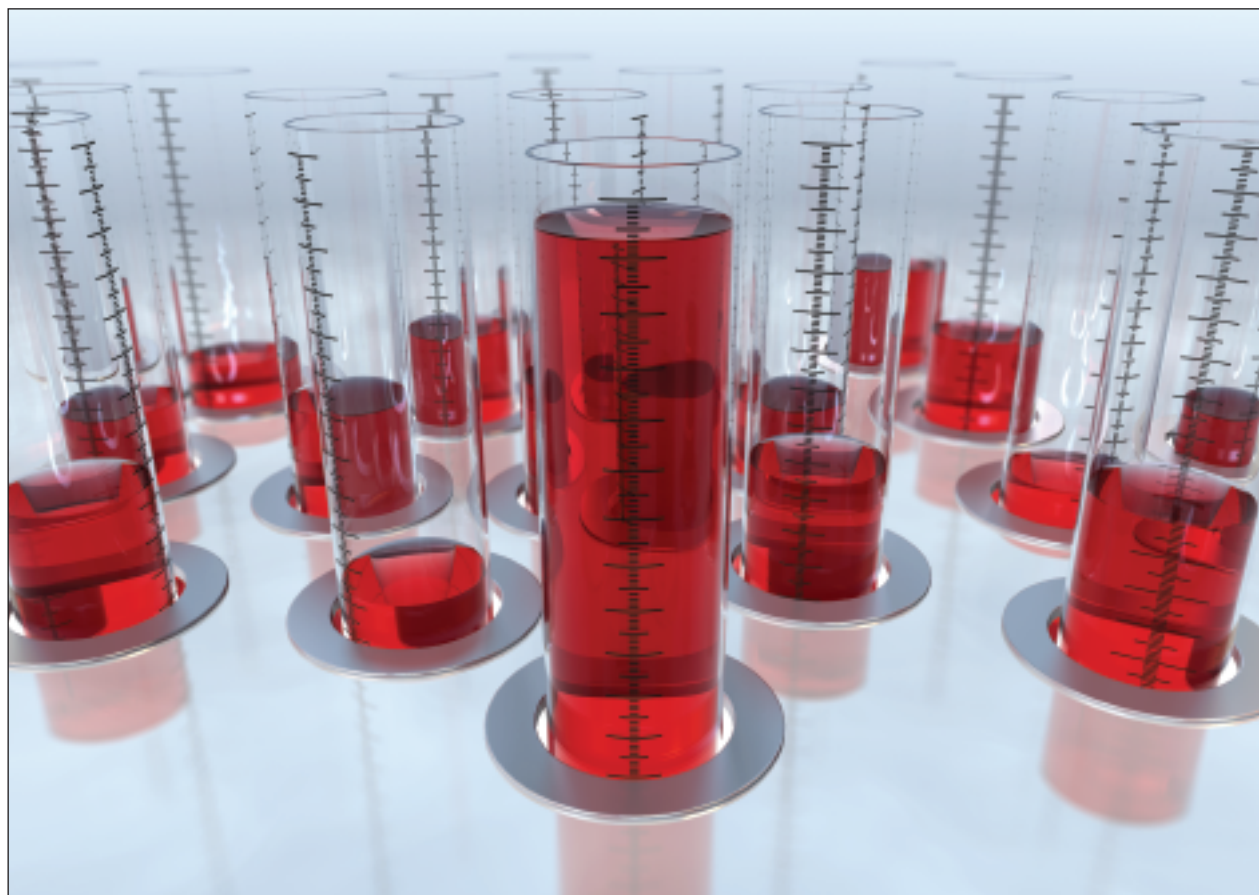


# Menorrhagia: recommended treatments in primary care

Shruti Mohan MRCOG, Louise Page MRCOG, Vivian Rusman BSc, MB BS and Jenny Higham FRCOG



Skyline Imaging Ltd

**A range of surgical and nonsurgical treatments for menorrhagia are now available to suit the needs of most patients. Our Drug review discusses the properties and efficacy of current therapies, followed by sources of further information.**

The condition of heavy menstrual bleeding (menorrhagia) is common, affecting about 22 per cent of otherwise healthy premenopausal women aged over 35 years in the UK. One in twenty women aged 30-49 years present to their GP with this problem annually, and it comprises 12 per cent of onward requests for a

gynaecological opinion.<sup>1</sup> Although treatment for menorrhagia can be initiated in primary care, not all GPs are willing to prescribe, with only 58 per cent of women receiving any medical therapy before referral to a specialist.

