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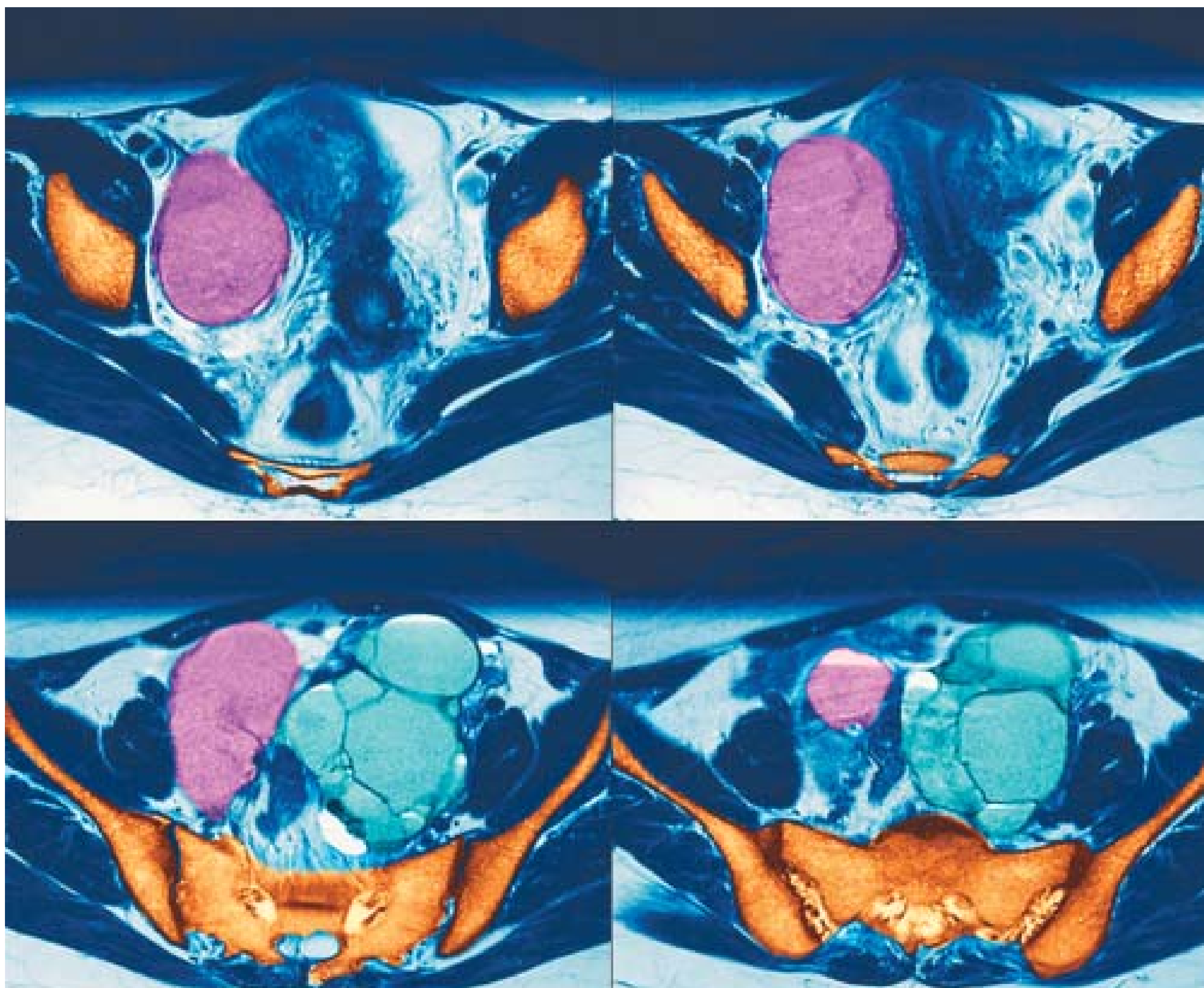

Endometriosis

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The authors

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Background

ENDOMETRIOSIS is a common condition affecting the health and wellbeing of 10-15% of Australian women of reproductive age.

Despite increasing awareness of this condition through the dedicated work of patient-support groups and continuing medical education, there remains a delay to diagnosis of 7-9 years.

If left untreated, endometriosis may result in significant disruption to a woman's life, including strain on interpersonal relationships and economic consequences for both the individual and society at large.

This article provides an up-to-date review to help GPs understand, identify, support and manage women with endometriosis.

What is it?

Endometriosis is defined as the presence of endometrial glands and stroma outside the uterine cavity. It is most often found on the pelvic peritoneum, including the uterosacral ligaments, anterior and posterior cul de sac, ovaries and pelvic sidewalls.

Similar to normal endometrium, endometriotic tissue outside the uterus responds to cyclical ovarian hormonal stimulation by swelling and bleeding. While normal endometrium is shed in menstrual fluid, ectopic endometriotic tissue implants on the surface of the pelvic peritoneum, forms cysts inside the ovaries and/or infiltrates into the walls of pelvic organs such as the rectum and bladder.

The recurrent, cyclical swelling-bleeding-scarring pattern results in an insidious, chronic inflammatory process and a variety of clinical and surgical presentations.

Incidence and prevalence

Endometriosis may affect women at any time from puberty to menopause. The finding of endometriosis among asymptomatic women is common (as high as 43%) based on incidental discovery at surgery for separate indications.

However, the incidence becomes more dramatic in patients with signs and symptoms such as pelvic pain and infertility. In women with dysmenorrhoea the finding may be as high as 40-60%.

Among women undergoing laparoscopy for an infertility workup, endometriosis may be found in 30-40% of cases.

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Aetiology

ALTHOUGH pelvic pain and dysmenorrhoea have been documented in historical medical texts, endometriosis has only been recognised as a pathological condition in the last century.

In the mid-1920s, Dr JA Sampson from the US introduced the theory of retrograde menstruation to explain endometriosis. While this remains the dominant theory, it alone does not explain this condition, as 70-90% of all women experience transtubal menstruation without developing endometriosis.

An altered immune response resulting in the body being unable to recognise or remove endometriosis implants may account for the susceptibility and development of this condition in some women.

Sampson's theory may be further expanded into a 'transplantation theory', which would include lymphatic and vascular spread of endometriosis. Cases of lung, brain and skin endometriosis would be explained by this type of spread and emphasise the importance of endometriosis as part of the differential diagnosis in any case of cyclical (catamenial) symptoms outside the pelvis.

