conceived by IUI.

Gonadotrophin releasing hormone agonists (GnRHa) temporarily stop the body's natural ovarian cycle. This improves the IVF success rates by reducing the number of cancelled cycles and preventing premature ovulation of the eggs developing within the ovaries. Prolonged (at least 60 days) treatment with Gonadotrophin releasing hormone agonists before IVF in those with moderate or severe endometriosis may result in higher pregnancy rates (Nakamura et al. 1992), although this approach may make stimulation of the ovaries more difficult. GnRHa treatment will also help relieve pain.

Many published trials have reported poor IVF success rates in those with moderate or severe endometriosis compared to those with minimal or mild disease. However, IVF with GnRHa treatment after surgical treatment results in good pregnancy and live birth rates, comparable to other causes of infertility.

National data statistics quote a 26% live birth rate per IVF cycle started for women below the age of 38 and 14% for women of all ages. This figure is lower, because age itself is a significant factor reducing female fertility.

The presence of small endometriotic ovarian cysts (endometrioma) does not affect the success of IVF. However, there is an increased risk of developing a pelvic infection following transvaginal egg (oocyte) collection. It is generally suggested that endometriotic cysts over 4cm in diameter should be removed surgically prior to IVF.

ICSI (intra-cytoplasmic sperm injection)

ICSI is used with IVF. A single sperm is injected into the egg, giving it the best chance of fertilizing. It is often recommended if there is a low sperm count or if other problems have been identified with the sperm. It can also be used if there are very few eggs collected from the patient to maximise fertilisation.

In vitro maturation (IVM)

IVM is where eggs collected from the ovaries are matured in the laboratory before being fertilised by sperm. It is different from IVF because the eggs are immature when they are collected. This means that the patient needs to take fewer fertility drugs.

PGD (Pre-implantation Genetic Diagnosis)



Pre-implantation genetic diagnosis is a process that tests the embryos for specific problems. It is used to test for a specific serious genetic problems carried within a family. The drawbacks are that IVF is required to create the embryos that can be tested and there may be no healthy embryos to replace.

PGS (Pre-implantation Genetic Screening)

Pre-implantation genetic screening is a process that tests the embryos for common genetic conditions such as Down's syndrome. It was thought that screening would benefit older mothers who have a higher chance of having a baby with Down's syndrome. Like PGD, the drawbacks are that IVF is required to create embryos that can be tested and there may be no healthy embryos to replace.

Egg or sperm donation

Donated eggs or sperm can be used in fertility treatment. This can be used for patients who do not have a male partner, or may be recommended when treatment is unlikely to be successful if you were to use your own eggs or partner's sperm. The Government has changed the law around donation in April 2005. Children born from eggs, sperm or embryos donated after April 2005 will, when they are 18, be able to find out who the donor was.

Surrogacy

Surrogacy is where another woman carries the baby for you. The baby can be conceived by IUI using the surrogate's eggs and your partner's sperm. Alternatively, the surrogate can have embryo transfer with embryos created from your eggs and your partner's sperm or from donor eggs and/or sperm. Surrogacy is a very complicated legal area and you will need to get legal advice before going ahead. Surrogacy may be the only option for women without a uterus or who have a medical condition that means that it is impossible or dangerous for them to undergo a pregnancy or give birth.

Does endometriosis affect pregnancy?

Endometriosis can cause delay in getting pregnant, and your experience during pregnancy may differ from others with or without endometriosis. In general, endometriosis pain improves during pregnancy, the increased levels of progesterone can help manage endometriosis deposits, but pain may return after giving birth as periods return. For others, there may be no improvement or increased endometriosis symptoms during pregnancy, this is due to the growth of the womb (uterus), it can pull and stretch tissue causing discomfort. Research suggests that there is a slightly higher risk of miscarriage and ectopic pregnancy (where the fetus grows outside of the womb, usually in the fallopian tube) in women with endometriosis, although this is based on low/moderate quality data. If vaginal bleeding and abdominal pain are experienced in the first trimester (first 12 weeks of pregnancy) it is advised that you seek medical attention to check there are no complications with the pregnancy

Further information about fertility treatment

 The Human Fertilisation & Embryology Authority has lots of information on fertility treatments on their website.

https://www.hfea.gov.uk/treatments/



 ESHRE Information for women with endometriosis. <u>https://www.eshre.eu/-/media/sitecore-files/Guidelines/Endometriosis/ESHRE-GUIDELINE-</u> ENDOMETRIOSIS-2022 2.pdf?la=en&hash=E1628E24D374F3EE6C9651EDB33235F8EB8ACBDA

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Feedback:

If you have any comments about this leaflet, please contact us at admin@endometriosis-uk.org

Support:

If you'd like to find out more about Endometriosis UK support services, please visit our website.

www.endometriosis-uk.org Helpline: 0808 808 2227

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