Menorrhagia is objectively defined as a blood loss of 80ml or more per menstrual cycle, with normal average menstrual loss of around 30-40ml per period, although in practice either is rarely measured. The complaint of heavy bleeding is, therefore, highly subjective. For clinical purposes menorrhagia should be defined as excessive menstrual blood loss that has a negative effect on quality of life, which can occur alone or in combination with other symptoms.<sup>2</sup> When menstrual loss is measured in women who complain of menorrhagia,

TAMPON	1	2	3	4	5	6	7	8
CLOTS								
FLOODING								

TOWEL	1	2	3	4	5	6	7	8
CLOTS		50px1 1px2	1p x1					
FLOODING								

SAMPLE CHART  
Please stick this chart with the  
menstrual pads completed over time.

**Figure 1.** The pictorial menstrual blood loss chart allows for a more objective assessment of the quantities of blood lost

approximately half of them have blood loss of less than 80ml.

As routine laboratory measurement of blood loss is not performed, a scoring system – the pictorial blood loss assessment chart (see Figure 1) – was developed to help to try and assess heavy periods by non-laboratory means, although the majority of GPs correctly rely on a patient’s own perceptions.<sup>3</sup>

Excessive loss can lead to chronic anaemia and this, together with problems of containment, can have a significant physical and emotional impact on women.

The underlying mechanisms causing excessive blood loss are varied and as yet unknown. Factors considered have included abnormal prostaglandin production, with there being a preponderance of vasodilatory effects in the endometrium and myometrium. Fibroids, especially those located submucosally, polyps and the presence of a copper-containing intrauterine contraceptive device increase the likelihood of excessive loss. Anovulation may be associated with menorrhagia, particularly at the extremes of reproductive life – close to menarche and menopause. Only very rarely is it the result of a systemic coagulation defect.

In the initial assessment of menorrhagia, a careful history should be taken. This should include enquiry

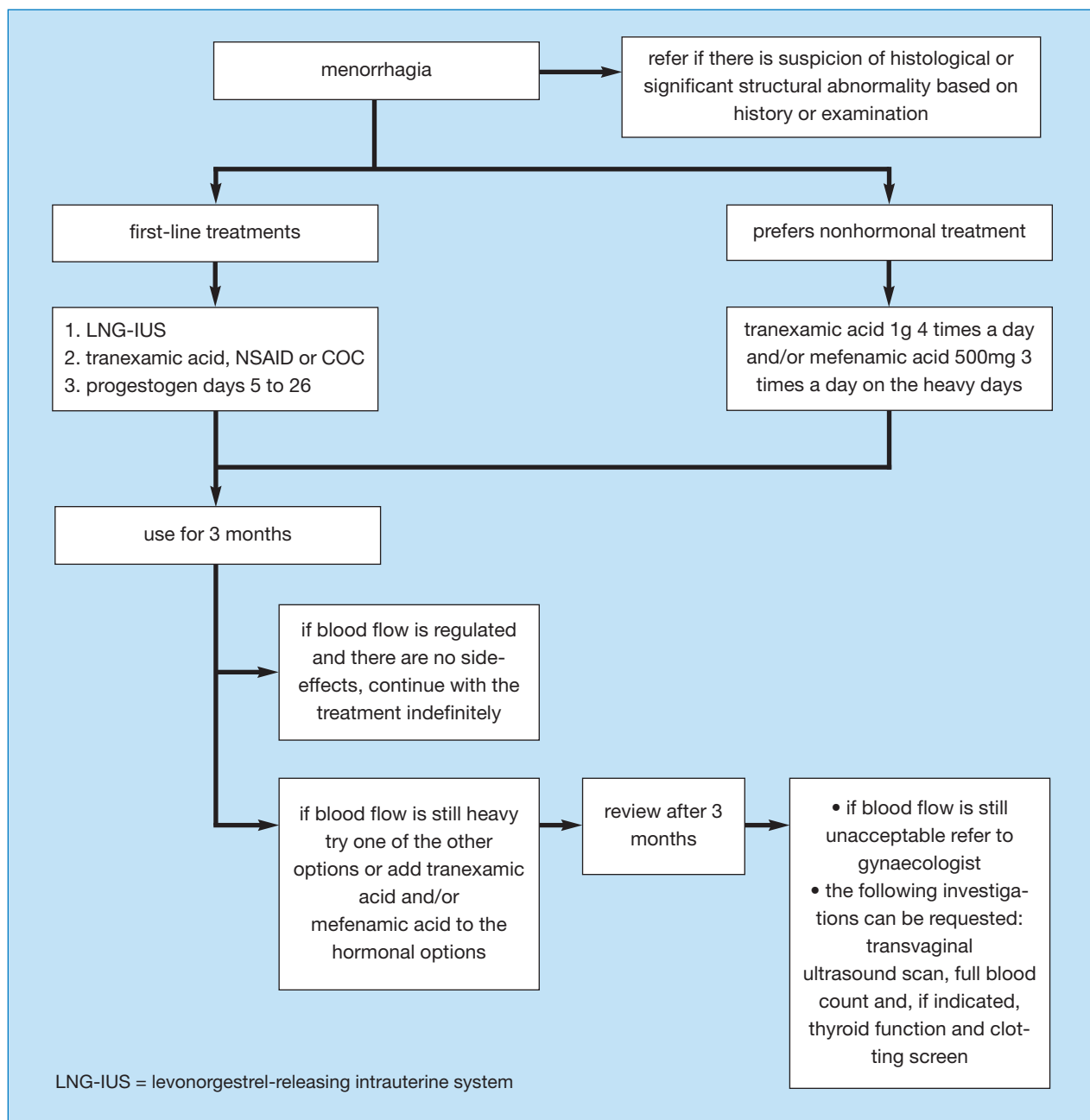
regarding the presence of associated symptoms such as intermenstrual or postcoital bleeding, pelvic pain or pressure symptoms. NICE guidance on heavy menstrual bleeding suggests that where heavy bleeding occurs in isolation, physical examination or other investigation may not be necessary prior to commencing treatment, unless the treatment choice is the levonorgestrel-releasing intrauterine system (LNG-IUS).<sup>2</sup> However, where the history raises the possibility of associated pathology, physical examination should be carried out. Examination is then needed to look for anaemia and exclude obvious pelvic pathology. Abdominal palpation should be performed to check for pelvic masses, and cervical inspection and vaginal examination will exclude conditions such as fibroids.<sup>4</sup>

