Adenomyosis

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INTRODUCTION

ADENOMYOSIS, the presence of ectopic endometrial tissue within the myometrium, can be a debilitating condition significantly affecting women's quality of life. It is far more prevalent than previously realised in clinical practice because of a lack of awareness. In the past, definitive diagnosis was only made on hysterectomy.

The clinical symptoms of heavy menstrual bleeding (HMB) and dysmenorrhoea are non-specific.[1] Adenomyosis remains an underrecognised, underdiagnosed and potentially mismanaged condition, which is often neglected in the absence of specific tests.[2] With the advent of high-quality transvaginal sonography (TVUS) and MRI, accurate diagnosis is now possible.[3]

Accurate diagnosis on imaging has allowed for the evaluation of medical therapies, as well as uterine preserving procedures, such as uterine artery embolisation (UAE).

It is estimated (from Medicare data) that about 30,000 hysterectomies are performed in Australia each year, with more than 90% performed for benign indications, including adenomyosis.

This How to Treat aims to raise awareness of adenomyosis at the primary care level, with the hope that GPs will make the diagnosis earlier, thus optimising conservative medical therapy and applying minimally invasive procedures to reduce unnecessary hysterectomies.

PATHOLOGY

ADENOMYOSIS is a benign condition of the uterus caused by the presence of ectopic endometrial tissue within the myometrium (see figure 1), and reactive hypertrophy and hyperplasia of the surrounding myometrium.[4]

Typically, the uterus is enlarged and globular in shape. Glandular foci may contain brown haemosiderin deposits. There is no clear consensus on the depth of endometrial penetration required for a diagnosis of adenomyosis, therefore the percentage of hysterectomy specimens containing adenomyosis varies from 5% to 70%.[4]

The prevalence in the general population is estimated at 20-28%, but is likely to be higher in subfertile populations.[5]

Using MRI criteria, adenomyosis is found in 12% of healthy women, 15% of women with a history of pre-term delivery and 9% with a history of normal delivery.[4]

Pathophysiology

Human and experimental studies support the theory of endometrium invagination.[6] There may be a 'weakness' of the uterine smooth muscle tissue or an increased intrauterine pressure, or both. De-novo development of ectopic adenomyosis from Mullerian rests is another theory.[6]

Relatively high oestrogen concentration and impaired immune-related growth control are needed for the maintenance of adenomyosis. Smooth muscle cell hyperplasia and hypertrophy are probably reactive changes secondary to endometrial proliferation.[6] ▸

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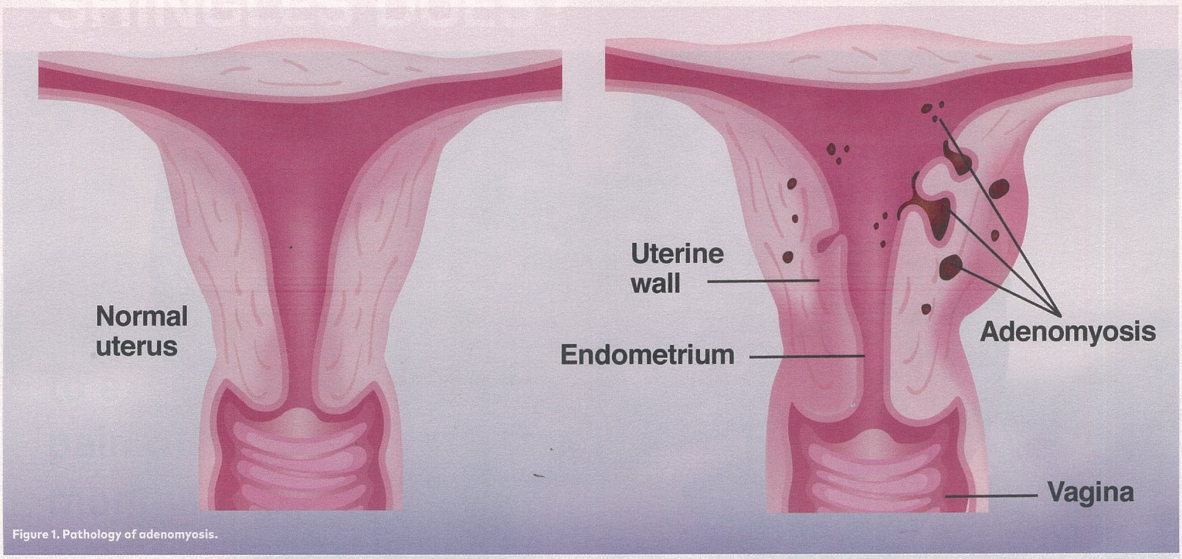

Figure 1. Pathology of adenomyosis.

Heavy menstrual bleeding may be due to improper uterine contractions and increased endometrial surface. Dysmenorrhoea may be related to uterine irritability or pseudodecidual oedema around the foci of adenomyosis.[7]

Risk factors

The risk factors for adenomyosis may be divided into mechanical and hormonal (see box 1). Curettage for termination of pregnancy or miscarriage may lead to disruption of the endometrial-myometrial interface, embedding endometrium into myometrium.[8,9] Previous caesarean section is also a risk factor.[10]

Adenomyosis is associated with age and parity. As an oestrogen-dependent pathology, the extent of oestrogen exposure may be a risk factor.[11]

Adenomyosis may be associated with depression and use of antidepressant medication.

Direct exposure of the uterus to prolactin and hyperprolactinaemia secondary to selective serotonin reuptake inhibitor (SSRI) use appear to be capable of inducing adenomyosis.[12]

CLINICAL FEATURES

WOMEN with adenomyosis may present with HMB, dysmenorrhoea, premenstrual pain, chronic pelvic pain, dyspareunia and abdominal bloating. Bimanual examination typically reveals a tender boggy uterus.[13]

Clinical evaluation

It is important to establish the severity and chronicity of HMB as perceptions differ. There are specific questions that are helpful to objectively assess the severity of HMB and assess treatment outcomes (see box 2). The severity of dysmenorrhoea can be assessed using a Visual Analog Scale (VAS) or assessing the use of analgesics and limitation of normal activities, such as work, school, exercise, family function and social engagement.