Genetic predisposition for developing this condition has been investigated through familial and twin studies, revealing a definite inheritance pattern among some women. Research has found the risk of endometriosis is seven times greater in women who have an affected first-degree relative. The pattern of familial spread is complex and likely to be multifactorial.

Diagnosis

DIAGNOSING endometriosis requires a careful history, examination and appropriate complementary investigations.

History

The symptoms and signs of endometriosis vary greatly among women. Pelvic pain is a classic symptom of endometriosis; however, women may also report abnormal bleeding, bowel and bladder symptoms and/or difficulties conceiving. It is useful to consider the many different presentations of endometriosis under the common complaints that women may experience when affected by this disease process (table 1).

These symptoms and signs may occur alone or in combination. All patients with these chief complaints require a detailed pain and gynaecological history to explore and rule out other causes of pain (table 2).

A focused history would also include reproductive health questions, including age of menarche, cycle frequency and regularity, previous pregnancies, use of oral contraception or hormonal treatments, contributory medical and surgical history and a family history of endometriosis or gynaecological cancers.

Examination

Physical examination in the primary care setting is essential to help diagnose and triage patients for appropriate care and to rule out other pathology or acute conditions that may require immediate attention (eg, surgical abdomen from appendicitis).

Examination should include a vaginal assessment to determine the position, size and mobility of the uterus; a fixed retroverted uterus may suggest severe adhesive disease.

Rectal examination is often a useful adjunct to the vaginal exam in patients who have bowel symptoms. Palpation of the uterosacral ligaments and rectovaginal septum may reveal tender nodules, which are typical of severe endometriosis. Adnexal masses may be discovered on physical examination and may suggest ovarian endometriomas.

Table 1: Symptoms and signs in women with endometriosis

Pain
- Painful menstruation (dysmenorrhoea)
- Painful intercourse (deep dyspareunia)
- Painful micturition (dysuria)
- Painful defecation (dyschesia)
- Chronic pelvic pain
- Lower-back or abdominal discomfort

Abnormal bleeding
- Premenstrual spotting
- Heavy menstrual bleeding (menorrhagia)
- Irregular bleeding

Bowel symptoms
- Diarrhoea or constipation
- Abdominal bloating
- Symptoms suggestive of irritable bowel syndrome

Infertility
- Difficulty conceiving after one year of unprotected intercourse, when all other causes of infertility have been evaluated and excluded

Atypical presentations
- Cyclical leg pain or sciatica
- Cyclical rectal bleeding or haematuria
- Chronic fatigue

In adolescents and non-sexually-active women, pelvic examination may be confined to rectal assessment and/or pelvic imaging.

Investigations

Ultrasound is the first-line investigational tool in the workup of endometriosis. It allows detection of ovarian cysts or other pelvic pathology such as uterine fibroids.

There is little support for the routine use of blood work or other imaging in the primary workup of these cases. Although serum CA125 level may be elevated in moderate to severe endometriosis, it should not be used as part of the routine workup of patients.

The gold standard for diagnosis is direct visualisation at laparoscopy (figure 1). Disease severity is best described through a description of the appearance of the endometriosis, its location and any organ involvement.

The American Society of Reproductive Medicine (ASRM) has also developed a classification to allow staging of endometriosis at laparoscopy. This type of classification has limited utility for clinical management, as disease stage may not correlate with the patient's symptoms.

It is important to appreciate that the diagnosis and description of disease as minimal, mild, moderate or severe is highly subjective and will vary among practitioners.

Women in the reproductive age group with symptoms of irritable bowel syndrome have a high chance (some evidence indicates as high as 25-50%) of having endometriosis as the underlying or coexisting pathology.

This finding suggests that laparoscopy should be considered in some patients with symptoms suggestive of IBS. If bowel symptoms are prominent, colonoscopy should be considered to rule out the possibility of bowel endometriosis involvement.

Diagnostic laparoscopy is not required in all patients presenting with pelvic pain and is ideally used in patients who require diagnosis and active treatment. Although laparoscopy is considered a minimally invasive procedure, it still carries the risks of surgery, including bowel and bladder perforation and vascular injury.

The risk of minor complications such as nausea and shoulder tip discomfort is in the order of 3%, while the major complications (vascular and bowel injury) are less commonly found at 0.6-1.8 per 1000 cases.

Figure 1: Normal pelvis at laparoscopy.

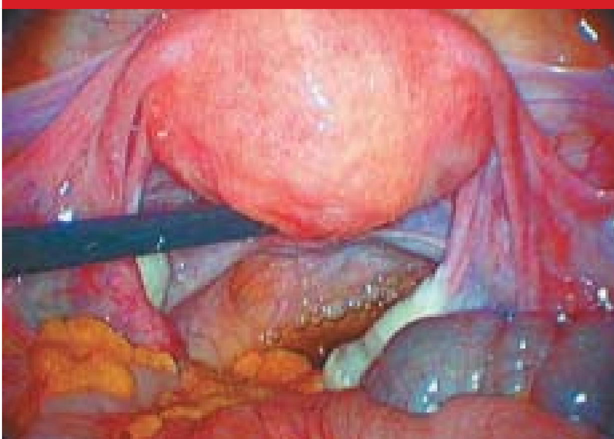


Figure 2: Classic black-brown implants of endometriosis along pelvic peritoneum.

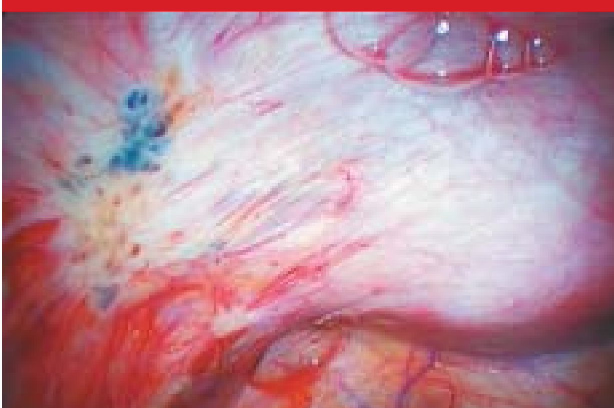


Figure 3: Bilateral ovarian endometriomas occupying cul de sac.