In terms of investigations, a full blood count should be performed on all women with heavy menstrual bleeding in parallel with the commencement of treatment.<sup>2</sup> A routine serum ferritin is not needed for all women with heavy menstrual bleeding.<sup>2</sup> If there are any other symptoms to suggest thyroid dysfunction, this should be checked. Clotting disorders should be considered in women who have experienced heavy menstrual bleeding since menarche or who have a relevant family history.

An ultrasound may be valuable to assess the uterine size and cavity – specifically looking for fibroids and endometrial polyps and to exclude ovarian pathology. Indications for imaging, most commonly by ultrasound scanning, include a uterus that is palpable abdominally, a pelvic mass of unknown origin or in women where pharmaceutical treatment fails.<sup>2</sup>

Underlying pathology is found in less than 50 per cent of patients. However, indications for referral to secondary care include a uterus that is palpable abdominally, intracavity fibroids on scan or a uterus of over 12cm in length.<sup>2</sup> All women referred for specialist care should be given a patient information leaflet on heavy menstrual bleeding outlining investigation and treatment options, prior to their outpatient consultation.<sup>2</sup> A hysteroscopy and endometrial biopsy are considered in secondary care for women over 45 years of age, or for a woman of any age when there is a suspicion of structural or histological abnormality or when heavy loss is unresponsive to therapy.<sup>2,5</sup>

Excessive menstrual blood loss can be treated medically or surgically, and the medical treatment involves both hormonal and nonhormonal therapy. Figure 2 summarises the management of menorrhagia in primary care.



**Figure 2.** Primary care management of menorrhagia with indications for referral to secondary care

**Medical treatment**

Pharmaceutical treatments should be considered in the following order.<sup>2</sup>

*Levonorgestrel-releasing intrauterine system*

The LNG-IUS is a good alternative to the surgical treatment of menorrhagia, and is highly effective (see Figure 3). The reduction in measured blood loss is progressive in the months following initial insertion and a 90 per cent plus diminution in loss has been demonstrated in those women that keep the device

in; amenorrhoea is not uncommon. The device also provides effective reversible contraception. Prior to inserting an LNG-IUS, pregnancy should be excluded and the patient counselled that the initial three to six months postinsertion are typically accompanied by tiresome protracted, if lighter, blood loss.