A list of the causes of secondary dysmenorrhoea appears in box 3.

Pelvic examination may reveal suspicious pelvic masses. Speculum examination is useful in excluding cervical lesions and facilitates a cervical screening test.

The presence of abnormal iron studies and iron deficiency anaemia indicate severity and/or chronicity, and suggest that more proactive treatments than just iron supplementation may be needed.

CA 125 may be raised in adenomyosis, but it is neither sensitive nor specific for adenomyosis.[14,15] It is not recommended as a screening tool.

TVUS is part of the initial evaluation, and may detect endometrial hyperplasia, intracavitary lesions (polyps or fibroids) and wall lesions (fibroids and adenomyosis).

Irregular menstrual bleeding may be related to underlying hormonal disturbance and should be evaluated accordingly.

Investigate atypical bleeding patterns, like intermenstrual, post-coital and postmenopausal bleeding, for more sinister causes. Investigation for potential malignant causes of abnormal uterine bleeding is beyond the scope of this article (see Online resources).

INVESTIGATIONS

Medical imaging

MODERN TVUS and MRI achieve a high level of diagnostic accuracy for adenomyosis. Meta-analysis shows MRI has higher sensitivity and specificity than TVUS (see table 1), making a correct diagnosis more often than TVUS.[3] Studies showed more variability in accuracy with TVUS than MRI.

TVUS is widely available and less expensive but is operator-dependent and less reproducible. MRI is less accessible and more expensive, and currently not Medicare-funded for the investigation of adenomyosis.

Uterine fibroids may obscure TVUS assessment of adenomyosis while focal adenomyosis can be mistaken for fibroids.

Some women with severe symptoms may have adenomyosis in a small or normal sized uterus, where TVUS signs are subtle or absent. When adenomyosis is suspected clinically, GPs need to indicate this clearly on the imaging request to alert the sonographer to look for these subtle signs.

In real-world practice, fibroids and adenomyosis coexist in about 50% of cases.[16] In our audit of 117 symptomatic women with adenomyosis diagnosed on baseline MRI prior to uterine artery embolisation, in 71% of cases the TVUS failed to report the presence of adenomyosis (unpublished data).

Both TVUS and MRI may demonstrate an enlarged globular uterus with asymmetrical anterior and posterior myometrial wall thickness. TVUS (see figure 3) often detects heterogeneous myometrial echotexture suggestive of adenomyosis (see box 4).

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Box 1. Risk factors for adenomyosis

Mechanical
- Multiparity
- Termination of pregnancy
- Uterine curettage
- Previous caesarean section

Hormonal
- Age
- Early menarche
- Short menstrual cycles
- Obesity
- Tamoxifen use
- Depression and use of SSRI

Source: Riggs JC et al 2014[10], Abbott JA 2017[11], Taran FA et al 2010[12]

Box 2. Clinical assessment of HMB

Assessing the severity
- What kind of sanitary pad/tampon do you use (regular/super/maternity/incontinence)?
- How often do you change during daytime and at night?
- Have you ever soiled clothing or linen?
- Do you pass clots? If so, how big?
- Do you experience flooding?
- Do you have to stay at home, miss work or school due to HMB?
- Do you experience symptoms of anaemia like lethargy, dizziness and SOB?

Assess response to treatment
- Are your periods still heavy, back to normal or lighter than normal?

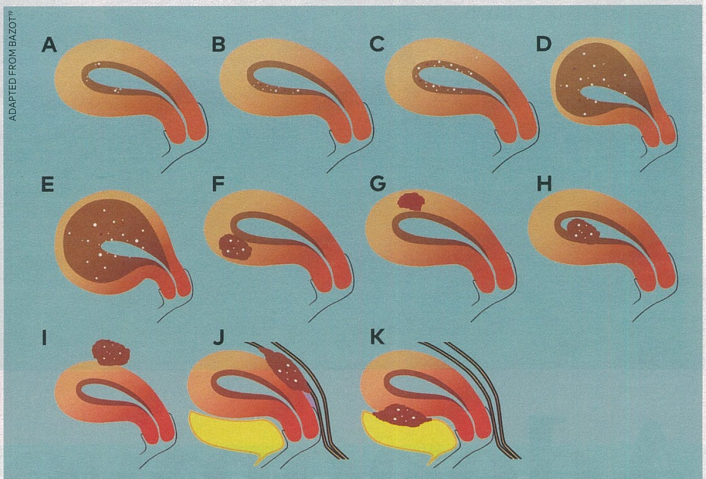

Figure 2. Different types of adenomyosis as demonstrated on MRI.

A, B and C: Superficial adenomyosis; D and E: Diffuse adenomyosis; F: Intramural adenomyoma; G: Cystic adenomyoma; H: Submucosal adenomyoma; I: Subserosal adenomyoma; J: Posterior external adenomyosis; K: Anterior external adenomyosis.

Box 3. Causes of secondary dysmenorrhoea
- Adenomyosis
- Endometriosis
- Fibroids
- Cervical stenosis
- Obstructive endocavitary lesions
- Pelvic congestion syndrome
- Intrauterine contraceptive device
- Chronic pelvic inflammatory disease
- Intrauterine or pelvic adhesions
- Congenital obstructive Müllerian malformations
- Ovarian cysts

◀PAGE 18 More specific signs, such as myometrial cysts and subendometrial striations, representing ectopic endometrial tissue, are less commonly seen.

MRI (see figure 4) may demonstrate direct signs of ectopic endometrial tissue and haemorrhage (see box 5). These signs are more specific but less commonly seen.

Junctional zone (JZ) thickening representing myometrial hyperplasia is often observed. A thickness of more than 12mm is regarded as diagnostic of adenomyosis. MRI can exquisitely demonstrate a wide spectrum of adenomyotic changes.

A classification of different types of adenomyosis based on MRI has been proposed (see figure 2).[19] Many studies on various aspects of adenomyosis in the past have yielded conflicting results, possibly due to inclusion of different types of adenomyosis by different study groups.

Hysterosalpingogram

Hysterosalpingogram may demonstrate features suggestive of adenomyosis but it has low sensitivity and specificity. Features could include small spicules extending from the endometrium into the myometrium, with saccular endings. Accumulation of contrast material in the myometrium may produce a honeycomb appearance.[20] Hysterosalpingography may be performed with lipiodol for the investigation and treatment of infertility.

