

Heavy menstrual bleeding

Treatment and referral options

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Heavy menstrual bleeding affects about one in four women. After excluding malignancy, first-line management in primary care is with pharmaceutical treatments. Other treatment options include endometrial ablation and hysterectomy.

KEY POINTS

- Heavy menstrual bleeding (HMB) affects about 25% of women of reproductive age.
- Comprehensive assessment is essential to determine the likely cause of the bleeding and its impact on a woman's life; it includes exclusion of anaemia, iron deficiency and reproductive tract cancer.
- Many women with HMB of benign causes can be managed in general practice with pharmaceutical treatment including the levonorgestrel-releasing intrauterine system.
- Less-invasive surgical options such as endometrial ablation are appropriate for some women.
- Hysterectomy offers definitive treatment of HMB of benign causes when other treatment options have been ineffective or are unsuitable.



Hheavy menstrual bleeding (HMB) is defined as excessive menstrual blood loss that interferes with a woman's physical, emotional, social and material quality of life, and which can occur alone or in combination with other symptoms such as pelvic pain.¹ The term HMB is based on a history of excessive bleeding that affects a woman's wellbeing and replaces the earlier term menorrhagia that was based on quantifying blood loss objectively rather than assessing its impact.

HMB is the most common presentation of abnormal uterine bleeding in premenopausal women, affecting 25% of women of reproductive age.² Anecdotally, there may be delay in diagnosing HMB due to a patient's lack of awareness of what is normal in relation to menstrual blood loss, and missed diagnostic opportunities.

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1. INTERNATIONAL FEDERATION OF GYNECOLOGY AND OBSTETRICS CLASSIFICATION OF ABNORMAL UTERINE BLEEDING³

Structural lesions

- Polyps
- Adenomyosis
- Leiomyoma (fibroids)
- Malignancy and hyperplasia

Nonstructural conditions

- Coagulopathy
- Ovulatory dysfunction
- Endometrial
- Iatrogenic
- Not otherwise classified

Classification system for abnormal uterine bleeding

The International Federation of Gynecology and Obstetrics classification system for abnormal uterine bleeding stratifies causes into nine categories arranged according to the acronym PALM-COEIN (Box 1).³ Abnormal uterine bleeding includes any departure from normal menstruation or from a normal menstrual cycle pattern. HMB is the most common type; other types include intermenstrual bleeding and postcoital bleeding, which are distinct from HMB and must be investigated separately.

Assessment and diagnosis

A comprehensive history that includes assessment of the bleeding pattern and amount and its impact on the woman's quality of life is essential to determine the likely causes of HMB and to guide appropriate investigations, referral and management of patients with the condition. It is essential to exclude gynaecological malignancy in all women, and differential diagnoses such as miscarriage or endometriosis must be considered. Box 2 provides a guide to the important elements in history taking.

An abdominal and bimanual pelvic examination should be performed to identify any palpable mass or abnormal uterine size (except in young women who are not yet sexually active or in those who decline). A speculum examination may be performed to assess the cervix and a cervical screening test or a co-test (human papilloma virus and liquid-based cytology) performed in accordance with the National Cervical Screening Program guidelines.⁴

Pregnancy must always be considered, with urine beta human chorionic gonadotropin testing as required. Test for chlamydia and gonorrhoea if risk factors for a sexually transmitted infection are present. It is also important to assess iron status and exclude anaemia with a full blood count (haemoglobin should be above 110g/L) and ferritin level (should be above 50 mcg/L). Other investigations are determined by the initial assessment and may include thyroid testing and a coagulation profile for women with HMB since menarche or a relevant family history (e.g. Von Willebrand disease).⁵

The role of ultrasound

A pelvic ultrasound provides important information about structural uterine and endometrial abnormalities. A transvaginal ultrasound (TVUS) is the first-line imaging modality if the patient has risk factors for malignancy or other abnormality is suspected on history and examination. A TVUS is usually performed in conjunction with a transabdominal ultrasound. A transabdominal ultrasound can be ordered if TVUS is unavailable or inappropriate, but it is less accurate for assessing the endometrium.⁶

The ultrasound should, where feasible, be performed between days five and 10 of the menstrual cycle when the endometrium is thinnest. This timing allows for the most accurate measurement of endometrial thickness and optimal detection of polyps and submucosal fibroids. The report should include stage of the cycle (e.g. day 7), endometrial thickness (in mm), uterine dimensions and the presence and location of structural abnormalities.