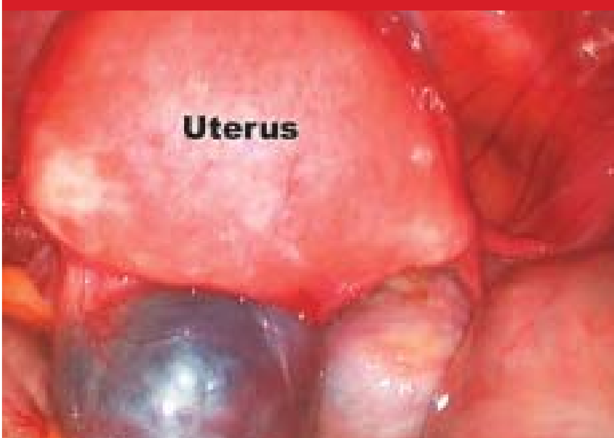
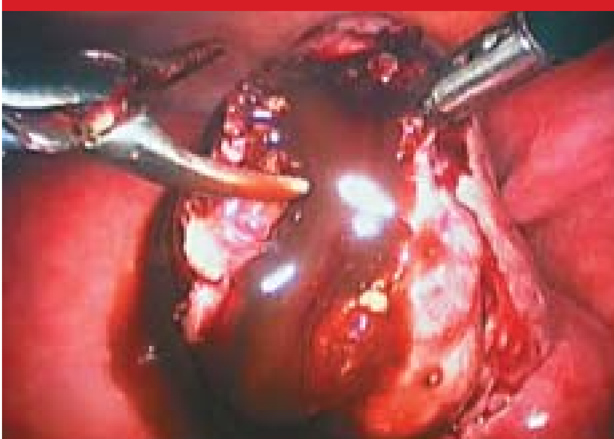


Figure 4: Ruptured ovarian endometrioma ('chocolate cyst').



What does endometriosis look like?

Endometriosis has several different appearances at laparoscopy. Typically it is seen superficially over the pelvic peritoneum, covering the side walls, uterus, ovaries, bowel or bladder (figure 2). It may appear as:
- A superficial 'powder burn'.
- Black, dark-brown or bluish lesions, nodules or small cysts.
- Red, serous or clear vesicles.
- Plaques or scars.

Ovarian endometriomas are cysts filled with old blood from invaginated endometriosis that appear as 'chocolate cysts' after they have ruptured or drained (figures 3 and 4). These cysts may enlarge to significant sizes and be detectable on clinical examination. They are best seen at pelvic ultrasound, with a classic sonographic appearance.

Table 2: Differential diagnosis for pelvic pain

Uterine
- Primary dysmenorrhoea
- Adenomyosis

Bowel
- Irritable bowel syndrome
- Inflammatory bowel disease
- Chronic constipation

Bladder
- Interstitial cystitis
- Urinary tract infection
- Urinary tract calculi

Ovarian
- Mittleschmerz (ovulation pain)
- Ovarian cysts (rupture, torsion, etc)
- Ovarian remnant syndrome

Fallopian tube
- Haematosalpinx (after sterilisation or endometrial ablation)
- Ectopic pregnancy (acute and chronic)

General
- Endometriosis
- Myofascial pain
- Neuropathic pain
- Pelvic congestion

Managing endometriosis pain

PELVIC pain is a complex clinical scenario with many sources other than endometriosis, including uterine (adenomyosis), bladder (interstitial cystitis) or musculoskeletal (pelvic floor muscle spasms).

Furthermore, pelvic pain has a profound effect on the overall quality of life, including mental and sexual health. The GP's supportive counselling will be invaluable in these difficult cases.

Because endometriosis may present with different clinical manifestations, its treatment must be tailored to the individual's symptoms with consideration given to the underlying differential diagnosis. Pelvic pain secondary to endometriosis is managed primarily by medications and patient support.

Surgical intervention is reserved for patients who are refractory to first-line treatment or present with severe disease such as large endometriomas or rectal disease (see Surgical options, below).

Medical options

Medical treatment is an effective first-line approach to pain associated with endometriosis. Although medical treatment provides effective temporary relief for symptoms, it has not been shown to alter the natural history of the disease.

In women treated successfully with medical therapies, symptoms often recur after stopping treatment. Education, support and awareness of the chronic nature of this condition are vital to management success.

NSAIDs

These medications are the first-line therapy for dysmenorrhoea but their role in endometriosis-specific pain (eg, dyspareunia, dyschesia) has not been validated. GPs should quantify the amount and type of NSAID used by patients to avoid complications of these medications such as gastric ulceration and renal dysfunction.

While NSAIDs offer a logical first-line approach for dysmenorrhoea, hormonal options are found to be better for the overall management of symptoms associated with this condition.

Hormonal treatments

The two main mechanisms of hormonal management are initiation of a 'pseudo-pregnancy' or 'pseudo-menopause' state. All hormonal options are relatively efficacious in controlling pain in endometriosis, with the main differences being cost, route of administration and side-effect profile (table 3).

Compliance may present a problem with some daily medications, while other medications may have adverse profiles after prolonged use.

The oral contraceptive pill

The oral contraceptive pill is an effective and safe method of symptom control. It may be used as a continuous or cyclical regimen. The continuous method involves daily ingestion of a monophasic combination pill, which suppresses the monthly menses.

This type of treatment may be effective for women who predominantly have dysmenorrhoea ('no period = no pain'). Although effective, the continuous OCP may result in some irregular spotting, and some patients may be uncomfortable with the idea of missing or "skipping" their period.

Gonadotrophin-releasing hormone agonists

Through suppressing the hypothalamic-pituitary-ovarian axis, GnRH agonists result in a 'pseudo-menopause' state. These medications are very effective at treating pain associated with endometriosis.

The side effects include menopausal symptoms such as hot flushes, vaginal dryness and mood swings. Bone loss will also occur if these agents are used alone for more than six months, which limits their long-term application.

GnRH agonist with 'add-back therapy' refers to providing women with hormone replacement (low-dose oestrogen/progestin) to counteract the menopausal symptoms and bone loss. When low-dose hormone replacement is used the benefit of pain control is maintained and allows for improved compliance and prevents bone loss with extended use.

The limiting factor for this medication is its cost and side-effect profile.

Progestins

Progesterone in women helps stabilise and control endometrial gland and stromal proliferation. Progestin is the synthetic counterpart to the naturally existing hormone and is widely used for contraception, menorrhagia and endometriosis. Progestins may be used orally, as an IM injection or as an implant.

The IM preparation of medroxyprogesterone acetate (Depot Provera) is effective at controlling pain related to endometriosis and is only required every three months. This may help with compliance in some women.