Laparoscopy

Laparoscopy is indicated for the investigation of endometriosis, but not if adenomyosis is suspected clinically. Endometriosis and adenomyosis often coexist.

Women with both conditions are likely to continue to have pain following surgical excision of endometriosis.[21] Similarly, women who have persistent pain after UAE may need laparoscopy to exclude endometriosis (see later).

Table 1. Imaging accuracy for adenomyosis

	TVUS	MRI
Sensitivity	72%	77%
Specificity	81%	89%

Source: Champaneria R et al 2010[3]

Box 4. TVUS Features of adenomyosis

- Heterogeneous myometrial echotexture (highest sensitivity 80.8%)
- Globular-appearing uterus
- Asymmetrical thickness of myometrial wall
- Venetian blinds artefacts
- Myometrial cysts
- Poor definition of the endometrial-myometrial junction
- Subendometrial echogenic linear striations (highest specificity 95.5%)

Source: Kepkep K, et al 2007[17]

Box 5. MRI Features of adenomyosis

- Bright T2 myometrial foci (endometrial tissue)
- Bright T1 myometrial foci (haemorrhage)
- Bright T2 endometrial-myometrial linear striations (endometrial invagination)
- Junctional zone thickness of >12mm (myometrial hyperplasia)
- Junctional zone (JZ) 8-12mm and the following ancillary signs:
  - JZ to myometrial thickness ratio of >40%
  - JZ difference between anterior and posterior wall >5mm

Source: Agostinho L, et al 2017[18]

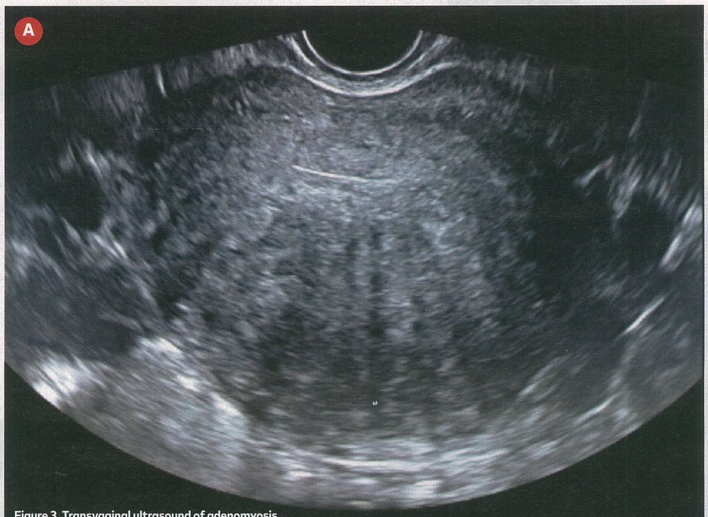

Figure 3. Transvaginal ultrasound of adenomyosis.

Figure 3a. Adenomyosis is seen as asymmetrical wall thickening, Venetian blinds artefacts and subtle small myometrial cysts.

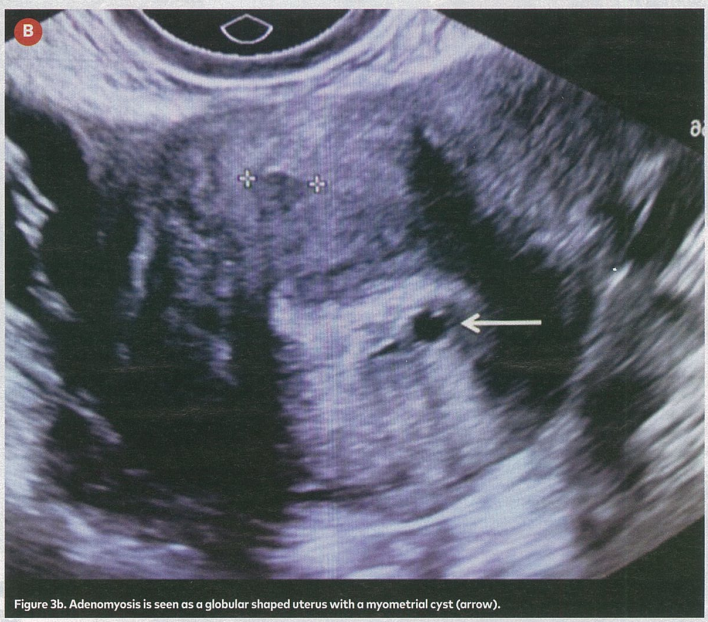

Figure 3b. Adenomyosis is seen as a globular shaped uterus with a myometrial cyst (arrow).

MANAGEMENT

Medical therapy

MEDICAL therapies such as tranexamic acid, NSAIDs, progestins or low-dose continuous combined oral contraceptive pills (COCP) are often used as first-line treatment for symptomatic control (see table 2).[22,23] Although most of these treatments have not been tested specifically for adenomyosis, they are still recommended in the current Australian Clinical Care Standard for the symptomatic management of HMB.[4,24]

TRANEXAMIC ACID

Tranexamic acid is an antifibrinolytic that reversibly blocks fibrinogen degradation by lysine.[25] It is more effective in the treatment of HMB than NSAIDs such as mefenamic acid or luteal phase progestogens.[25] Side effects include gastrointestinal disturbance and alteration of colour vision. In the event of the latter, cease the drug immediately.

A specific concern is the potential for thromboembolic disease. Tranexamic acid is contraindicated in patients with a history of active thrombotic or embolic disorders.[26]

The WHO database records 528 cases of suspected reactions including deep vein thrombosis, pulmonary embolus, cerebral embolism and arterial thrombosis.[26]

NSAIDS

There are no studies on the use of NSAIDs specifically for the treatment of adenomyosis.