The device releases 20µg levonorgestrel every 24 hours and is effective for up to five years. The local progestogenic dose is high at the endometrial surface and this continuous exposure induces endometrial atrophy. However, as the circulating dose is low,

systemic side-effects are minimal after the first few months of insertion, but initially complaints of bloating and breast tenderness do get reported. Discussion with the patient prior to insertion is required regarding possible discomfort and the risk of uterine perforation at insertion. Spontaneous expulsion of the device is infrequent, more common in nulliparous women, and should be considered when the device appears ineffective. Normally, ovarian activity is not inhibited.

The high effectiveness of the LNG-IUS means that it has been shown to be more acceptable to many women than oral medications and it should be offered to women as a first-line treatment, providing at least 12 months' use is anticipated. It has dramatically reduced the need for surgical interventions such as hysterectomy. The LNG-IUS's efficacy is similar to that of endometrial ablation techniques. Women with an

LNG-IUS report more progestogenic side-effects, but no difference in their perceived quality of life. Thus, the LNG-IUS is a cost-effective and successful means of treating menorrhagia, with high acceptability.<sup>6,7</sup>

### Nonhormonal medical treatments

**Antifibrinolytics** Tranexamic acid works by inhibiting plasminogen activator, so slowing the speed of dissolution of fibrin plugs and thereby reducing vessel bleeding. The typical reductions in menstrual blood loss are by 40-50 per cent of the total, confirmed in a number of studies where this was measured.<sup>8</sup> It does not alleviate menstrual pain.

Tranexamic acid has the advantage of needing to be taken only during the period itself, but must be ingested regularly with a dose of 1g four times a day on the heavy days being usual. Typically side-effects are

*continued on page 46*

	Benefits	Limitations (including contraindications)	Side-effects
<i>Levonorgestrel-releasing intra-uterine system (LNG-IUS)</i>	up to 90% reduction in blood loss reversible contraception minimal systemic side-effects cost-effective treatment	irregular bleeding up to 3-6 months postinsertion, initial discomfort, risk of uterine perforation at insertion	bloating breast tenderness
<i>Tranexamic acid</i>	reduces blood loss by 40-50% only needs to be taken during the period itself suitable for women wishing to conceive	does not alleviate menstrual pain contraindicated in women with a history of thromboembolic disease	nausea vomiting diarrhoea leg cramps
<i>NSAIDs</i>	reduce blood loss by 30-50% reduce menstrual pain only need to be taken during the period itself	contraindicated in women with a history of hypersensitivity to aspirin or other NSAIDs	gastrointestinal discomfort diarrhoea
<i>Combined oral contraceptive pill</i>	reduces blood loss by 50% alleviates menstrual pain and irregularity provides contraception	not suitable for heavy smokers and obese and older women in view of increased risk of thromboembolism	headaches breast tenderness bloating and weight gain alteration in libido depression
<i>Progestogens</i>	reduce blood loss by 30% (more in anovulatory women) ability to control and predict onset of menses can be used for the treatment of acute heavy bleeding	long-term use limited because of side-effects	weight gain bloating breast tenderness breakthrough bleeding

**Table 1.** Pros and cons of drugs used in the treatment of menorrhagia



**Figure 3.** The efficacy of the LNG-IUS has reduced the need for surgical treatment

mild nausea, leg cramps and diarrhoea. Very rarely there is a disturbance in colour vision.

Although tranexamic acid is an antifibrinolytic, there is no evidence of an increased risk of thrombotic events when prescribed to the general population. Its use is, however, contraindicated in women with a history of thromboembolic disease. Compared with NSAIDs and luteal phase progestogens, tranexamic acid is generally more effective at reducing excessive menstrual bleeding. As it has a short half-life and is given only during menstruation, it can be taken while trying to conceive.

The use of etamsylate (Dicynene), which reduces capillary bleeding in the presence of a normal number of platelets, is not recommended.<sup>2</sup>

**NSAIDs** These drugs act by inhibiting the enzyme cyclo-oxygenase and reducing the production of prostaglandins and thromboxanes. As vasodilatory prostaglandin levels are elevated in women with menorrhagia, this is the mechanism by which NSAIDs are thought to act. Furthermore, the reduction in prostaglandin-mediated uterine contractions is suppressed, which is why this group of drugs is so effective at also reducing menstrual pain. Like tranexamic acid, these drugs are taken during menstruation.