It should be noted that recent data have shown that use of this preparation over two years leads to reversible bone loss, so women should be counselled to maintain adequate calcium and vitamin D supplementation in addition to close monitoring.

Table 3: Hormonal treatment options for endometriosis

Medication	Route	Side effects	Comments
Combined hormonal contraception	Oral, transdermal, vaginal	Nausea, irregular bleeding	Continuous administration of a monophasic medication offers an alternative to cyclical methods
Progestins	Oral daily, IM every three months or SC implant three-yearly	Weight gain, bloating, acne, irregular bleeding	Long-term depot progestin may result in reversible osteopenia
GnRH analogue ± 'add-back' therapy of low-dose oestrogen/progestin	IM or nasal spray, varying frequency	Hot flushes, vaginal dryness (hypo-oestrogenic symptoms), osteopenia	Add-back therapy will allow extended use to counter side effects and bone loss. Without add-back, GnRH analogue should not be used for more than six months
Levonorgestrel intrauterine system	Intrauterine device (5 years)	Irregular bleeding	Will reduce menstrual blood loss and provide excellent contraception
Danazol	Oral daily	Androgenic (weight gain, acne, hirsutism)	Effective. Must be balanced with side-effect profile

Figure 5: Endometriosis lesion along right pelvic sidewall.

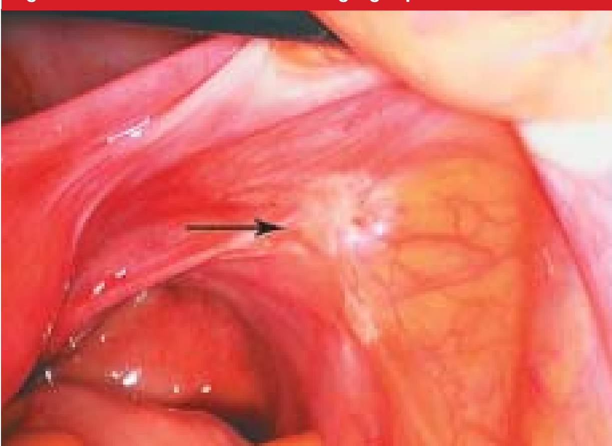


Figure 6: Excision of lesion for treatment and histopathological diagnosis.

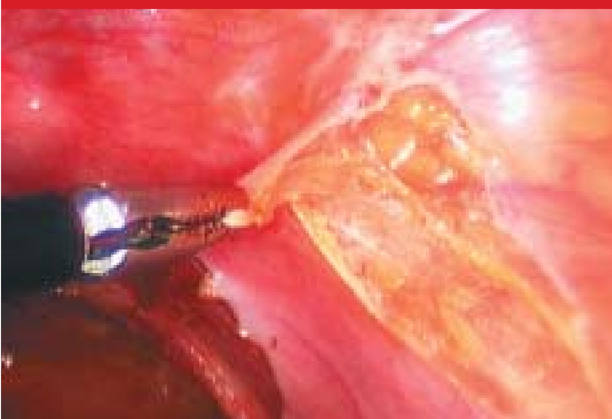
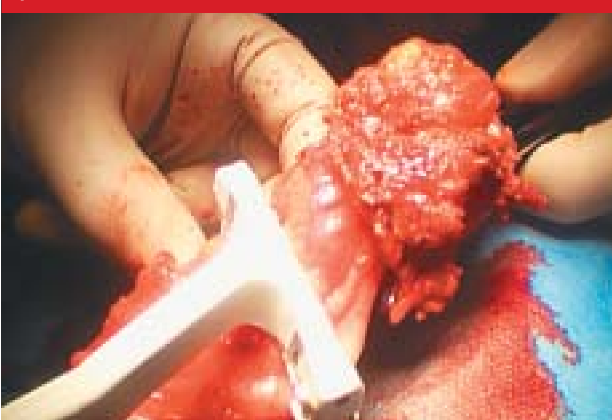


Figure 7: Rectal endometriosis: nodule from a bowel resection specimen.



Progestin intrauterine system

Progestin-lined intrauterine devices (Mirena) have become extremely popular for managing menorrhagia. It has now become apparent that, in addition to minimising uterine bleeding and providing effective contraception, this therapy may also help patients with pain due to endometriosis. The upfront cost may seem considerable, but over five years it is more cost-effective than other hormonal treatments.

Table 4: Indications for surgical management of endometriosis

- Diagnosis after failed medical management for symptoms suggestive of endometriosis
- Infertility investigation and treatment
- Endometrioma >3-4cm in diameter
- Failure of medical therapy
- Significant impact on quality of life
- Patient request for surgical management
- Secondary organ involvement (rectum, bladder)

Danazol

This hormonal option is just as effective as the other options discussed but the side-effect profile is less acceptable and includes androgenic symptoms such as oily skin, hirsutism, weight gain and acne. Long-term use has been associated with permanent virilisation such as voice changes.

Although effective in many cases, hormonal treatments may not always provide relief, and alternative treatments or surgical intervention may be required.

Surgical options

Surgical management is indicated if medical therapy fails, a patient desires pregnancy or presents with ovarian endometriomas on ultrasound (table 4). The current standard would involve laparoscopic management over laparotomy because of the greater visualisation through the magnified view, quicker patient recovery and return to normal activity.

Endometriosis may be ablated or excised using various energy modalities, including electrosurgery and carbon dioxide laser. Ablation refers to local destruction without removal of tissue. Excision involves removal of peritoneal implants or nodules to allow pathological diagnosis and treatment simultaneously (figures 5 and 6).

While there is considerable debate as to the benefits and risks of each method, one thing is clear: operator experience predicts the success of diagnosis and treatment.

Ovarian endometriomas >3-4cm in diameter also require surgical management. Current recommendations suggest surgical excision is superior to drainage to enable histopathological evaluation and to prevent recurrence.

Definitive treatment

Definitive treatment for patients with refractory pain secondary to severe endometriosis is to induce menopause through surgical or medical (GnRH agonists) options.

The surgical approach involves removing both ovaries (with or without hysterectomy) and results in immediate surgical menopause. Definitive surgery requires thorough counselling and support by a specialist.

In addition, the importance of postoperative calcium, vitamin D and possibly hormonal supplementation should be discussed with patients because of the earlier expected onset of bone loss and menopausal symptomatology.

If started three months after definitive surgery, HRT after bilateral oophorectomy is unlikely to cause recurrence of disease in most patients.