A Cochrane review in 2010 concluded that NSAIDs are an effective treatment of dysmenorrhoea but there was insufficient evidence to determine the most effective and safest individual NSAID.[27]

Another Cochrane review in 2013 showed that NSAIDs reduced HMB when compared with placebo, but were less effective than other therapies such as tranexamic acid or hormonal treatments (danazol or levonorgestrel-releasing intrauterine system).[28]

HORMONAL THERAPY

The aim of hormonal therapy is to suppress the cyclical changes of ovarian hormones, inhibiting pituitary gonadotropins and preventing the mid-cycle oestrogen surge. The effect is limited to the duration of treatment.

Hormonal treatments for symptomatic relief include progestogens, COCPs and gonadotropin-releasing hormone analogues (GnRHa).[29]

The proposed mechanism of actions includes: decidualisation and then atrophy of endometrial tissue; hypoestrogenism effect; and antiproliferative effect.[30]

Progesterone-releasing IUD

Levonorgestrel-releasing intrauterine system (LNG-IUS) releases 20mcg levonorgestrel per day for up to five years. It is currently the best-evaluated and the most efficacious non-surgical treatment of adenomyosis.[29,31]

A randomised controlled trial comparing LNG-IUS and hysterectomy with 43 women in each arm showed comparable increases in haemoglobin and similar quality-of-life scores at 12 months.[32]

A three-year follow-up study on 94 women who had LNG-IUS inserted for adenomyosis-related dysmenorrhoea showed a significant drop in pain score from 78 to 16 at 12 months. However, there was a 22.6% discontinuation rate (12% expulsion and 11% premature removal). Patient satisfaction rate was only 56.3% at 12 months. Prolonged light bleeding (25%) or irregular bleeding (14%), and other side effects, such as weight gain, ovarian cyst, lower abdominal pain and acne, contributed to the less-than-ideal satisfaction rate.[33]

LNG-IUS is less effective in women with extensive adenomyosis. Treatment discontinuation is more likely with a uterine volume larger than 150mL, with a discontinuation rate of 70% noted in women with a uterine volume larger than 314mL.[34]

Combined oral contraceptive pill

Low-dose, continuous COCP with withdrawal bleeds every 4-6 months may be effective in relieving HMB and dysmenorrhea.[35] There are, however, no well-conducted RCTs available to support its use in adenomyosis.

There are more than 30 COCP registered brands available in Australia. A guide has been developed to help GPs to choose the right one for their patients (see Online resources).[36]

Gonadotropin-releasing hormone agonists

GnRHa cause suppression of pituitary gonadotropins and ovarian function, resulting in a medical menopause. GnRH receptors have been found in endometriosis, adenomyosis and fibroid tissue. GnRHa may also exert a direct antiproliferative action within the myometrium.[30] GnRHa can induce amenorrhoea, reduce pelvic pain and cause shrinkage of uterine volume.[37]

The use of GnRHa is associated with hypoestrogenic side effects, including vasomotor symptoms, reduced bone mineral density, genital atrophy, and mood instability.[30]

Generally, treatment is limited to 3-6 months. After cessation of therapy, symptoms may return, and uterine volumes may increase

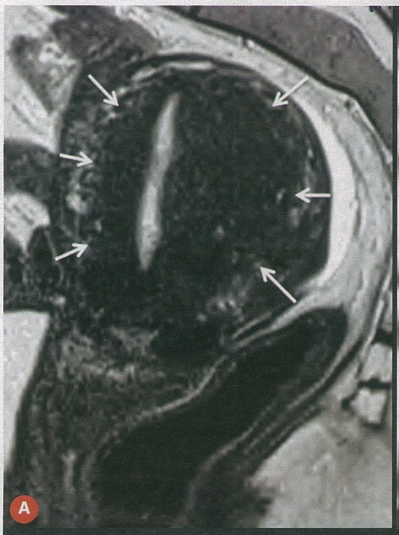

Figure 4. MRI of adenomyosis.

Figure 4a. Adenomyosis with junctional zone thickening of the posterior wall.

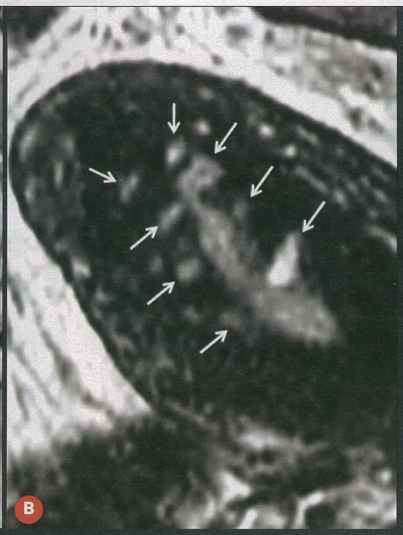

Figure 4b. Adenomyosis with multiple bright signal foci (ectopic endometrial tissue) within the thickened junctional zone (reactive myometrial hyperplasia).

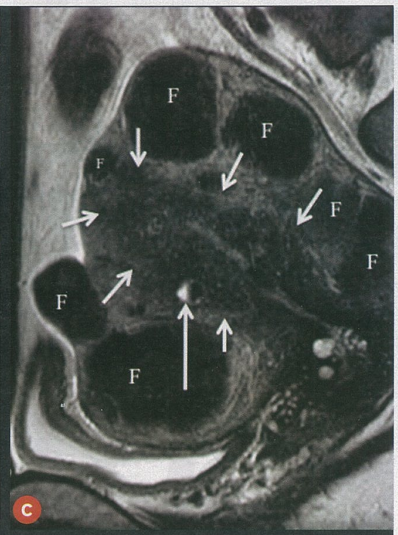

Figure 4c. Adenomyosis is seen as irregular junctional zone thickening (short arrows) with a haemorrhagic cyst showing fluid-fluid level (long arrow). Coexisting fibroids are marked with 'F'. Note: fibroids are easily distinguished from adenomyosis.

to pretreatment size.[38] Pregnancy is possible after cessation of treatment, making it a viable treatment option for women wishing to conceive.[39]

Danazol

Long-term vaginal administration of one 200mg danazol tablet daily seems to be effective in reducing HMB and pain.[30,40] However, the use of this androgen, similar to testosterone, is limited by the high incidence of androgenic side effects, including weight gain, acne, hirsutism, hot flushes, and voice changes, which might be irreversible.

