

Endometriosis

Endometriosis is a chronic oestrogen-dependent condition characterised by the growth of endometrial tissue in sites other than the uterine cavity, most commonly the pelvic cavity (including the ovaries), the uterosacral ligaments, the pouch of Douglas, the rectosigmoid colon, and the bladder and distal ureter.

Other sites are rarely involved but include the umbilicus, scar sites (eg, following caesarean section and laparoscopy), the pleura and pericardium, and the central nervous system.

Adenomyosis is the invasion of the myometrium by endometrial tissue. Extrauterine endometrial tissue causes inflammation, pain and the formation of adhesions. Clinically its significance is as a cause of chronic pelvic pain, dyspareunia and female infertility^[1].

Epidemiology^[1] ^[2]

- Endometriosis is one of the most common gynaecological disorders in women of reproductive age. Endometriosis is the second most common gynaecological condition (after fibroids).
- The prevalence is not known accurately because of variability in clinical presentation. Some women with endometriosis may be asymptomatic.
- The only reliable diagnostic test is laparoscopy. It takes an average of 7.5 years from the onset of symptoms before endometriosis is diagnosed.
- Endometriosis affects approximately 10% of women of reproductive age in the UK.
- The prevalence of endometriosis in women with infertility is about 30–50%.

Risk factors

- Risk factors include: an early menarche, late menopause, late first sexual encounter, delayed childbearing and nulliparity.
- Obstruction to vaginal outflow - eg, hydrocolpos, female genital mutilation or defects in the uterus or Fallopian tubes.
- Genetic factors:
 - Risk for first-degree relatives of women with severe endometriosis is six times higher than that for relatives of unaffected women.
 - Familial aggregation has been shown in clinical and population-based samples and in twin studies^[3].
- Other risk factors include white ethnicity, low body mass index (BMI) and smoking.

Aetiology^[1]

The exact cause of endometriosis is unknown. It is thought that endometriosis may develop as a result of a combination of the following possible theories/factors:

- Retrograde menstruation: endometrial cells flow backwards from the uterine cavity, through the Fallopian tubes, and implant on pelvic organs.
- Lymphatic or circulatory dissemination: it has been suggested that endometriotic tissue may also be able to travel to distant sites (such as the lungs, eyes, and brain) through the lymphatic system or in the bloodstream.
- Genetic predisposition.
- Metaplasia: cells in the pelvic and abdominal area change into endometrial-type cells. of the germinal epithelium.
- Environmental factors: this theory suggests that certain environmental toxins can affect the body, immune system, and reproductive system and cause endometriosis.

- Immune dysfunction: many women with endometriosis appear to have reduced immunity to other conditions.

Presentation

Common symptoms include:

- [Dysmenorrhoea](#).
- [Dyspareunia](#).
- Cyclical or chronic [pelvic pain](#).
- [Subfertility](#).

Other symptoms may include bloating, lethargy, constipation and low back pain. Less common symptoms include cyclical rectal bleeding, menorrhagia, diarrhoea and haematuria.

The clinical presentation is variable, with some women experiencing several severe symptoms and others having no symptoms at all. The severity of symptoms tends to increase with age.

- Women with endometriosis may have no symptoms and be diagnosed incidentally or during investigations for infertility.
- The appearance or worsening of symptoms *at the time of menstruation, or just prior to it*, suggests endometriosis.
- Other symptoms include [lower urinary tract symptoms](#) (eg, dysuria), painful defecation, abdominal pain, backache, menstrual irregularity, and cyclical pain or bleeding (eg, epistaxis, haemoptysis) at extrapelvic sites.

Signs

- Examination is often normal.

- However, there may be:
 - Posterior fornix or adnexal tenderness.
 - Palpable nodules in the posterior fornix or adnexal masses (endometriosis can cause cystic lesions on the ovaries, known as 'chocolate cysts').
 - Bluish haemorrhagic nodules visible in the posterior fornix.

The National Institute for Health and Care Excellence (NICE) recommends abdominal and pelvic examination for women with suspected endometriosis to identify abdominal masses and pelvic signs, such as reduced organ mobility and enlargement, tender nodularity in the posterior vaginal fornix, and visible vaginal endometriotic lesions. If a pelvic examination is not appropriate, offer an abdominal examination to exclude abdominal masses

[4]

Differential diagnosis

- Pelvic inflammatory disease.
- Ectopic pregnancy.
- Torsion of an ovarian cyst.
- Appendicitis.
- Primary dysmenorrhoea.
- Irritable bowel syndrome.
- Uterine fibroids.
- Urinary tract infection.

Investigations

- For a definitive diagnosis of most forms of endometriosis, laparoscopy is the gold standard investigation but it is invasive with a small risk of major complications - eg, bowel perforation^[3].

- Symptoms and laparoscopic appearance do not always correlate.
- Transvaginal ultrasound scanning appears to be a useful test, both to make and to exclude the diagnosis of an ovarian endometrioma^[3].
- MRI scan may be a useful non-invasive tool in diagnosis, especially for subperitoneal deposits.
- CA 125 measurement has limited value as a screening test or diagnostic test^[3].

In an acute setting, blood tests (eg, FBC), urinalysis and MC&S, cervical swabs (MC&S, [chlamydia](#) testing) and beta human chorionic gonadotrophin (beta-hCG) may be helpful in excluding some important differentials.

