



## THEME

Pelvic pain



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# Endometriosis

## An update

### BACKGROUND

Endometriosis is one of the major causes of pelvic pain and subfertility in women.

### OBJECTIVE

This article discusses the diagnosis and treatment of endometriosis.

### DISCUSSION

Empiric treatment in women presenting with pain symptoms suggestive of endometriosis is the usual first option.

Ultrasound does not diagnose peritoneal disease but will recognise endometriomas. Laparoscopy remains the gold standard for diagnosis and surgical removal at that time should be first line treatment.

Medical treatment is proven effective for superficial disease. It is most frequently used where surgical skills do not allow removal of the endometriosis or where incomplete removal is suspected in severe disease. Long term treatment after surgical removal with diet, exercise and hormones provides long term pain control and may reduce the risk of recurrence. Medical treatment has no place in infertility treatment, however surgical removal of milder disease enhances pregnancy rates. Early referral for assisted reproduction treatment is suggested with severe disease.

**Endometriosis is a condition where endometrial glands and stroma are found in sites outside the endometrium and myometrium of the uterus. These implants are most commonly found in the pelvis but can occur in many other sites. Endometriosis is a chronic disease causing significant interference to quality of life. Important concerns for women include delayed diagnosis, chronic pain management, acceptability and tolerance of treatments that may require long term usage and potential infertility.**

### Diagnosis

#### Symptoms

Symptoms are varied and nonspecific, which often leads to a diagnostic delay if clinical suspicion is not high. The commonest pain symptoms are dysmenorrhoea, pelvic pain (especially midcycle), and dyspareunia. Less common complaints are cyclical bowel and bladder symptoms, which are suspicious of more severe disease. Nonspecific symptoms such as tiredness, lethargy or premenstrual tension are also common. Infertility is the other major presenting symptom. Symptoms have a pervasive effect on lifestyle and may interfere with education, employment, sexual relationships and social functioning. A treatment plan needs to be tailored to make use of treatment options acceptable to the individual woman.

### Examination

Most women with endometriosis exhibit no abnormality or minimal findings on physical examination. Clues to the diagnosis include uterine, adnexal or pouch of Douglas tenderness, a tender fixed adnexal mass or a fixed retroverted uterus. The most suggestive sign is tenderness and nodularity in the pouch of Douglas or uterosacral ligaments. In any pelvic examination where endometriosis is suspected, a conscious effort should be made to palpate this area by running the vaginal fingers behind the cervix and onto the pouch of Douglas. The palpation should then continue laterally to define the bordering uterosacral ligaments. Nodularity in this area is highly suggestive of endometriosis.

Positive findings are often associated with more severe disease and should increase clinical suspicion. This may prompt more immediate recourse to specialist opinion or surgery. They may also influence preoperative planning, counselling and the use of bowel preparations.

### Ultrasound

Transvaginal ultrasound is not useful in diagnosing the majority of cases of endometriosis as the peritoneal implants and adhesions involved are not detectable. A negative ultrasound could never be used as definitive evidence of the absence of endometriosis. However, ultrasound remains a

vital preoperative investigation because of its ability to detect ovarian endometriomas.

An ultrasound report should provide a clear and detailed description of the ovaries and any cyst involved as well as a possible diagnosis or differential. In particular, any concerning features should be mentioned. If this level of detail is not provided, you should speak to your ultrasound service about its provision.

Endometriomas are described as having a 'ground glass' appearance on ultrasound as the thick altered blood within the cyst has some echogenic properties. The main differential is a haemorrhagic corpus luteum. If surgery or referral for specialist opinion is not immediately planned, sorting out this differential is best achieved by repeating the scan. This should be done 6–8 weeks later, preferably in the first half of the menstrual cycle. By this time, the corpus luteum should have resolved whereas the endometrioma will have remained unchanged. Other ultrasound clues are that endometriomas are often bilateral and the ovary is immobile to probing as it is fixed to the pelvic side wall by inflammatory adhesions.

Using transvaginal, transrectal or renal ultrasound to define the extent of deeply infiltrating disease in the rectovaginal septum, bladder or ureters, along with magnetic resonance imaging (MRI), is finding application in preoperative planning. This currently remains the domain of specialist gynaecological ultrasound services and gynaecologists with a special interest in difficult operative laparoscopy.