Dienogest

Dienogest has a high selectivity for progesterone receptors. It causes a mild inhibition of ovarian function and has an antiproliferative action on the endometrium.[30] It seems to be effective in reducing pain, but 30% of women developed irregular bleeding and worsening anaemia, limiting its use in adenomyotic women who might already be anaemic.[41]

Interventional radiology procedures

UTERINE ARTERY EMBOLISATION

Uterine artery embolisation (UAE) is a minimally invasive angiographic procedure that can be performed under local anaesthetic and light conscious sedation. It requires usually only a one-night hospital stay and one week's recovery. It is now a well-established treatment option for symptomatic fibroids. Seven randomised controlled trials and a Cochrane review in 2014 concluded that UAE was as effective as hysterectomy in treating fibroids, in terms of symptom relief, patient satisfaction and quality of life improvement. Several studies over the past 15 years have documented the safety and efficacy of UAE for adenomyosis.[42]

During UAE, an angiographic catheter is used to selectively cannulate each of the two uterine arteries. Embolic particles are then suspended in contrast medium and injected into the uterine arteries to induce ischaemia (see figure 5). Normal uterine myometrium has many dormant arteries that are normally shut down, but has an immense capacity to recruit these dormant arteries to survive the ischaemic insult. Within the adenomyotic tissue, however, all the vessels stay open and will be blocked with embolic particles. Pathological lesions like adenomyosis or fibroids do not have the capacity to recruit new vessels and therefore will undergo irreversible ischaemic infarction.

Post-embolisation pain can be managed with paracetamol, NSAIDs and patient-controlled analgesia. The pain is worst in the first 12 hours and gradually subsides with revascularisation of the normal uterine tissue.

A meta-analysis of 30 studies in 2018 included 1049 adenomyotic women treated with UAE (see table 3).[42] Reported complications included: persistent amenorrhoea in 28 (6.3%) out of 445 women (all were aged over 40); one false aneurysm treated with thrombin injection; 10 cases of fibroid expulsion; four cases of suspected endometritis treated with antibiotics; and one calf DVT requiring no treatment. There were no deaths or major complications.[42]

Our recently published local Australian data showed similar results.[16]

The local study is among the largest ever performed, treating 117 women with adenomyosis using UAE. Overall clinical success was achieved in 89% of women with a mean follow-up period of 22.5 months. HMB was successfully controlled in 88% of women; dysmenorrhoea was successfully treated with significant average visual analog scale pain score reduction (from 7.45 to 1.32). The hysterectomy rate was 5%, because of unsatisfactory symptom relief rather than UAE complications. There were no major complications.[16]

Uterine artery embolisation is now a well-established treatment option for symptomatic fibroids.

To study the durability of UAE, the same Australian cohort was followed further for a mean period of 50 months. Clinical success with satisfactory control of symptoms was maintained in 88%. For those women with recurrence of symptoms (7/58,12%), the mean time to failure was 39 months (unpublished data).

An RCT comparing UAE with hysterectomy is now underway in the Netherlands.[43]

There is now sufficient data to suggest that UAE is a safe and effective treatment for adenomyosis, especially for those women who desire to retain their uterus.

Table 2. Suggested medical therapy for HMB in general practice

Drug	*Tranexamic acid*	*Mefenamic acid*	*COCP*	*Progesterone-releasing IUD*
Action	Antifibrinolytic	Inhibits prostaglandin synthesis	Stabilises lining of uterus, suppresses cyclical hormone changes, prevents mid-cycle oestrogen surge	Endometrial atrophy
Effect	Reduces bleeding	Reduces pain and bleeding	Amenorrhoea with continuous use	Reduces menstrual loss, reduces pain
Dose	2 x 500mg tabs QID	2 x 250mg tabs TDS		
Indication	HMB (consider alternative if not effective after three cycles)			
Contra-indications	History or risk of arterial or venous thromboembolic disease		Thromboembolic risks, obesity, hypertension, smoking	
Caution	Concomitant use with COCP	Not as effective as tranexamic acid or progestogen	Monitor fibroid growth No specific studies that COCP reduces HMB in fibroids or adenomyosis	Submucosal fibroid, bleeding due to friction, difficult to insert or expulsion
Side effects	Nausea, vomiting, dizziness, visual disturbance, seizure	GIT irritation	Spotting, headache	Similar to oral progestogen; continuous spotting or bleeding.

HIGH-INTENSITY FOCUSED ULTRASOUND

High-intensity focused ultrasound induces focal thermocoagulation necrosis. The treatment can be monitored with MRI or ultrasound. The target region is mapped out with 3-5mm treatment spots. Focused ultrasound energy is delivered to heat the treatment spot to 70-90 degrees Celsius. Real-time monitoring with temperature feed-back is required. Focal adenomyosis can be treated in a single session; diffuse adenomyosis is treated in two sessions. Each session is, on average, four hours in duration.[45]

Despite ultrasound- or MRI-guided high-intensity focused ultrasound systems being available for many years, these are not readily accessible in Australia. Long-term durability of the treatment is yet to be reported. Short-term results vary widely between different series.[45]

Many patients are excluded from this treatment because of safety concerns (target lesion too close to skin, bone, nerve plexus or bowel), or efficacy concerns (target lesion too big, too deep or too vascular).[46] Like many procedures, patient selection is the key to success. Small intramural focal adenomyosis may be ideal for this treatment.

Surgical treatment

ENDOMETRIAL ABLATION

In this approach, heat energy is used to destroy the endometrial lining. It only treats a few millimetres depth of tissue and is only effective for superficial adenomyosis. Studies have shown increased failure rates for adenomyosis deeper than 2.5mm.[47,48] As an MRI diagnosis requires an imaged depth of invasion of 8-12mm (equivocal) or 12mm (definitive), it is clear that a 6mm depth of treatment as seen with endometrial ablation will most likely be ineffective.