The NICE guidelines for the management of endometriosis advise on recognition of symptoms and diagnosis, as well as treatments for symptom control and when a couple are trying to conceive^[4] :

- Transvaginal ultrasound can be used to investigate suspected endometriosis even if the pelvic and/or abdominal examination is normal and also to identify endometriomas and deep endometriosis involving the bowel, bladder or ureter.
- Pelvic MRI should not be used as the primary investigation to diagnose endometriosis in women with symptoms or signs suggestive of endometriosis. However, it might be used to assess the extent of deep endometriosis involving the bowel, bladder or ureter.
- When pelvic MRI scans are used in assessment of pelvic pain symptoms, they should be interpreted by a healthcare professional with specialist expertise in gynaecological imaging.

Management^[5] ^[6]

- The treatment of endometriosis is usually individually based, depending on the nature and severity of symptoms and the need for future fertility.

- Medical treatment may reduce symptoms in 80–90% of patients but none of the treatment options has been shown to reduce recurrence of symptoms once treatment has stopped^[3] .
- Suppression of ovarian function for at least six months is the basis for most medical treatment, and the options include the combined oral contraceptive (COC) pill, medroxyprogesterone acetate and gonadotrophin-releasing hormone (GnRH) agonist.
- The levonorgestrel intrauterine system has been shown to be effective even after three years of use.
- Surgical options include removing severe and deeply infiltrating lesions (which may reduce pain related to endometriosis), ovarian cystectomy (for endometriomas), adhesiolysis and bilateral oophorectomy (often with a hysterectomy).
- NICE recommends that the evidence for uterine artery embolisation for treating adenomyosis shows that the procedure is effective for symptom relief in the short and medium term and there are no major safety concerns^[7] .
- Management may also include pain management specialists and clinical psychologists.

Pain

For pain, the general principle is to create a pseudo-pregnancy or pseudo-menopause, whilst the treatment of infertility requires a different approach.

- For laparoscopically confirmed disease, suppression of ovarian function for six months reduces endometriosis-associated pain.
- Effective hormonal drugs include the COC pill, danazol, oral or depot medroxyprogesterone acetate, the levonorgestrel intrauterine system and GnRH analogues. Approximately 80–85% of patients improve with treatment.
- Ablation of endometrioid lesions reduces endometriosis-associated pain. The smallest effect is seen in patients with minimal disease.

Drugs^[8]

- Non-steroidal anti-inflammatory drugs (eg, naproxen) may be effective in reducing the pain associated with endometriosis, although the evidence to date is inconclusive^[9] .
- Paracetamol, with or without added codeine, is an alternative.
- If there is no evidence of a pelvic mass on examination, there may be a role for a therapeutic trial of a COC pill (monthly or tricycling) or a progestogen to treat pain symptoms suggestive of endometriosis, without a diagnostic laparoscopy first.
- Danazol is effective in treating endometriosis but its use is limited by androgenic side-effects^[10] .
- GnRH analogues (GnRH agonists) appear to be effective at relieving pain associated with endometriosis^[11] .
- GnRH agonist therapy given for three months may be as effective as treatment given for six months in relieving endometriosis-associated pain. If longer or repeated treatment is required, GnRH agonist use can be extended with 'add-back' therapy (a low-dose oestrogen, progestogen or tibolone to relieve menopausal side-effects and prevent bone loss)^[3] .

Referral

NICE recommends to consider referring women to a gynaecology service for an ultrasound scan or gynaecology opinion if^[4] :

- They have severe, persistent or recurrent symptoms of endometriosis.
- They have pelvic signs of endometriosis.
- Initial management is not effective, is not tolerated or is contra-indicated.

Surgical

- Laparoscopic excision at the time of diagnostic laparoscopy. Excision should be considered in preference to ablation^[1] .
- Hysterectomy with salpingo-oophorectomy is reserved for women as a last resort.

- Laparoscopic surgery has been shown to reduce pelvic pain when compared to diagnostic laparoscopy alone^[12] .

Fertility

- Medical treatment for endometriosis should be avoided for women who are trying to conceive^[3] .
- In minimal-mild endometriosis, suppression of ovarian function to improve fertility is not effective but ablation of endometrioid lesions plus adhesiolysis is effective compared to diagnostic laparoscopy alone.
- The use of laparoscopic surgery in the treatment of subfertility related to minimal and mild endometriosis may improve future fertility^[13] .
- There is insufficient evidence available to determine whether surgical excision of moderate-to-severe endometriosis enhances pregnancy rates.
- In vitro fertilisation (IVF) is appropriate treatment, especially if there are co-existing causes of infertility and/or other treatments have failed^[14] .

Complications

- A review found an association between endometriosis and some histological subtypes of ovarian cancer^[15] :
 - Endometriosis was associated with a significantly increased risk of clear-cell, low-grade serous and endometrioid invasive ovarian cancers.
 - No association was noted between endometriosis and risk of mucinous or high-grade serous invasive ovarian cancer, or borderline tumours of either subtype.
- Infertility: moderate-to-severe endometriosis can cause tubal damage leading to infertility. Lesser degrees of endometriosis, even in the absence of any obvious tubal damage, are also associated with subfertility and increased risk of ectopic pregnancy.

- Adhesion formation may occur due to the endometriosis or following surgery.
- Women with endometriosis have an increased risk of inflammatory bowel disease^[16].

Prognosis^[1]

- The prognosis is variable. It is unclear whether endometriosis is always progressive, remains stable, or improves with time.
- Endometriosis can be a chronic disease affecting women throughout their reproductive lives, and sometimes beyond the menopause.
- For the majority of women, symptoms can be controlled with hormonal treatment. Some women have complex needs and require long-term support.
- Studies in untreated women with infertility suggest that endometriotic deposits can spontaneously regress in up to 30% of women, and progress is around 50% over 6–12 months.
- Recurrence after surgery ranges from 10–50% at one year and increases over time.

Further reading

- [Endometriosis UK](#)

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