

## Endometriosis, Fertility and Pregnancy

This leaflet covers endometriosis and fertility. It provides information for women who have been diagnosed with endometriosis who would like to know if and how this can affect their fertility, and for women who have been trying to conceive and have been diagnosed with endometriosis during their investigations.

The sections cover surgical, medical and fertility treatment including in-vitro fertilisation (IVF or test-tube baby). 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 problem. It does not necessarily cause infertility or pain. Minimal to mild endometriosis is common and it is far more likely that you will have no difficulty conceiving naturally. With increasing severity of endometriosis, scar tissue (*adhesions*) becomes more common and the chance of natural conception decreases. There is an association between infertility and endometriosis, but cause has not been fully established. Even with severe endometriosis, natural conception is still possible.

The main factor that influences fertility is a woman's 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 as women age. The reason for this is that a woman is born with her lifetime supply of eggs (*oocytes*) within her ovaries. They undergo maturation and ovulation, but no new eggs are produced. A man produces new sperm every three months and can father a child into old age although there is evidence emerging that the chance of miscarriage also relates to the man's age.

### Will I be able to conceive naturally if I have endometriosis?

Anatomical distortion and adhesions caused by endometriosis, particularly in moderate and severe disease, reduces the chance of natural conception. The chance of conceiving with minimal to mild endometriosis is not very different from normal. The more severe the endometriosis, the smaller the chance of getting pregnant naturally. This is because there are more adhesions that trap the egg and prevent it from getting down the Fallopian tube.

100 women without endometriosis, all start trying for a baby  
At the end of one year, 84 will be pregnant.

100 women with minimal-mild endometriosis, all start trying for a baby  
At the end of one year, 75 will be pregnant.

100 women with moderate endometriosis, all start trying for a baby  
At the end of one year, 50 will be pregnant.

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## Endometriosis, Fertility and Pregnancy

100 women with severe endometriosis, all start trying for a baby  
At the end of one year, 25 will be pregnant.

### Grade or severity of endometriosis

Endometriosis is classified into minimal, mild, moderate and severe using the American Fertility Society Revised Classification of Endometriosis (AFS) score. This classification helps to predict the chance of getting pregnant naturally and does not always agree 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 laparoscopy. The pelvis is carefully inspected at laparoscopy. A score is worked out from 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.

### Why does endometriosis cause infertility?

Scar tissue (*adhesions*) is similar to cobwebs and can be fine, or dense. Adhesions are more common in moderate and severe endometriosis. This scar tissue distorts the pelvic anatomy. 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 pocket is covered by adhesions, then the chance of getting pregnant is also lower.

It is less clear why minimal or mild endometriosis causes infertility. In minimal-mild endometriosis, there may be spots of endometriosis, and minimal or no scar tissue.

Evidence that minimal-mild endometriosis affects fertility comes from studies of women having donor insemination because of male fertility problems. It was found that women with minimal to mild endometriosis had less chance of conceiving than women who had no endometriosis. The study was biased because only 11 women had endometriosis and not all the men were completely infertile.

If endometriosis is linked with fertility, then treatment of endometriosis should improve the chance of pregnancy. This has been proven by a large Canadian study (Marcoux et al 1998) that reported that surgical treatment of minimal to mild endometriosis increased the chance of getting pregnant naturally compared to diagnostic (look and see) laparoscopy. Exactly how the endometriosis was treated (laser, excision (cutting out) or diathermy) did not appear to matter.

Theories for why minimal to mild endometriosis causes infertility:

- Toxins in peritoneal fluid (naturally occurring fluid within the body cavity)
- Problems with egg transport down the fallopian tube

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## Endometriosis, Fertility and Pregnancy

- An abnormal immune response (*antibodies*)
- Failure of the egg sac (*follicle*) to release its egg (*luteinised unruptured follicle syndrome*)

### What happens if I decide to do nothing about my endometriosis?

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, it is thought that endometriosis slowly gets worse over time.