## Laparoscopy

Laparoscopy is the gold standard investigation for the diagnosis of endometriosis and now provides the main tool of treatment. Visual recognition is the means of diagnosis, although histological confirmation is also recommended as visual diagnosis alone varies in accuracy.

## Treatment

### Treatment of pain

Endometriosis is a chronic condition that interferes with the quality of life. Recurrence rates are high. Treatment goals include removal of the endometriotic implants and prevention of their return. However, the main aim is the treatment of the associated pain and subfertility. It is imperative that the woman is counselled carefully about the potential benefits and likely side effects of any proposed treatment. Nothing is more likely to cause frustration with the treatment suggested than unrealised expectations or unexpected side effects. Initial treatment should involve the least invasive and least expensive option.

As symptoms are nonspecific and definitive diagnosis requires an invasive procedure, many women with endometriosis are no doubt treated adequately with simple analgesia and hormonal manipulation without a formal diagnosis ever being made. Women presenting with pain symptoms possibly related to endometriosis should be tried on these conservative measures first.

## Empirical treatments

Empirical treatments include simple analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), progesterones, and the combined oral contraceptive pill (COCP), as well as exercise, nutrition and multiple alternate therapies.

A 2003 Cochrane review looking at NSAIDs in the treatment of primary dysmenorrhoea concluded that they were more effective in control of pain than placebo.<sup>1</sup> It is likely that a significant number of women in this trial had endometriosis.

There is a lack of evidence regarding the benefit or otherwise of modern low dose COCPs in the treatment of dysmenorrhoea.<sup>2</sup> Anecdotally they are considered effective and can be used safely in the long term.

Progesterones (medroxyprogesterone acetate, orally or depo; norethisterone, dydrogesterone or the levonorgestral intrauterine device, Mirena) have been shown to be as effective as any of the medical treatments available in dealing with confirmed endometriosis.<sup>3,4</sup> Due to their benign side effect profile and safety for long term use they remain suitable empiric treatments.

## Pharmacological

Hormone therapy to treat endometriosis diagnosed on laparoscopy was the mainstay of treatment for peritoneal endometriosis before the development of operative laparoscopy. Multiple randomised controlled trials have noted these to be effective for the treatment of endometriosis related pain.<sup>4–7</sup> The main agents used have been:

- progesterones (including Mirena IUD)
- continuous COCP
- danazol
- gestrinone, and
- the GnRH agonists (see *Table 1* for their methods of action and side effect profile).

No agent has proven to be more effective; therefore cost, side effect profile and personal preference usually dictate choice. As an alternative to surgery they are appropriate where surgical skills do not allow removal of the endometriomas where severe disease makes the excision incomplete.

Evidence is mixed as to the benefits of preoperative medical treatment,<sup>8–10</sup> however, trials have established postsurgical medical treatment gives significantly long

control of pain.<sup>11–13</sup> This should usually be in the form of a progesterone or COCP due to their milder side effect profile and ability to be used long term.

### Surgery

Peritoneal implants can be removed by excision, diathermy ablation or laser vaporisation. Randomised controlled trials have shown these to be effective means of treating pain,<sup>14–15</sup> however no technique has been demonstrated to be superior to the other. Many surgeons believe that excision of the endometriosis allows potentially more complete treatment as deep nodules can appear as superficial implants until excision is attempted (*Figure 1, 2*). Such nodules may not be fully treated by ablation or vaporisation. Excision also allows vital structures on the pelvic side wall (eg. ureters) to be recognised and protected and provides histological evidence to confirm the visual diagnosis.

Endometriomas are best stripped from the ovary and completely excised. This has been shown to give better symptomatic relief than drainage and ablation.<sup>16–17</sup> It also provides histology to exclude rare malignancies. The potential downside is a greater loss of ovarian tissue and follicle reserve.

Treatment of women with severe symptomatic disease involving obliteration of the pouch of Douglas and involvement of the bowel, bladder or ureters should be referred to centres specialising in complicated operative laparoscopy. This surgery will often be performed in consultation with a colorectal surgeon or urologist and

may involve bowel or bladder resections or reimplantation of ureters.

Oophorectomy and hysterectomy have become less common measures as modern surgical treatment has concentrated on removal of disease and restoration of normal anatomy. They remain an option where conservative measures have failed to provide adequate relief and fertility is not required. Care should be taken to ensure any remaining pelvic endometriosis is removed at the same time.