The role of specialists

General gynaecologists have the necessary laparoscopy skills to help diagnose endometriosis or other pelvic pathology, when indicated. However, it is now known that a specialist with an interest in endometriosis will be more likely to make an accurate diagnosis and assessment and be better able to surgically manage the disease.

Mild to moderate endometriosis may be managed by direct ablation or simple excision procedures, but severe endometriosis including bowel involvement requires greater training and experience (figure 7).

This is especially important for women with chronic pelvic pain and severe endometriosis requiring greater care and intervention.

Lifestyle management

IN addition to the traditional medical therapies outlined previously, the general wellbeing of the individual must be considered. This includes adherence to a well-balanced diet, regular exercise and stress management.

Counselling patients to make lifestyle changes when necessary is difficult but should be encouraged. Simple changes that will improve the ability to cope with pain associated with endometriosis include:

- Endometriosis education.
- Dietary changes, including high-fibre and low-fat foods.
- Weight loss if indicated.
- Reducing caffeine intake.
- Regular exercise.
- Adequate sleep.
- Adequate hydration.
- Stress reduction and relaxation techniques.

Coping with endometriosis varies tremendously between women and depends largely on their coping capabilities and support system. The severity of disease at laparoscopy does not always correlate with the level of subjective pain described by patients. If a woman is thought to have minimal endometriosis at laparoscopy, she may have more pain than someone labelled with severe disease.

Labels in these cases may minimise the impact of this diagnosis on a woman's quality of life, social function and mental health. Support groups may be of value in some patients suffering from endometriosis (see Online resources, page 32).

Not enough attention has been paid in our Western medical literature to these aspects of health and their impact on pelvic pain and endometriosis. As a result, the complementary medicine niche in this area has grown tremendously for women looking for alternative options.

Complementary therapies for endometriosis

From the perspective of Western medicine practitioners, our ability to counsel and prescribe herbal or other complementary medicines and therapies is often limited. We depend on the scientific method of evaluation, on society guidelines and expert recommendations.

At present there are no clear guidelines for alternative therapies in the treatment of endometriosis, and the following information is provided more for general awareness than clinical guidance.

While the evidence may be lacking in the area of complementary medicine or 'natural' therapies, women may be exploring many options while under your care (table 5). Patients should not be criticised for exploring options; however, they should understand there are only limited safety and efficacy data available in this area, especially with unregulated substances.

The dietary recommendation popular among complementary practitioners for endometriosis focuses on altering 'oestrogen dominance', although there are no clear guidelines or evidence for the routine that should be followed, or its efficacy.

Progesterone cream also has no clear evidence-based guidelines to support its use in endometriosis. Nevertheless it is being used by many patients with gynaecological complaints. Cream preparations generally come as 1.5-3% creams and are provided by some compound chemists.

The side-effect profile is said to be minimal; however, there is no clear information on its systemic effects, including changes on the uterus or breast.

With limited evidence from the classic scientific method, there is insufficient evidence to suggest or to dispel the effectiveness of the alternative therapies discussed above.

Table 5: Nutritional and complementary therapies used in endometriosis-related conditions*
Progesterone cream
Herbal treatment (vitex *Agnus castus*)
Homeopathy
Reflexology
Traditional Chinese medicine
Acupuncture
Dietary treatments (ie, macrobiotic diet)
Meditation and stress-management exercises

* There is only limited safety and efficacy data available in this area

Special scenarios

Endometriosis and fertility

Aetiology

INFERTILITY is a growing and common medical presentation that requires specialised support, investigations and treatment. Endometriosis must be considered as part of the evaluation for infertility.

Although not clearly established, endometriosis likely results in subfertility due to mechanical or inflammatory changes in the pelvis and uterus. Tubal blockage or destruction may occur secondary to severe adhesive disease.

Alternatively, the peritoneal fluid to which the oocyte is exposed after ovulation may also negatively impact on motility and maturation because of the inflammatory mediators released by ectopic endometrial glands and stroma.

A recent suggestion has proposed that a hostile uterine environment in women with endometriosis may prevent ideal implantation for conception.

Evaluation

Although laparoscopic evaluation is not always required in assessing infertility, it is generally advised in cases of:

- Unexplained infertility.
- Concomitant pelvic pain.
- Previous history of endometriosis or pelvic adhesions.

At laparoscopy, the gynaecologist will thoroughly evaluate the abdomen, pelvis, uterus, tubes and ovaries. A simultaneous tubal dye test helps document tubal patency, and a hysteroscopy may help rule out uterine cavity abnormalities.

Management

Management of infertility secondary to endometriosis requires specialised care, which often means referral to a specialist in infertility or a gynaecologist who manages endometriosis.

Young women with endometriosis often have a delayed diagnosis because their pain may be attributed to primary dysmenorrhoea and hence a 'normal' part of growing up.

While medical therapies may aid in pain relief, they do not improve spontaneous conception on their own and often will prevent conception in the case of hormonal therapies. Surgical management or advanced reproductive technologies are the primary treatment options for women with infertility.

Intrauterine insemination has been shown to be effective in improving fertility outcomes in women with minimal to mild endometriosis. In vitro fertilisation is also used to treat these patients, especially if tubal occlusion is present, there is male-factor infertility and/or other treatment options have failed.

However, it is recommended that large ovarian endometriomas (cysts ≥4cm diameter) be removed by laparoscopic cystectomy before any advanced reproductive technologies are used.

Use of GnRH agonists 3-6 months before IVF in women with endometriosis has been found to increase pregnancy rates.

Surgical management (ablation or excision at laparoscopy) of mild to moderate endometriosis will improve pregnancy rates, compared with diagnostic laparoscopy alone, for 9-12 months after surgery.

Surgery for severe endometriosis has not been well studied and the impact on fertility is not as clear. However, it is probable that tubal reconstruction resulting in reversing tubal obstruction would improve fertility.

Evaluation, diagnosis and management of women with infertility should always include endometriosis as a possible cause or comorbidity, to allow appropriate referral and management.

Relationship between endometriosis and cancer

Endometriosis should be considered a benign disease; however, rare instances of ovarian carcinomas (especially clear-cell and endometrioid subtypes) may be found among women with endometriomas. As a result, it is standard practice to at least biopsy if not completely excise the ovarian cyst capsule for ovarian endometriomas being surgically managed.