Sealing the endometrial surface may in fact worsen dysmenorrhoea.[47,48] Even with more recent ▸

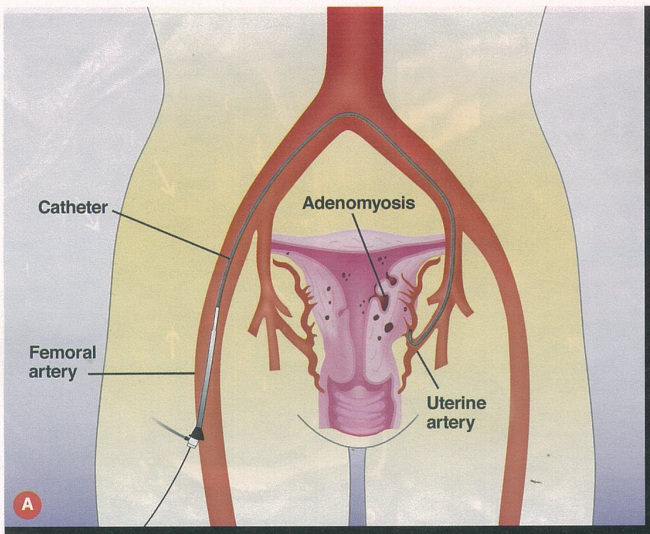

Figure 5a. Uterine artery embolisation.

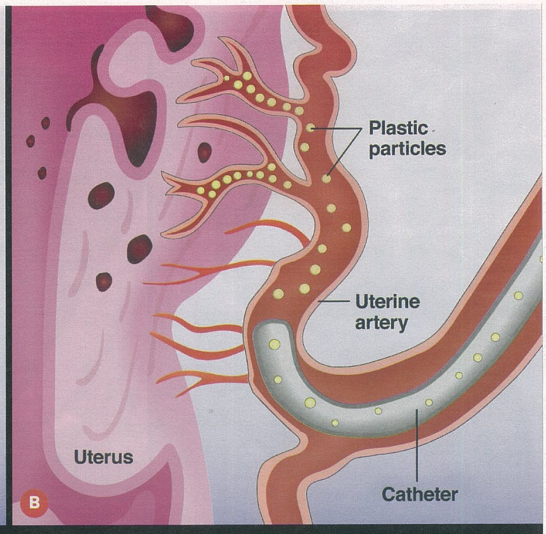

Figure 5b. Uterine artery embolisation.

technology, deep adenomyosis (more than 2.5mm) is a risk factor for failure of endometrial ablation, resulting in a higher rate of subsequent hysterectomy.[49]

UTERINE SPARING SURGERY

Focal adenomyosis or adenomyoma can simulate fibroids on TVUS. Surgical resections may have been attempted with the incorrect preoperative diagnosis. Unlike fibroids, the boundary between adenomyosis and the adjacent myometrium is indistinct, therefore adenomyotic tissue cannot be enucleated.

Uterine-sparing surgery should not be undertaken lightly for adenomyosis. A high degree of surgical skill is required for such fertility-sparing procedures (see later).[11]

A recent meta-analysis of uterine-sparing surgery for adenomyosis reported reduced dysmenorrhoea in 82%.[50] The HMB reduction rate was 69% if the resection was complete; but only 50% when excision was incomplete.[50]

HYSTERECTOMY

Hysterectomy is clearly required in the treatment of malignant disease of the uterus, but exercise care before recommending it for benign disease. Because there are many less invasive treatment options to deal with adenomyosis-related symptoms, hysterectomy should be the last resort when less invasive treatments have failed.

Hysterectomy can be performed transvaginally or transabdominally (open, laparoscopic or robotic). Recovery time varies from one to six weeks depending on the type of hysterectomy.

The surgical approach depends on the size of the uterus and underlying pathology.

Why should women avoid hysterectomy?

Hysterectomy is a major surgical procedure with a mortality rate up to 1.5/1,000 in Australia.[51] Women who have undergone hysterectomy enter menopause almost four years earlier.[52] Blood supply to the ovary may be compromised during surgery by ligation, spasms or thrombosis.

Table 3. UAE meta-analysis 2018

Features	Short-term (less than 12 months)	Long-term (more than 12 months)
Pure adenomyosis		
Symptom improvement	275/307 (89.6%)	318/430 (74%)
Secondary hysterectomy	8/307 (2.6%)	31/430 (7.2%)
Combined adenomyosis and fibroid		
Symptom improvement	133/141 (94.3%)	171/146 (85.4%)
Secondary hysterectomy	2/141 (1.4%)	12/146 (7%)

Source: de Bruijn et al 2017[42]

Table 4. Long-terms adverse effects of hysterectomy

Adverse effect	Possible pathophysiology
Early menopause	Disruption of ovarian blood supply due to ligation, spasm or thrombosis
Prolapse and incontinence	Loss or damage to ligamentous support of the cervix and vagina
Loss of libido	Unclear
Alteration to the character of orgasm	Loss of sensation from uterus
Altered sensation for woman and partner	Vaginal anatomy change
Constipation	Nerve damage
Post-hysterectomy syndrome	Possibly due to hormonal changes causing depression and lethargy
Increased cardiovascular risk	Secondary to ovarian dysfunction, despite ovarian conservation

Hysterectomy weakens pelvic supports and can cause urinary stress incontinence.[53]

Removal of or division of the ligamentous supports of the cervix and upper vagina may predispose to development of prolapse. Further, the effectiveness of prolapse repair is compromised by the removal the cervix and ligaments, which are used to anchor an effective repair.

Studies regarding the effect on a woman's sex life after hysterectomy may be confusing. Women whose sex lives are affected by their menstrual symptoms may find hysterectomy improves this.

Women whose sex lives are unaffected should be aware that decreased libido and orgasm intensity have been noted after hysterectomy, especially total hysterectomy.[54] This may be as a result of nerve damage or alterations to the vaginal vault, resulting in altered sensation or loss of uterine contraction, leading to anorgasmia.

Constipation following hysterectomy may also be as a result of nerve damage.[55]

Patients who have had a hysterectomy take longer to recover than those who have undergone other major surgery.[56] Symptoms include urinary problems, tiredness and depression.

The underlying cause is uncertain, and the condition has been labelled post-hysterectomy syndrome.[56] It is thought to be due to hormone imbalance after hysterectomy.

Even with ovarian conservation, hysterectomy is associated with increased long-term risks of cardiovascular and metabolic conditions.[57] These are probably mediated by the effects on the ovaries. One theory for the increased risk is the loss of collateral blood flow to the ovaries caused by hysterectomy.