### Infertility

There is no evidence to suggest that hormone treatment is effective in treating infertility in mild or severe endometriosis. It should not be offered as treatment in this situation.<sup>18</sup>

In minimal to mild endometriosis, surgical removal plus adhesiolysis appears to improve fertility when compared to diagnostic laparoscopy alone.<sup>19–20</sup> While evidence in these trials has some weakness, it would seem a reasonable treatment. Where success is not achieved referral for assisted reproductive treatment in the form of ovulation induction with intrauterine insemination or in vitro fertilisation (IVF) is appropriate.

There is no reasonable data to answer this question where the disease is moderate or severe. As the disease becomes more severe pregnancy rates fall.<sup>21</sup> Where there is anatomical distortion of the pelvis rectifying this at the time of surgery would seem prudent. Early referral to assisted reproductive treatment is suggested and where

**Table 1. Options for hormone treatment of endometriosis**

|                                    | <b>Method of action</b>  | <b>Maximum treatment length</b> | <b>Side effects</b>  |
|------------------------------------|--|---------------------------------|--|
| COCP, continuous or cyclical       | Decidualisation of endometrium leading to atrophy  | Indefinite                      | Nausea, headache, breast tenderness, breakthrough bleeding (BTB), depression   |
| Progestones (including Mirena IUD) | Decidualisation of endometrium leading to atrophy  | Indefinite                      | Nausea, weight gain, fluid retention, BTB, depression, breast tenderness, possible bone density loss in the long term                        |
| Danazol                            | Multiple effects causing a high androgen low oestrogen environment inhibiting endometrial growth           | 6 months                        | Androgenic and hypoestrogenic – hot flushes, breast shrinkage, acne, hirsutism, weight gain, vaginal atrophy, voice deepening (irreversible) |
| Gestrinone                         | Androgenic and anti-oestrogenic, progestogenic and gonadotrophic activity causing endometrial degeneration | 6 months                        | Similar profile to danazol but tends not to be as severe   |
| GnRH analogues                     | Down regulation of gonadotrophic activity inducing a pseudomenopause                                       | 6 months                        | Hypo-oestrogenic (marked) – hot flushes, emotional lability, atrophic vaginitis, reduced libido, short term bone density loss                |

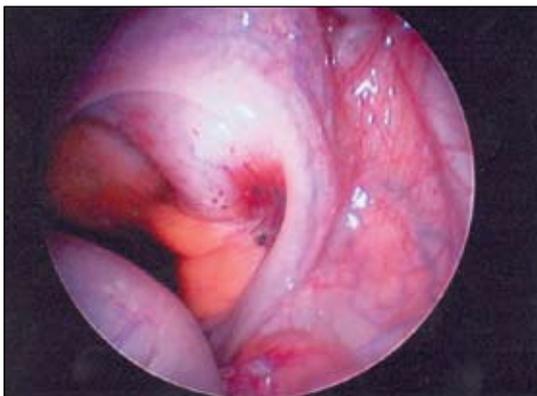


Figure 1. Endometriotic implant right uterosacral ligament (the area is distended by a swab in the vagina used to push the implant into view from under the ligament). This lesion may be mistaken as superficial on visual appearance alone



Figure 2. The implant which extended into the vagina and pararectal space has now been removed. The gauze swab is protruding through the opened vaginal wall which was subsequently sutured

adhesions, endometriomas or pelvic distortion exist, only IVF is likely to be appropriate.

### Long term considerations

Exploration of alternative therapies should not be discouraged or criticised. Support groups such as the Endometriosis Association of Victoria ([www.endometriosis.org.au](http://www.endometriosis.org.au)) provide assistance and validation for the many challenges endometriosis patients encounter.

### Conclusion

Endometriosis often requires many surgical and medical treatments. A clear explanation of the disease and its possible course must be provided from the outset. Women must be comfortable with therapies provided and expectations for their potential must be realistic. Options that don't conform to a woman's own beliefs and lifestyle are unlikely to be successful, even where the clinician believes them to be the best therapy. Future treatments will hopefully be able to deal with the underlying cause of endometriosis rather than dealing with current exacerbations and preventing recurrence.

Conflict of interest: none declared.

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