Adolescents and endometriosis

Young women with endometriosis often have a delayed diagnosis because their pain may be attributed to primary dysmenorrhoea and hence a 'normal' part of growing up. However, when pelvic pain interferes with daily activities (school or work) it requires attention and management. Up to 50-70% of adolescent girls with dysmenorrhoea not controlled by NSAIDs or the OCP have endometriosis.

One report found that 66% of women with endometriosis had symptoms starting before age 20 and that 47% of women had to see five or more doctors before a diagnosis was made.[1]

Early diagnosis and referral will help young women receive the necessary education regarding their symptoms and also help them obtain appropriate treatment.

Years of suffering and pain can effect a young woman socially and physically. School performance and attendance may be affected, leading to a 'slippery slope' of social deterioration. Early management may help return these young women to normal psychosocial development and self-esteem, improved scholastic performance and return to normal daily activities.

Adolescents with endometriosis typically present with pain symptoms such as progressive dysmenorrhoea and both cyclic and acyclic pelvic pain.

Pelvic examination of the young adolescent may be difficult but is invaluable to help rule out pelvic masses and abnormal anatomy, such as imperforate hymen and transverse vaginal septum. However, if the young patient declines or is unable to have such an exam, a pelvic ultrasound will provide additional information before referral.

Empirical treatment with NSAIDs and the OCP are adequate for most

cont'd page 32

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adolescents with dysmenorrhoea. However, young patients who do not respond to these medications require early referral for further investigations, which may include laparoscopy for diagnosis and treatment.

The referral and surgical threshold is lower in these patients because of the side effects of the other medical therapies, such as bone loss with GnRH agonists and depot progestin during adolescence.

Laparoscopy should be done by experienced surgeons, who will recognise that younger patients have slightly different appearances of endometriosis, including a greater number of clear vesicles and reduced likelihood of powder-burn-type lesions.

The OCP or other hormonal treatments do not have any effect on the progression of disease; they are used for symptom control only. As a result there is no known benefit or harm to future fertility in patients taking the OCP for endometriosis. This question is being studied further with newer medications such as aromatase inhibitors and selective progesterone-receptor modulators.

The adolescent with pelvic pain and endometriosis requires immediate attention and care. With an average of nine years from presentation of symptoms to diagnosis, the medical system warrants greater attention to this condition in younger patients.

Evidence-based practice

- Endometriosis should be suspected in all women with a history of dysmenorrhoea refractory to medical treatment.
- Physical examination may help detect endometriosis nodules and/or ovarian endometriomas.
- Pelvic ultrasound is the best imaging modality for characterising pelvic pathology found on pelvic examination.
- Serum CA125 is not useful in the diagnosis of endometriosis.
- Laparoscopy is the gold standard test for diagnosing endometriosis.
- Suppression of ovarian function for six months reduces endometriosis-related pain; however, symptom recurrence is common after completion of treatment.
- All hormonal treatments (OCP, danazol, medroxyprogesterone acetate, GnRH agonists) are equally effective at treating endometriosis-related pain.
- Surgical ablation and/or excision at laparoscopy reduces endometriosis-related pain, compared with diagnostic laparoscopy alone.
- Severe cases of endometriosis should be referred to units with the expertise to offer all available treatment options, which may include advanced operative laparoscopy and/or multidisciplinary consultations.
- Hormonal suppression alone is not effective for the treatment of endometriosis-associated infertility.
- Surgical management of minimal to mild endometriosis is effective for infertility, compared with diagnostic laparoscopy alone.
- Laparoscopic cystectomy is better than drainage for ovarian endometriomas.
- Treatment with intrauterine insemination in women with minimal to mild endometriosis improves fertility outcomes.

From the European Society for Human Reproduction and Embryology *Guidelines for the Diagnosis and Treatment of Endometriosis* (http://guidelines.endometriosis.org) and the Royal College of Obstetricians and Gynaecologists, Green-top Guideline No. 24, October 2006.

Future directions

ONGOING research into the field of endometriosis must focus on prevention and alternative therapies. Scientists are working throughout the world, including Australia, to help describe the aetiology, natural history and characteristics of this disease.

Newer medications such as aromatase inhibitors and selective progestin-receptor modulators may also provide alternative treatment options, possibly with fewer side effects.

Authors' case studies

Infertility and endometriosis

A 30-YEAR-old woman was referred for primary infertility. She and her husband had tried to conceive for the past two years with no success. She had regular menstrual cycles, no history of STIs and was otherwise healthy. There was also no history of pain with menses or intercourse.

Her GP had done a thorough initial fertility workup, including a normal semen analysis and hormonal profile. She had tried five cycles of clomiphene citrate, with no success.

On pelvic examination she was found to have a mobile uterus and nodularity along both uterosacral ligaments. Based on her history and physical examination, the patient was offered a laparoscopy for diagnosis and management of possible endometriosis.

At laparoscopy a significant amount of endometriosis was found adhered to both uterosacral ligaments, the rectum and sigmoid colon. The pelvic sidewalls had scattered endometriosis, as did the bladder flap. The ovaries and uterine cavity (at hysteroscopy) were normal. The fallopian tubes were otherwise normal and patent on testing.

The lesions of endometriosis were excised and sent for pathology, which confirmed the diagnosis. This was a difficult dissection because the lesions were close to the bowel and ureters. The colonic lesions were not excised because of a greater risk associated with this type of dissection.

On follow-up the patient's findings and management were discussed. She decided to try to continue with timed intercourse for the next six months.

Comment

This case highlights the variable presentation of this disease. In this case the patient had no pain yet had significant pathology.

Although the surgical management of mild to moderate endometriosis has been shown to improve fertility, the evidence is not as clear in cases of severe disease. If this patient has not conceived within six months, she will be advised to seek advanced reproductive technologies through an infertility specialist.

Endometriosis and pain

Annie, 19 and nulliparous, was seen for chronic pelvic pain. Since the age of 13 Annie has had painful periods, which resulted in a significant impact on her social life, including missing school on a regular basis.

At age 18 she was prescribed the OCP to help manage this pain. Although this treatment provided some relief; she had to discontinue the medication because of side effects, including headaches and nausea. Recently she had also developed painful bowel movements.

Her medical history was significant, with a laparoscopy for suspected appendicitis five years ago, which turned out to be 'ovarian cysts'. No other comment or pathology could be found regarding that surgery. She was also treated for presumed 'pelvic inflammatory disease' for this acute-on-chronic pain despite having no identifiable infection.