Mefenamic acid is licensed specifically for menorrhagia and dysmenorrhoea.<sup>9</sup> Other NSAIDs include naproxen, indometacin and ibuprofen, all having similar overall efficacy. Individual response to treatment varies, but average blood loss is reduced by a third to a half and typically pain is eased. In the treatment of dysmenorrhoea only, ibuprofen and naproxen have been shown to be more effective compared to mefe-

namic acid and aspirin. The use of paracetamol is no better than placebo.<sup>10</sup> Gastrointestinal side-effects are reportedly less with mefenamic acid than with naproxen sodium.

As NSAIDs and tranexamic acid have differing mechanisms of action, one could postulate that if taken together the reduction in menstrual bleeding would be enhanced in comparison with either drug alone. However, to date no study has been published on this approach. If a woman's symptoms are not eased by either tranexamic acid or NSAIDs, alone or in combination, after a trial treatment period of three cycles, they should be discontinued and alternative treatment options explored.<sup>2</sup>

### *Hormonal medical treatments*

**Combined oral contraceptive pill** The combined oral contraceptive pill (COC) is a useful, although unlicensed, treatment for menorrhagia, dysmenorrhoea and menstrual irregularity. From the small number of studies with objective blood loss measurement and much experience in clinical practice, there is evidence that the COC significantly reduces the menstrual blood volume by the order of 50 per cent and this loss is associated with less pain.<sup>11</sup> Other obvious benefits are contraception and predictability of loss, which may be appreciated by the patient.

The COC's mechanism of action is to inhibit ovulation, endometrial growth and development. Mild side-effects include headaches, breast tenderness, bloating and weight gain, alteration in libido, and depression. The increased risks of thromboembolism with the COC are exacerbated in older and/or obese and/or smoking women, often limiting its use in women in their 40s.

**Progestogens** The most commonly used progestogens are norethisterone, medroxyprogesterone acetate and dydrogesterone. These hormones, when given over a short period of the menstrual cycle, induce secretory change in the endometrium, yet when given over an extended period they initially inhibit proliferation and eventually induce endometrial atrophy. Understanding this mechanism explains why progestogens taken as a short course in the luteal phase of the cycle (from days 19 to 26) have no real beneficial effects on blood loss and therefore luteal-phase progestogens should not be used in the treatment of menorrhagia.<sup>2</sup>

Better suppression is seen when progestogens are started prior to ovulation in the proliferative phase, *ie* given for 21 days (from days 5 to 26 of the menstrual cycle inclusive). This will reduce menstrual blood loss by the order of 30 per cent, and often more than this

in the anovulatory patient. A benefit of progestogens is the ability to manipulate the timing of bleeding, and this ability to control and predict the onset of their menses may be greatly appreciated by the individual woman.

Progestogens also have a role in short-term menstrual delay or treatment for acute heavy bleeding.

Long-term use may be limited because of their side-effects such as weight gain, bloating, breast tenderness and breakthrough bleeding.

**Danazol** Danazol is a synthetic oral compound combining androgenic activity with antioestrogenic and antiprogestogenic activity. Danazol is licensed for the treatment of endometriosis but has been used, although unlicensed, in the treatment of menorrhagia. It should not be used in the routine treatment of heavy menstrual bleeding.<sup>2</sup> Danazol is rarely used for medium or longer-term management because of its unpleasant androgenic side-effects. It may be prescribed in the short term for endometrial preparation prior to endometrial destructive procedures.

**Gonadotrophin-releasing hormone (GnRH) analogues** consistently induce amenorrhoea and hence eradicate menorrhagia; they are unlicensed in the UK for this indication. They are not, however, useful for long-term treatment alone as they cause a menopausal hypo-oestrogenic state, with unwanted associated effects. Therapy prolonged for more than six months has a deleterious effect on bone mass and to avoid this and other adverse effects, studies using 'add-back' therapy with HRT have been described. GnRH analogues are more commonly seen in menorrhagia patients when used preoperatively prior to a myomectomy, hysterectomy or endometrial ablation.