2. IMPORTANT ELEMENTS OF HISTORY TAKING FOR WOMEN PRESENTING WITH HEAVY MENSTRUAL BLEEDING

- General medical history including medications (e.g. anticoagulants)
- Sexual, reproductive and contraceptive history, including plans for future fertility
- Cervical screening status
- Menstrual history including last menstrual period, duration, timing, heaviness (flooding, passing clots, 'accidents') and chronicity of bleeding
- Presence of postcoital and intermenstrual bleeding (different to HMB and require separate investigation)
- Use of sanitary protection (e.g. double pads, frequent changes)
- Impact on daily activities and quality of life
- Associated symptoms including dysmenorrhoea, dyspareunia, pelvic pressure
- Risk factors for endometrial cancer
 - increasing age
 - obesity (particularly with comorbid diabetes and/or hypertension)
 - nulliparity
 - anovulatory cycles
 - polycystic ovary syndrome (PCOS)
 - personal or family history of endometrial, ovarian or colon cancer or Lynch syndrome
 - use of unopposed oestrogen or tamoxifen
- Symptoms of iron deficiency, with or without anaemia
- Symptoms suggesting a bleeding disorder
- Symptoms associated with PCOS including acne, hirsutism and irregular menses
- Symptoms suggesting hypothyroidism

Cancer Australia recommends endometrial sampling in premenopausal women if the endometrium is more than 12mm and in perimenopausal women if it measures 5 mm or more.⁷

TABLE 1. OVERVIEW OF OPTIONS FOR ONGOING PHARMACEUTICAL MANAGEMENT OF HEAVY MENSTRUAL BLEEDING⁸

Medication	Reduction in mean blood loss (%)	Comments
Levonorgestrel-releasing intrauterine system	71–95%	Provides contraception
Combined oral contraceptive pill (cyclically or continuously)	35–69%	Provides contraception and cycle control
Tranexamic acid (for four days from the onset of bleeding)	26–54%	No additional benefits
NSAIDs (mefenamic acid or naproxen from the start of bleeding for up to five days)	10–52%	Benefits for dysmenorrhoea
Cyclic progestogen (norethisterone 15 mg orally daily from day five to day 26 of the cycle)	87%	Limited by side effects
Depot medroxyprogesterone acetate (injection every 12 weeks)	–	No studies for heavy menstrual bleeding but up to 47% of subjects have amenorrhoea at 12 months

Initial steps in managing HMB

When a woman initially presents with HMB it is important to offer immediate symptomatic relief to decrease blood loss in subsequent menstrual cycles. Useful options for women awaiting a TVUS or specialist appointment include the following. The choice will depend on a woman's reproductive life stage and the presence of comorbidities.

- **Tranexamic acid.** Initiate at a dose of two tablets three to four times daily as soon as menstruation starts and continue for the first four days of the period. Inhibits clot breakdown (antifibrinolytic).
- **NSAIDs.** Mefenamic acid (500 mg three times daily) or naproxen (500 mg immediately followed by 250 mg three to four times daily) reduce prostaglandin synthesis by inhibition of cyclo-oxygenase when started at the onset of bleeding for up to five days until heavy blood loss abates.
- **Combined oral contraceptive pill.** A short course of a PBS-listed low-dose oral contraceptive pill with levonorgestrel or norethisterone can be a good choice for women not wishing to conceive and/or with irregular cycles, with advice on skipping the nonhormonal sugar pills. (Evidence is lacking for differences

between estradiol formulations but all reduce bleeding by about 35%. There is, however, evidence from placebo-controlled trials that a combined formulation containing estradiol valerate and dienogest may be more effective but it is not available on the PBS.)

- **Norethisterone.** A 22-day course is given as 5 mg tablets three times daily from day five to day 26 of the menstrual cycle. Studies have found this to be less well tolerated than other treatments.

Longer-term primary care management

Once malignancy or significant abnormality have been excluded, many women can be effectively managed in the primary care setting in the long term with pharmaceutical treatment alone. The choice of treatment will be determined by the presence of associated symptoms such as dysmenorrhoea, medical contraindications, whether the bleeding is ovulatory or anovulatory, plans for conception and personal preference. Women should be provided with information about available options, the expected effect on their bleeding as well as possible side effects, and when to return for review.

Table 1 provides an overview of pharmaceutical treatments that can be

considered for use in the following order, based on evidence of effectiveness and adverse effects.⁸

1. Levonorgestrel-releasing intrauterine system (LNG-IUS), also referred to as the LNG-intrauterine device (LNG-IUD).
2. Combined oral contraceptive pills (tricycled or used continuously) or tranexamic acid or NSAIDs.
3. Cyclic norethisterone or injected long-acting progestogens (depot medroxyprogesterone acetate).