On examination the abdomen was slightly tender over the suprapubic region, as was the posterior fornix on pelvic exam. No masses were otherwise found. Ultrasound was normal.

In light of her six-year history of pelvic pain and dyschesia, the patient was offered a laparoscopy for diagnosis and treatment. At laparoscopy, severe endometriosis was documented and included a recto-vaginal nodule of endometriosis, bilateral uterosacral ligament nodules and pelvic sidewall implants.

The tubes, ovaries and uterus were otherwise normal. The diseased areas were excised and the patient experienced almost immediate relief. She was counselled regarding her diagnosis, and arrangements were made for continued follow-up.

Comment

This case illustrates the importance of early referral and management of women (including adolescents) for pelvic pain not responsive to medical management, to prevent delayed diagnosis and prolonged suffering. Endometriosis presents at any age during the reproductive years and thus requires heightened awareness for GPs treating these women.

GP's contribution

DR DIANNE CHAMBERS
Leichhardt, NSW

Case study

ANN is now aged 41. She has a long history of severe endometriosis. During her 20s and early 30s she struggled with severe pain, having only moderate success with NSAIDs and the OCP.

Laparoscopy and diathermy gave some temporary relief but, as pain was severe, she was finally treated with danazol. She had significant side effects but she persevered, as it gave her the best pain relief.

In 2000 she came off all treatment, planning to become pregnant. Predictably her pain levels escalated and she eventually had repeat laparoscopy in 2002. This showed severe endometriosis with a large right ovarian cyst densely adherent to the uterosacral ligament, the uterus, vagina and rectum. A right ovarian cystectomy was performed and, fortunately, both tubes were patent to dye at completion of surgery.

Shortly after, Ann presented with irregular vaginal bleeding. We were both alert to the possibility of ectopic pregnancy although ultrasound did not confirm this. As she was now 38 and her fertility was the major concern, she was referred to an IVF unit.

As it was almost two years since her large surgical clearance, further laparoscopic evaluation was sought as a prelude to IVF. This showed extensive endometriosis involving the right ovary and uterosacral ligament, and two endometriomas. Once again these were cleared and she proceeded to IVF. Fortunately, pregnancy was achieved and she is now a proud mother.

Questions for the authors

What is the risk of ectopic pregnancy

cont'd page 34

Reference

1. American College of Obstetricians and Gynecologists. Committee Opinion: *Endometriosis in Adolescents.* Number 310, April 2005.

Online resources

- Endometriosis newsgroup, Sydney, Australia: email sydney_endo@yahoogroups.com
- Endometriosis Association, International: www.endometriosisassn.org
- US-based information: www.endocenter.org
- European-based information: www.endometriosis.org
- Fertility.com: www.fertility.com/oceania
- Centre for Young Women's Health: www.youngwomenshealth.org

Recommended reading

- Ballweg ML. *Endometriosis: the Complete Reference for Taking Charge of Your Health.* McGraw-Hill Publishers, New York, 2004.
- Evans S. *Endometriosis and Other Pelvic Pain.* Piatkus Books Ltd, London, 2006.

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in association with endometriosis?

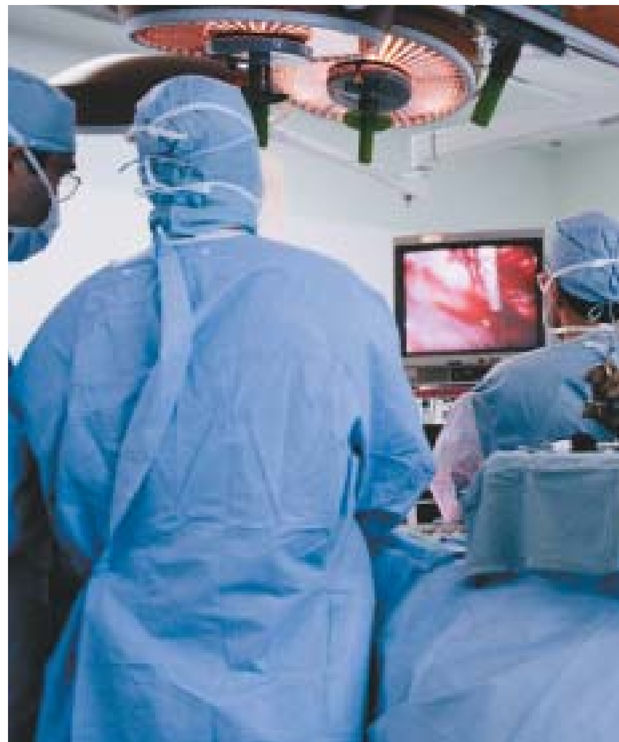
There is limited information about this association in the medical literature. In cases of severe disease with fallopian tube damage, patients would be considered at greater risk of subsequent ectopic pregnancy, as in pelvic inflammatory disease. Unfortunately, there are no clear data to quantify the risk in these cases.

In general, patients with a history of infertility are known to be at greater risk of subsequent ectopic pregnancy; whether some of these cases are due to underlying endometriosis is unknown.

What is the risk and time frame of endometriosis recurrence after surgery?

Recurrence of endometriosis is common after surgical management. One report found that up to one-third of women reported recurrent dysmenorrhoea within one year. Even after aggressive surgical excision, up to 20% of patients will return over five years for further treatment.

The laparoscopic approach has been found to have less scarring and inflammatory response compared with laparotomy.



Does the surgery itself contribute to later scarring and hence risk of infertility?

Surgery involves a healing and scarring process as the body responds to injury and inflammation. The laparoscopic approach has been found to have less scarring and inflammatory response compared with laparotomy. This is why laparoscopy is considered the preferred route of management for endometriosis.

In cases of mild to moderate endometriosis, laparoscopic ablation or excision has been shown to improve fertility up to one year after the surgery. Advanced or severe endometriosis is a destructive entity, often with significant tubal damage, adhered and retroverted uterus, obliterated cul de sac and adhesions.

The goal of surgical management is to reconstruct normal anatomy in these cases, and the risk of scarring from surgery must be considered in the context of damage already found.

In general, can you outline the pros and cons regarding early or deferred surgical interventions?

Early surgical intervention, when indicated (table 4, page 29), provides a diagnosis and treatment for patients who may otherwise be suffering from the impact of endometriosis. As noted, there is often a significant delay (7-9 years) in the diagnosis of endometriosis, and hence a delay in appropriate management.

It is important to advocate for your patients with severe disease through consultation with specialists with an interest in endometriosis to offer appropriate and long-term management and follow-up.