### Surgical treatment

Surgery may be indicated for women who have completed their family, when medical treatment is ineffective or not tolerated, or when there are other associated problems. The decision to proceed with surgery must depend upon the patient's individual wishes and history, not least because of its irreversible consequences in terms of fertility.

### Endometrial destruction techniques

A variety of endometrial resection or ablation techniques have been developed over the past 20 years. They aim to destroy the endometrium and the underlying basal glands, preventing regeneration and replacing the endometrial surface with fibrosis, thus reducing or stopping menstrual bleeding. Many modalities have been tried and those that remain in common use are resection using electrosurgery (especially where there are submucous fibroids that require resection along with the endometrium), microwave technology, thermal balloons and impedance-controlled bipolar radiofrequency ablation. These therapies may require pretreatment of the endometrium, or careful timing of the procedure to the postmenstrual phase to render the endometrium thin and enhance the likelihood of success.

Endometrial ablation provides a cost-effective alternative to hysterectomy, with fewer complications. Although safer than a hysterectomy there are risks including uterine perforation, infection, bleeding and fluid overload depending on the technique used. The short-term complication rate is about 4 per cent.<sup>12</sup> A range of outcomes following treatment is possible from amenorrhoea to a reduction of blood loss, or no beneficial effect (due to endometrial regeneration). Endometrial regeneration is more common the younger the patient is when treated as most younger women with menorrhagia still have ovulatory cycles. Repeat treatment or progression to hysterectomy may be necessary in a minority of patients.<sup>13</sup>

Overall endometrial ablative techniques usually require only an outpatient or short hospital stay with quick recovery and few complications. Pregnancy, although less likely, should be avoided after endometrial destruction and therefore some form of contraception is needed.

### Hysterectomy

Hysterectomy is seen as the final option when other treatments fail and guarantees a 100 per cent success rate in treating menorrhagia. Hysterectomy can be performed abdominally, vaginally or laparoscopically. There is good evidence that vaginal hysterectomy and



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laparoscopic-assisted vaginal hysterectomy are associated with shorter recovery time and fewer complications than the abdominal route, although this is in part due to the more complicated operation conducted via the abdominal route. Regardless of the method, the overall satisfaction rates after hysterectomy for menorrhagia are high, in the order of over 95 per cent three years after surgery.<sup>14</sup> The short-term complications and risks of a hysterectomy are: bleeding, infection, damage to surrounding organs (such as the bowel or ureters), urinary retention, thromboembolism and wound/vault haematomas.

### Summary

The variety of therapies available to treat menorrhagia means that they can be tailored to suit the individual patient. Her need for contraception is important, as are her desires to retain future fertility. The patient must be involved in the decision-making process regarding the suitable treatment options, including any potential side-effects and complications.

The efficacy of nonsurgical techniques means that, particularly where there is no other pathology present, these should be tried in the first instance, before resorting to surgery.

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*Miss Mohan, Miss Page and Dr Rusman are specialist registrars in obstetrics and gynaecology and Professor Higham is reader in obstetrics and gynaecology at Imperial College, London*

## Resources

### Groups and organisations

Women's Health Concern, 4-6 Eton Place, Marlow, Buckinghamshire SL7 2QA. Website: [www.womens-health-concern.org](http://www.womens-health-concern.org); tel: 01628 478 473; telephone counselling 0845 123 2319 (Mon-Wed 10-12) and e-mail counselling: see website. A charitable organisation which aims to help educate and support women with their healthcare. The website provides a factsheet on menorrhagia and its treatment.

Royal College of Obstetricians and Gynaecologists, 27 Sussex Place, Regent's Park, London NW1 4RG. Website: [www.rcog.org.uk](http://www.rcog.org.uk); tel: 020 7772 6200.

### Websites

NICE patient information on heavy menstrual bleeding: [www.nice.org.uk/guidance/index.jsp?action=download&o=30406](http://www.nice.org.uk/guidance/index.jsp?action=download&o=30406).

Patient UK: [www.patient.co.uk](http://www.patient.co.uk) has sources of information and/or support.

Medical information for patients: [www.medinfo.co.uk/conditions/heavyperiods.html](http://www.medinfo.co.uk/conditions/heavyperiods.html) provides a brief overview of menorrhagia and its treatment as well as some sources of further information.

Ability: [www.ability.org/Menorrhagia.html](http://www.ability.org/Menorrhagia.html) has links to further sources of information on menorrhagia.

### Further reading

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