Women with HMB and severe dysmenorrhoea might have underlying adenomyosis. Raising the clinical suspicion of adenomyosis is the first step in establishing the diagnosis. Imaging diagnosis can be made with TVUS, but more accurately with MRI. Optimise medical therapies before considering invasive procedures. GnRHa may be used to control symptoms in women who want to conceive. Failing medical therapies, UAE is an effective and safe non-surgical procedure. Many hysterectomies can potentially be avoided with a modern approach to treating adenomyosis.

ADENOMYOSIS AND FERTILITY

THERE is now increasing evidence to show that adenomyosis has a negative impact on fertility and pregnancy.[11] Women with adenomyosis are more likely to have premature delivery or premature rupture of membranes.[58]

Adenomyosis can also have a detrimental effect on IVF outcomes, with reduced pregnancy and live birth rates, and increased rates of miscarriage.[11] Fetal growth restriction and poorer neonatal outcome are reported.[11]

An early IVF study found that the spontaneous abortion rate was higher in women with a diffusely enlarged uterus without distinct uterine masses on ultrasound (suggestive of adenomyosis) compared with those with a normal looking uterus.[59]

Junctional zone thickness of more than 7mm (an MRI feature of adenomyosis) is associated with higher rate of implantation failure.

Disturbed uterine peristalsis and sperm transport, and destruction of normal myometrial architecture and function, are among proposed mechanisms for infertility in women with adenomyosis.[60]

Uterine-sparing conservative surgery to remove adenomyosis is technically challenging and should not be undertaken lightly.[11] Unlike fibroids, infiltrative adenomyosis tissue cannot be enucleated from the uterus without a natural surgical plane. Attempting complete excision of the affected area requires excision of normal uterine muscle.[61]

The resulting uterine wall may then be structurally and functionally defective. This can cause obstetric complications, such as miscarriage or uterine rupture.

Uterine rupture during pregnancy is rare, but it is a catastrophic obstetric event associated with maternal and fetal mortality.[62]

There are many reported series documenting possible successful term pregnancies following UAE for the treatment of fibroids.[63]

However, for adenomyotic women, there is currently insufficient data regarding impact of UAE on fertility and pregnancy.[42,16]

Following UAE for adenomyosis, there is a more than 90% chance the uterus can be retained, but it remains unclear if UAE will positively or negatively affect fertility and pregnancy outcomes.[16]

GnRHa treatment induces apoptosis, and reduces inflammatory reaction and angiogenesis in adenomyosis. GnRHa before IVF improves the pregnancy rate.[64] GnRHa treatment could be an option for women seeking symptom control and immediate fertility.

ADENOMYOSIS AND ENDOMETRIOSIS

IN ENDOMETRIOSIS, ectopic endometrial glands and stroma are located outside of the uterus, on the serosal or subperitoneal surface of the uterus.

A recent study has confirmed the strong association between adenomyosis with endometriosis, and vice versa, in 80-90% of cases.[65] It has been proposed that pelvic endometriosis and uterine adenomyosis are variants of the same disease.[66]

Persistent pelvic pain following optimal endometriosis surgery suggests the presence of

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◂PAGE 22 adenomyosis.[21] We propose that when dysmenorrhoea is accompanied by HMB, women are evaluated with a high-quality TVUS looking for adenomyosis. Follow with MRI if TVUS is inconclusive.

Since medical therapy for endometriosis and adenomyosis are rather similar, manage women conservatively with adequate medical therapy before performing invasive procedures for diagnosis and treatment. In those with severe dysmenorrhoea without HMB and an apparently normal TVUS, endometriosis is a likely diagnosis. When medical therapy has failed to control symptoms, laparoscopy is indicated to exclude/confirm endometriosis.

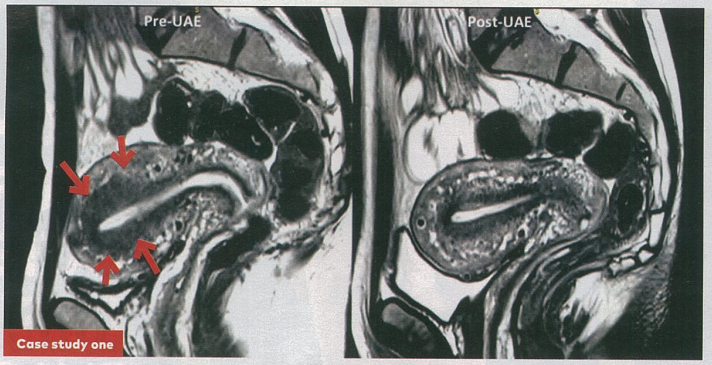
Since both endometriosis and adenomyosis impact negatively on fertility, fully counsel and appropriately manage subfertile women with either diagnosis, before embarking on IVF.

CASE STUDIES

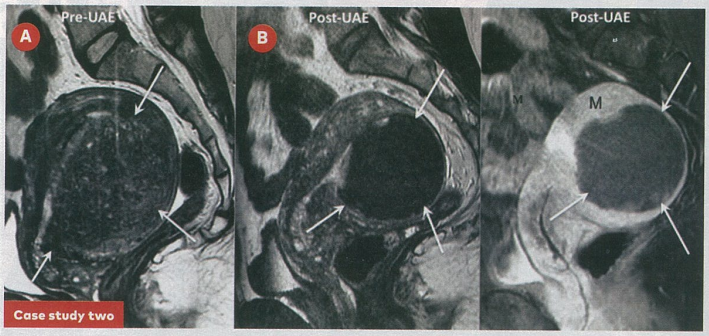
Case study one

AMY, a 28-year-old mother of three young children, complains of HMB and always feeling tired. She is incapacitated for a few days each month by her severe dysmenorrhoea. NSAIDs have not improved the condition, and despite taking tranexamic acid, Amy is still changing large pads every two hours. A progestogen IUD was not tolerated because of acne and continuous spotting.

Her uterus is reported as normal on ultrasound. Because of her severe symptoms, an MRI is performed, revealing thickening of the junctional zone (arrows) confirming adenomyosis.