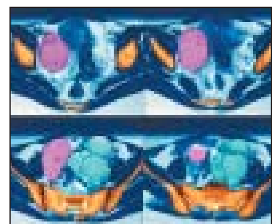
General questions for the authors

You suggested a rectal examination as part of the assessment of endometriosis. What in particular do you expect to find which could not be found with vaginal examination and ultrasound? If laparoscopy is the gold standard, do you consider that the information found on rectal examination is sufficiently important to warrant the distress, particularly in non-sexually active women?

Rectal examination is an important part of our assessment of patients with endometriosis and concomitant bowel or back symptoms. The vaginal-rectal examination allows clinical evaluation of the recto-vaginal septum, which may contain endometriosis nodules and infiltration.

We counsel our patients regarding this component of the exam and only proceed if the patient is comfortable. Occasionally, ultrasound may be needed because of patient discomfort at examination or refusal to allow examination. In our experience this is usually not the case and most patients understand the reasons for a thorough examination.

Through a better understanding of the disease location we may plan our referrals and management appropriately. If there is a significant recto-vaginal nodule with bowel symptoms, a referral to a specialist with experience in treating severe disease is more appropriate, including consultation with a colorectal surgeon.



How to Treat Quiz

Endometriosis — 03 August 2007

INSTRUCTIONS

Complete this quiz to earn 2 CPD points and/or 1 PDP point by marking the correct answer(s) with an X on this form. Fill in your contact details and return to us by fax or free post.

FAX BACK	FREE POST	ONLINE
Photocopy form and fax to (02) 9422 2844	How to Treat quiz Reply Paid 60416 Chatswood DC NSW 2067	www.australiandoctor.com.au/cpd/ for immediate feedback

1. In regard to incidence and prevalence of endometriosis, which TWO statements are true?
- ❑ a) Endometriosis affects up to 3-4% of Australian women of reproductive age
- ❑ b) It only presents in women aged 20-30
- ❑ c) The risk of endometriosis is seven times greater in a woman whose mother or sister has endometriosis
- ❑ d) It can occur outside the pelvis, including skin, brain and lungs

2. In the treatment of endometriosis which TWO statements are correct?
- ❑ a) Endometriosis can be asymptomatic and require no treatment
- ❑ b) The mechanism of hormonal therapy is to try to suppress a woman's menstrual cycle
- ❑ c) The Mirena (levonorgestrel) IUD is not suitable as a treatment option, as it does not provide therapeutic doses of progesterone beyond the uterine cavity to the deposits of endometriosis
- ❑ d) Progesterone cream has been demonstrated to provide safe and effective pain relief in many women with endometriosis

3. Jennifer, 23 and nulliparous, presents with severe dysmenorrhoea for the past three years. Which TWO other symptoms are suggestive of endometriosis?
- ❑ a) Pre-menstrual spotting
- ❑ b) Cyclical vaginal discharge
- ❑ c) Deep dyspareunia
- ❑ d) Vaginal itch and burning

4. On examination, which THREE features may be found in endometriosis?
- ❑ a) Cervical erythema
- ❑ b) A fixed retroverted uterus
- ❑ c) Adnexal masses
- ❑ d) Tender nodularity of the uterosacral ligaments and Pouch of Douglas

5. In regard to investigations for Jennifer, which TWO statements are true?
- ❑ a) Ultrasound may be useful to detect ovarian cysts and exclude other pathology
- ❑ b) CA125 testing is a useful tool in diagnosing and monitoring the extent of endometriosis
- ❑ c) Serum inflammatory markers, ESR and CRP are frequently elevated in endometriosis and are good monitoring tools
- ❑ d) Direct visualisation at laparoscopy is the gold standard for diagnosis

6. Jennifer requests treatment for pain. She is reluctant to have surgery. Regarding medical therapy for endometriosis, which TWO statements are true?
- ❑ a) NSAIDs are not effective in managing the pain from endometriosis
- ❑ b) She may be offered a monophasic oral contraceptive pill on a continuous basis
- ❑ c) The side effects of danazol may include permanent virilisation, including voice changes, hirsuitism, weight gain and acne
- ❑ d) GnRH antagonists are well tolerated and can be useful in the long term

7. If on ultrasound Jennifer had bilateral ovarian cysts 4.5 and 5cm in diameter, which ONE of the following would be the recommended therapy?
- ❑ a) Observing the cysts with serial ultrasounds, and treating medically for pain relief only
- ❑ b) Surgical incision and drainage
- ❑ c) Ablative therapy
- ❑ d) Surgical excision and histopathological evaluation

8. Medical therapy has not been successful in controlling Jennifer's pain without side effects. Which would be TWO preferred surgical options?
- ❑ a) Laparotomy, as this provides superior visualisation
- ❑ b) Laparoscopic surgical ablation using electrosurgery or laser therapy
- ❑ c) Laparoscopic surgical excision of peritoneal implants or nodules
- ❑ d) Bilateral oophorectomy to render her menopausal, followed by HRT three months later

9. Belinda, 29 and G1P1, has been trying to get pregnant for 12 months. She has noticed increasing dysmenorrhoea during this time. Which TWO statements are true?
- ❑ a) Endometriosis is unlikely to be the problem, as Belinda had no problems getting pregnant with her first child
- ❑ b) Endometriosis may be responsible for up to 30-40% of women requiring treatment for infertility
- ❑ c) Pregnancy will exacerbate endometriosis
- ❑ d) Surgical treatment of endometriosis would be best for Belinda

10. Regarding treatment options for Belinda, which TWO statements are correct?
- ❑ a) Intrauterine insemination and in vitro fertilisation can be beneficial in improving fertility in women with endometriosis
- ❑ b) GnRH agonists are sometimes used for some months before IVF to increase success
- ❑ c) Belinda's fertility should improve for at least five years after surgical management
- ❑ d) If Belinda has tubal obstruction surgical management will not help

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Quiz: **Dr Heather Knox**

The mark required to obtain points is 80%. Please note that some questions have more than one correct answer. Your CPD activity will be updated on your RACGP records every January, April, July and October.

NEXT WEEK The next How to Treat focuses on Duchenne muscular dystrophy as a paradigm for the approach to diagnosis and management of muscular dystrophy generally. The author is **Dr Kristi Jones**, staff specialist in clinical genetics, The Children's Hospital at Westmead; and consultant clinical geneticist, Westmead Hospital, NSW.