The LNG-IUS is the most effective pharmaceutical treatment for HMB. It is associated with high levels of continuation and satisfaction and provides highly effective contraception for women who do not wish to conceive.⁹ Choosing whether to use an LNG-IUS will depend on medical contraindications, uterine size and shape and the acceptability to the patient of potential side effects, including initial spotting and hormonal effects, as well as their personal preference. After a TVUS and any other appropriate investigations to exclude serious abnormality, an LNG-IUS can be inserted by a primary care practitioner. Ensuring there is a trained IUD-inserter in the practice or having rapid referral pathways to other GP practices or family planning services is important for increasing access to this effective management option.

When to refer patients for further investigation

Early referral for endometrial biopsy is essential when there are findings suggestive of malignancy on assessment. A higher index of suspicion is required for women aged 45 years or more. Specialist referral is also essential for significant pelvic abnormality on ultrasound such as an endometrial polyp, or when there is a lack of response to pharmaceutical treatment after about six months (or earlier as required). Red-flag factors are listed in Box 3.

Beyond primary care management

Specialist options beyond those already mentioned, and which the GP may need to discuss with their patient, include treatment with ulipristal acetate and minimally invasive surgical procedures such as endometrial ablation and/or removal of any local abnormality causing bleeding (fibroids and polyps). Fibroids can be removed abdominally or hysteroscopically depending on their site in relation to the uterine cavity. Polyps, even small ones, can cause HMB and may rarely be malignant so should be removed through hysteroscopic polypectomy or dilatation and curettage. Hysterectomy for HMB of benign causes may be considered when alternative medical and procedural options cannot be used for clinical reasons, are ineffective or intolerable, or when it is the woman's informed choice.

Ulipristal acetate

Ulipristal acetate is a selective progesterone receptor modulator that reversibly blocks the progesterone receptor. It acts on the endometrium and myometrium to reduce menstrual blood loss. When taken for three months at a daily dose of 5 mg it significantly reduces menstrual bleeding and leads to amenorrhoea in more than two-thirds of women. Ulipristal acetate also reduces fibroid volume by 25 to 45%.¹⁰⁻¹³ It potentially has a key role in reducing the size of fibroids in women

wanting to retain fertility, and in enabling less invasive surgery. Even though most women taking a therapeutic dose of ulipristal acetate will be anovulatory, a nonhormonal contraceptive method is recommended during treatment because hormonal methods may be adversely impacted by the medication.¹³

Ulipristal acetate is currently subject to a pharmacovigilance investigation by the European Medicines Agency due to cases of severe liver disease, so its use in Australia is restricted and no new patients should start treatment for the time being.

The 5 mg tablets are approved by the TGA for treatment courses of up to three months each for moderate to severe symptoms of fibroids. Ulipristal acetate has not been approved for subsidisation under the PBS. The product information states that ulipristal acetate should only be initiated by, or after a consultation with, a gynaecologist. Follow up could then be managed by the GP, with gynaecologist review as clinically indicated.¹⁴

Uterine artery embolisation

Uterine artery embolisation (UAE) can be used to reduce HMB caused by fibroids. UAE is performed by interventional radiologists. The patient is sedated and an angiographic catheter is used to access the uterine arteries via the common femoral artery. Small polyvinyl particles are injected into the uterine arteries.¹⁵ The resulting reduction in uterine blood flow produces ischaemic injury to the fibroids, causing necrosis and shrinkage.

The procedure is not currently recommended for women wishing to conceive, because the effects on fertility and pregnancy are uncertain. Potential side effects include pain, discharge and fever as the fibroid tissue dies, and venous thromboembolism. A recent meta-analysis comparing UAE with surgery for symptomatic fibroids found no significant differences in major and minor complications; however, there was an increased chance of reintervention for UAE compared with

3. FACTORS THAT MAY TRIGGER IMMEDIATE REFERRAL TO A SPECIALIST

- Significant abnormality on ultrasound (polyps, fibroids)
- Endometrial thickness of more than 12 mm if premenopausal or 5 mm or more if perimenopausal
- Risk factors for endometrial cancer (e.g. obesity, anovulation)
- Age 45 years or more with significant symptoms (flooding, large clots)
- Associated abnormal symptoms (intermenstrual or postcoital bleeding)
- Lack of response to pharmaceutical treatment by six months (consider placing the patient on recall)

myomectomy (28.4 to 32% at five years compared with 2.0 to 10.7% for the surgical groups).¹⁶

Endometrial ablation

Endometrial ablation is a surgical procedure undertaken to destroy or remove the endometrial cell lining of the uterus. This prevents the monthly proliferation and shedding of the lining, decreasing the amount of menstrual flow or eliminating it altogether.