Case study one



Case study two

Amy is treated with UAE. MRI six-months post-treatment shows normalisation of the junctional zone. She now has regular periods that are very light and the pain has almost completely gone. Amy is energetic and can actively play with her children. She is very happy with the marked improvement in her quality of life.

Case study two

Susan, 45, has had HMB and period pain for years. Tranexamic acid and progestogens are no longer effective. She expelled two progestogen IUDs and had a failed endometrial ablation. Susan declined a hysterectomy. Her MRI shows a large area of adenomyosis (arrows in A) in the posterior myometrium.

Six months post-UAE, MRI shows infarction of adenomyosis (arrows in B), and shrinkage from 272mL to 115mL. Note the normal viable myometrium(M). Her periods are now lighter and no longer painful.

Key points

- Adenomyosis can cause debilitating heavy menstrual bleeding and dysmenorrhoea.
- Adenomyosis can impair fertility and pregnancy.
- Adenomyosis often coexists with fibroids and endometriosis.
- Heightened awareness and clinical suspicion are keys to early diagnosis.
- Ultrasound signs can be subtle; MRI is more accurate but not readily available.
- Medical therapy is aimed at reducing heavy menstrual bleeding and dysmenorrhoea
- Uterine artery embolisation is an effective non-surgical alternative to hysterectomy.

CONCLUSION

ADENOMYOSIS is a seemingly benign disease of the uterus but can cause debilitating heavy menstrual bleeding and dysmenorrhoea, significantly affecting a woman's quality of life. Adenomyosis is associated with endometriosis, fibroids and infertility. Clinical suspicion is the key to early diagnosis. TVUS should be the initial imaging evaluation, although MRI is more accurate.

Conservative medical treatment includes non-hormonal therapy with tranexamic acid and NSAIDs. Hormonal treatments may be progestogens, low-dose COCPs, and progestogen-IUDs. GnRH agonist can be used for women who wish to conceive.

Failing conservative therapies, uterine artery embolisation is an emerging interventional radiological treatment that is safe and effective. Hysterectomy should only be performed as the last resort, when less invasive options have failed.

ONLINE RESOURCES

- **Cancer Australia Abnormal vaginal bleeding in pre- and perimenopausal women: A diagnostic guide for GPs and gynaecologists.** bit.ly/2WQvACf
- **Stewart M and Black K. Choosing a combined oral contraceptive pill. Australian Prescriber 2015; 38:6-11.** bit.ly/2uSJeITf
- **Dr Eisen Lang's website: Patient and doctor's information on adenomyosis** www.adenomyosis.com.au

References

Available on request from howtotreat@adg.com.au

How to Treat Quiz.

ADENOMYOSIS

GO ONLINE TO COMPLETE THE QUIZ **www.ausdoc.com.au/howtotreat**

1. **Which TWO statements regarding the pathology of adenomyosis are correct?**
   - a Using MRI criteria, adenomyosis is found in 9% of healthy women.
   - b Adenomyosis is a benign condition of the uterus caused by the presence of ectopic endometrial tissue within the myometrium, and reactive hypertrophy and hyperplasia of the surrounding myometrium.
   - c Dysmenorrhoea may be related to uterine irritability.
   - d Relatively high progestogen concentration and impaired immune-related growth control are needed for the maintenance of adenomyosis.
2. **Which THREE are risk factors for adenomyosis?**
   - a Uterine curettage.
   - b Obesity.
   - c Depression and use of SSRIs.
   - d Nulliparity.
3. **Which THREE are causes of secondary dysmenorrhoea?**
   - a Fibroids.
   - b Pelvic congestion syndrome.
   - c An intrauterine contraceptive device.
   - d Ovarian cysts.
4. **Which TWO may be presenting features of adenomyosis?**
   - a Amenorrhoea.
   - b Chronic pelvic pain.
   - c Dyschezia.
   - d Abdominal bloating.
5. **Which TWO statements regarding the imaging for adenomyosis are correct?**
   - a TVUS signs maybe subtle.
   - b MRI returns a correct diagnosis more often than TVUS.
   - c A positive finding of adenomyosis on ultrasound excludes endometriosis.
   - d Most women with fibroids also have adenomyosis.
6. **Which THREE statements regarding tranexamic acid are correct?**
   - a It is contraindicated with a history or risk of arterial or venous thromboembolic disease.
   - b Side effects include nausea, vomiting, dizziness, visual disturbance and seizure.
   - c It acts by stabilising the lining of the uterus, suppressing cyclical hormone changes and preventing mid-cycle oestrogen surge.
   - d Use with caution concomitantly with the COCP.
7. **Which ONE drug has the side effects of vasomotor syndrome, reduced bone mineral density, genital atrophy, and mood instability?**
   - a Progesterone-releasing IUD.
   - b Gonadotropin-releasing hormone agonists.
   - c Combined oral contraceptive pill.
   - d Danazol.
8. **Which THREE statements regarding uterine artery embolisation are correct?**
   - a UAE is a safe and efficacious treatment for adenomyosis.
   - b Adenomyosis and fibroids have immense capacity to recruit new vessels.
   - c UAE can be performed under local anaesthetic and light conscious sedation.
   - d Persistent amenorrhoea is uncommon following UAE for adenomyosis.
9. **Which THREE statements regarding management options for adenomyosis are correct?**
   - a High-intensity focused ultrasound is first-line management for adenomyosis.
   - b Endometrial ablation is only effective for superficial adenomyosis.
   - c The boundary between adenomyosis and the adjacent myometrium is indistinct, and therefore adenomyotic tissue cannot be enucleated.
   - d Hysterectomy for adenomyosis should be the last resort when less invasive treatments have failed.
10. **Which THREE conditions may occur as a result of adenomyosis?**
    - a Increased risk of premature delivery/rupture of membrane.
    - b Reduced IVF pregnancy and delivery rate.
    - c Fetal macrosomia.
    - d Risk of uterine rupture following surgical treatment.

CPD POINTS

- We have a new How to Treat website (www.ausdoc.com.au/howtotreat) where you can read this article and take the quiz to earn CPD points.
- Each article has been allocated 2 RACGP QI&CPD points and 1 ACRRM point.
- RACGP points are uploaded every six weeks and ACCRM points quarterly.