In a study of women with endometriosis either treated with a drug called gestrinone or placebo, laparoscopy after six months treatment showed that the endometriosis had improved or resolved in all the women treated with gestrinone. In the 17 women who were taking placebo, endometriosis improved in 9 women, but worsened in 8. In three women, this included the appearance of new adhesions around the tubes and around the ovaries. This study shows that endometriosis can get better as well as get worse in women without treatment.

### Is there any treatment to slow the progression of endometriosis?

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

If you are planning a family sometime in the future, but not just now, the Combined Oral Contraceptive Pill (COCP) may help to slow the progression of endometriosis. It reduces pain, is well tolerated and can be continued long-term for the control of symptoms. In healthy non-smoking women, 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 without the side effects.

### Does drug treatment improve fertility

Drug treatment (medical treatment) for endometriosis does not improve fertility, either during or after treatment. It is only indicated for treatment of pain associated with endometriosis or as a preparation for surgery.

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.

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## Endometriosis, Fertility and Pregnancy

Medical treatment of endometriosis produces no improvement in pregnancy rates compared to no active treatment (*expectant management*). Research has shown that medical treatment with danazol, buserelin, medroxyprogesterone acetate or gestrinone was no more effective than placebo or no active treatment in improving pregnancy rates.

Perhaps most importantly of all, it has also been shown that complete elimination of 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 (*endometriomata*) generally recur after drainage alone and need to be formally removed by removing the cyst, or draining the cyst and destroying the lining.

Surgical treatment of endometriosis helps the chance of getting pregnant. Research has shown that surgical treatment of minimal to mild endometriosis improves the chance of pregnancy compared to diagnostic laparoscopy (look and see) (Marcoux et al., 1998). Endometriosis was treated by cutting out (*excision*), destruction by heat (*electrocautery*) or laser. The different types of treatment all appeared just as good as each other. In the treated group, 50 of 172 (31%) became pregnant within 36 weeks compared to 29 of 169 (18%) in the diagnostic group. The miscarriage rate in both groups was 20%.

Criticisms of the study were that the type of surgical treatment varied. Only the typical blue-black spots of endometriosis were included and we now recognise many more appearances of the disease. Some women also had treatment of adhesions, and some were told what treatment they had had on discharge from hospital, which may have introduced a bias. However, as a result of this study, it is reasonable to wait about a year after the operation to see if you will get pregnant naturally before going on to fertility treatment.

A smaller study found no difference between surgical treatment and diagnostic laparoscopy (Parazzini, 1999). In the treated group, 10 of 51 (19.6%) and 10 of 45 (22.2%) in the look and see group became pregnant within one year following laparoscopy. It is possible that the lack of difference in this study was due to the smaller number of women (not enough statistical power).

### Combination of medical and surgical treatment

Medical (drug) treatment after surgical treatment may delay the return of pain symptoms in a woman who does not wish to start trying to conceive immediately.

## Endometriosis, Fertility and Pregnancy

If surgery was to treat significant pain and a woman does not plan to have a family immediately, post-operative medical treatment 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 for up to a year after surgery.

### What type of fertility treatment should I choose?

There are several types of fertility treatment available. What type of fertility treatment depends on the severity of endometriosis, the woman's age, how long the couple have been trying to conceive, whether the couple have conceived in the past and whether there are other fertility factors such as blocked tubes or sperm problems.

The main drawbacks of fertility treatment include over-stimulation of the ovaries (*ovarian hyperstimulation*) and high order multiple pregnancy (triplets or more). 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 irregular periods, stimulating the ovaries to release an egg (*oocyte*) each month. It is suitable for young women with healthy fallopian tubes, who do not ovulate regularly, have minimal or mild endometriosis and whose partner has good numbers of healthy sperm.

### IUI (Intrauterine insemination)

Intrauterine insemination (IUI) of partner or donor sperm is suitable for young women with healthy fallopian tubes, who ovulate regularly, have minimal or mild endometriosis and whose partner has 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 a woman's fertility so that she produces several eggs in one month (usually 3 or 4). It is more effective than either no treatment or IUI alone in women 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 or GIFT should be considered.