First-generation endometrial ablation techniques involved filling the uterus with fluid and resecting the endometrium with an electrosurgical loop. Second-generation techniques do not require direct visualisation of the uterine cavity but instead involve placing a device that moulds to the shape of the cavity and releases energy in the form of microwaves, heat or radiofrequency.¹⁷ There are two second-generation devices used in Australia, one that uses radiofrequency and one that uses a thermal balloon. These techniques are safer and more effective than the earlier methods and result in a 12-month amenorrhoea rate of 10 to 40%.¹⁸

Most women who undergo endometrial ablation do not require retreatment and are able to avoid hysterectomy. Endometrial ablation results in significant

scarring of the cavity and the treatment is not suitable for women who may want a pregnancy in the future because of the risk of placenta accreta. Effective contraception is required after the procedure.¹⁸

Myomectomy

Surgical removal of fibroids can be useful for women who want to preserve their uterus and/or fertility. Depending on the site of the fibroids, the procedure is undertaken laparoscopically, by laparotomy or transvaginally. Myomectomy can result in a large amount of blood loss so is best reserved for removal of only one or a few fibroids.¹⁹ Depending on the site of the fibroid and the extent of the surgery, myomectomy can increase the risk of rupture of the uterus in a subsequent pregnancy.

Hysterectomy

Hysterectomy provides definitive treatment of HMB but carries greater risks of morbidity and mortality compared with less-invasive surgical procedures. The procedure can be undertaken laparoscopically, through an abdominal incision, vaginally or as a laparoscopically-assisted vaginal hysterectomy.²⁰ Risks associated with hysterectomy include irreversibility and consequences for childbearing, infection, other organ damage and blood loss. The impact of time in hospital and post-operative recovery must also be considered. Nevertheless, hysterectomy remains a valid choice for informed women and may result in a better quality of life for some women in the long term due to its definitive nature.

The heavy menstrual bleeding clinical care standard

Recent data gathered for the Australian Atlas of Health Care Variation, produced by the Australian Commission on Safety and Quality in Health Care, showed great variability in the management of HMB across Australia.²¹ There was a 6.6-fold variation in hospitalisations for non-malignant hysterectomy in women aged

15 years and older across the country in 2014–15, with the highest rates in regional areas compared with remote and inner-city areas. Although variation is expected and can reflect a responsive health system, it can also reflect low use of less-invasive treatments. The rate of endometrial ablation was 21 times higher in some parts of the country compared with others, which suggests that some women may be missing out on potentially useful alternatives to hysterectomy.

The most effective medical intervention is the long-acting intrauterine progestogen device

In response to this variation, the 2017 Heavy Menstrual Bleeding Clinical Care Standard was developed by the Commission in collaboration with an expert topic working group of clinicians, researchers and consumers.²² The standard includes eight quality statements covering assessment and diagnosis, informed choice and shared decision making, pharmaceutical treatment as the initial treatment, quality ultrasound, intrauterine hormonal devices, uterine-preserving alternatives to hysterectomy and hysterectomy. It has been developed to inform patients about the care they can expect to receive, and to ensure patients have the opportunity to make an informed choice from a range of options. It also aims to provide guidance for health professionals, so they can deliver appropriate high-quality care, and to identify systems that health

services need in place to support and monitor appropriate care. The standard provides a useful framework for the management of HMB in primary care, gynaecology and radiology and is a valuable resource for patients wanting to understand their options for this relatively common condition.

Conclusion

For most women, HMB of benign causes can be managed in primary care with pharmaceutical treatment. The most effective medical intervention is the long-acting intrauterine progestogen device and, in the absence of significant uterine abnormality, about 80% of women using this will not require surgical intervention for at least five years. It is important for women and their healthcare practitioners to know about the less-invasive procedural interventions including uterine artery embolisation, endometrial ablation, polypectomy and myomectomy. Medical treatment of HMB, combined with active promotion of treatment, has significantly reduced the need for major surgery, and hysterectomy should be reserved mainly for women in whom other treatment options have failed or are contraindicated. **MT**

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS: Dr Bateson has attended advisory committee meetings and received support to attend conferences from Bayer Healthcare as part of her role at Family Planning NSW. Dr Black has attended one international advisory board meeting on postpartum contraception for Bayer Healthcare for which her airfare and accommodation were paid.

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