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## Endometriosis, Fertility and Pregnancy

### **GIFT (Gamete Intrafallopian tube Transfer)**

The eggs are collected from the woman's ovaries, usually by laparoscopy. The healthiest eggs are mixed with sperm before being placed inside the fallopian tube. Fertilisation takes place in the Fallopian tube. GIFT is suitable for women with healthy fallopian tubes whose endometriosis is not severe; those who have failed to conceive by IUI; older women; women trying to conceive a long time; and couples with several factors causing infertility.

### **IVF (In Vitro Fertilisation) or 'Test-tube baby' and Embryo Transfer**

IVF and embryo transfer is an established and successful treatment for endometriosis-related infertility. IVF is suitable for women with damaged or blocked tubes; women with moderate or severe endometriosis; women with minimal or mild endometriosis with a partner who has sperm problems; and women who have failed to conceive by IUI.

Gonadotrophin releasing hormone agonists (GnRHa) remove 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 women with moderate or severe endometriosis results in higher pregnancy rates (Nakamura et al. 1992). GnRHa treatment will also help relieve pain.

Many published trials have reported poor IVF success rates in women with moderate or severe endometriosis compared to women 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 (*endometriomata*) does not decrease 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 are 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 women to maximise fertilisation.

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## Endometriosis, Fertility and Pregnancy

### **In vitro maturation (IVM)**

In vitro maturation is a new technique. About 300 children have been born around the world from this technique. There is no evidence to suggest that it is unsafe, neither is there enough evidence to be certain that it is a safe treatment. 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 woman needs to take fewer fertility drugs.

### **PGD (Pre-implantation Genetic Diagnosis)**

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

### **PGS (Pre-implantation Genetic Screening)**

Pre-implantation genetic screening tests the embryos for common genetic conditions such as Down's syndrome. Healthy embryos are replaced by embryo transfer. It was thought that screening would benefit older mothers who have a higher chance of having a baby with Down's syndrome. 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 may be recommended when treatment is unlikely to be successful if you were to use your own eggs or sperm. Donor sperm can also be used for women who do not have a male partner. 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 eggs donated from another woman and your partner's 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 who have a medical condition that means that it is impossible or dangerous for them to undergo a pregnancy or give birth.

## Endometriosis, Fertility and Pregnancy

### Pregnancy and Endometriosis

Endometriosis can cause delay in getting pregnant, but once you are pregnant, pregnancy is expected to be no different from normal. There are reports of women who had more pain in the first few months of pregnancy. In general, pain improves, but may return after giving birth as periods return.

### Complementary treatments

There are numerous complementary therapies available. A lack of research evidence makes it difficult to recommend complementary treatments. Acupuncture, homeopathy and herbal medicine may help. Self help groups can help sufferers improve their symptoms.

### Medical References

Marcoux S., Maheux R., Berube S (1987). Laparoscopic surgery in infertile women with minimal or mild endometriosis. Canadian Collaborative Group on Endometriosis. *New England Journal of Medicine*; 337: 217-22.

Sutton C.J., Ewen S.P., Whitelaw N., Haines P (1994). Prospective randomised double-blind controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal, mild and moderate endometriosis. *Fertility and Sterility* **62**: 696-700.

Sutton C.J., Polley A.S., Ewen S.P., Haines P (1997). Follow-up report on a randomised controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal to moderate endometriosis. *Fertility and Sterility* **68**: 1070-4.

### Further information about fertility treatment

Free from The Human Fertilisation & Embryology Authority. The patients' guide to infertility & IVF. Human Fertilisation & Embryology Authority, Paxton House, 30 Artillery Lane, London E1 7LS.

Free from The Human Fertilisation & Embryology Authority. The patients' guide to IVF clinics. Human Fertilisation & Embryology Authority, Paxton House, 30 Artillery Lane, London E1 7LS.

Infertility the Facts written by Melanie Davies, Lisa Webber & Caroline Overton. Published 2008 by Oxford University Press.





## Endometriosis, Fertility and Pregnancy

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