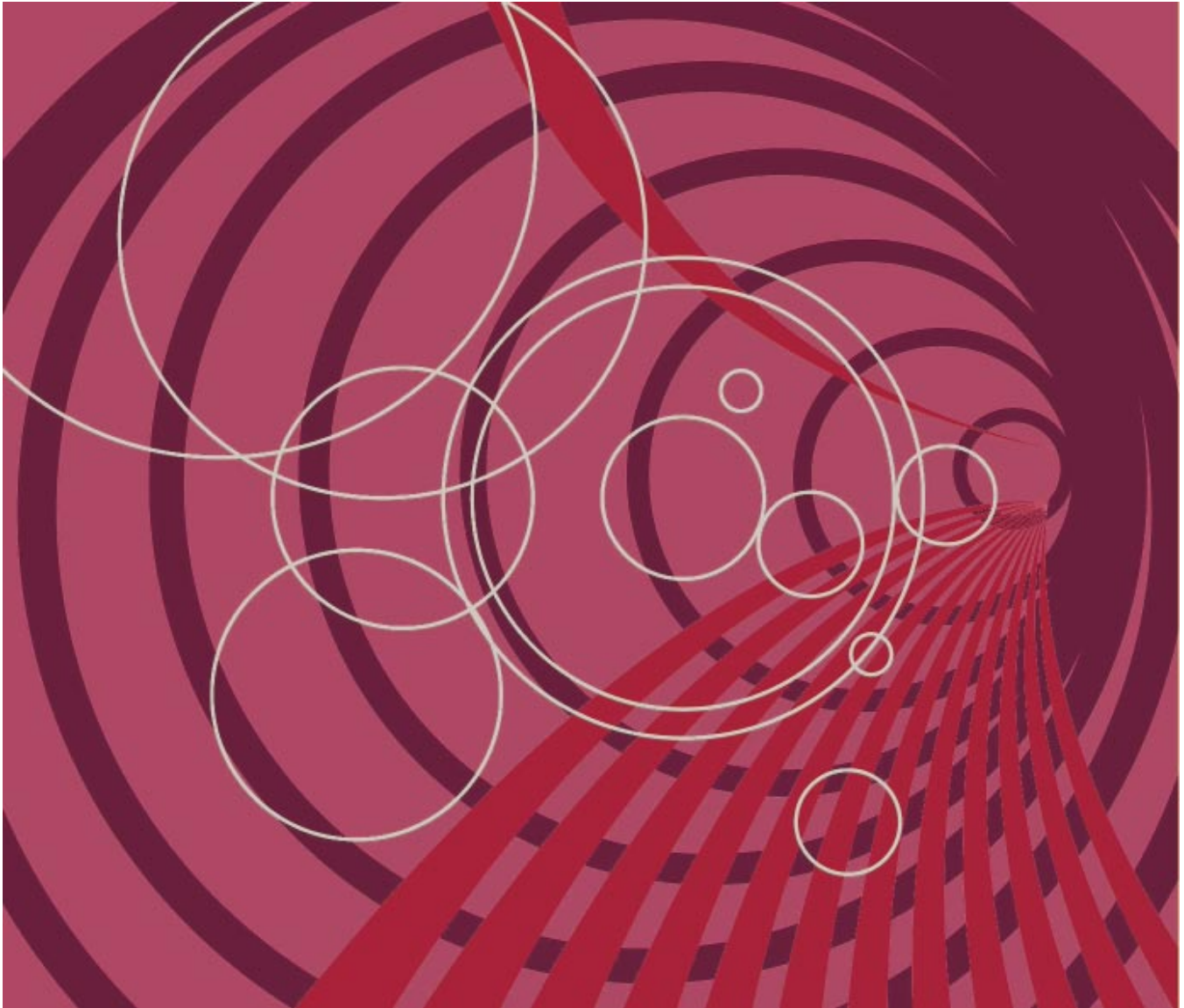

The Need for Proper Diagnosis and Treatment of Menorrhagia

by Michelle Warren, MD



Menorrhagia is a common and treatable medical condition that affects more than 10 million women annually. It is a major contributor to hysterectomy, accounting for about 20% of the more than 600,000 hysterectomies performed in the United States each year. Although hysterectomy is the best choice for some women with menorrhagia, many others are candidates for a variety of safe and effective treatment options.

Excessive menstrual bleeding arising from benign causes, known as menorrhagia, is one of the most common complaints encountered by gynecologists and primary care physicians.¹ It affects more than 10 million American women annually.² About 50% of those affected are in the 40 to 50 years³ of age group—otherwise known as the perimenopausal years. The most common reason for seeking treatment is that the patient notices a change in her normally reliable menstrual pattern and becomes concerned.¹

Menorrhagia, which is defined as regular, normal intervals of menstruation with excessive volume and duration of flow, is rarely life threatening. However, it may interfere with physical activity, work and sexual activity. In a study of 214 women, more than 70% reported that prior to treatment for menorrhagia, heavy bleeding had a severe impact on their quality of life, and 40% reported an inability to work outside the home during their menstrual period.⁴

A survey of 445 women conducted in 2000 showed similar results, with nearly half of those polled (44%) reporting that they had adjusted their lives to accommodate their period (including adjusting their personal life, work life, activities with children, or travel or vacation scheduling); 40% reported suffering an embarrassing moment because of heavy bleeding.⁵ Menorrhagia may progress to menometrorrhagia.

Menorrhagia is a major contributor to the high incidence of hysterectomies

performed among women in their later reproductive years. In fact, of the 600,000 hysterectomies performed annually in the United States, approximately 20% are performed to treat menorrhagia.^{6,7} Indeed, the highest proportion of hysterectomies are in women between the ages of 40 and 50 years. In addition, 40% of the approximately 555,000 dilation and curettage (D&C) procedures performed each year are for the purpose of alleviating heavy periods,⁸ but these procedures offer women only temporary relief at best. Because menorrhagia is so rarely discussed, few women may realize that the condition can be treated with minimally invasive options, making hysterectomy an extreme choice and D&C an ultimately ineffective one.

Causes of Menorrhagia

Menorrhagia can have hormonal or non-hormonal causes. Common nonhormonal causes include fibroids and polyps, which cause structural uterine bleeding. Infection of the uterus or cervix and cancer of the uterus, cervix or vagina also can cause excessive menstrual bleeding. Given the range of etiologies, it is critical that menorrhagia be properly diagnosed in order for it to be treated appropriately.

Normal menstrual bleeding caused by postovulatory estrogen-progesterone withdrawal is stable and precisely regulated.⁹ The normal menstrual cycle is so predictable that women come to expect a characteristic pattern of flow. Therefore, minor deviations in their expected use of sanitary napkins or tampons may cause women considerable concern.

The usual duration of menstrual flow is 4 to 6 days, but many women may have a flow for as little as 2 days or as many as 7 days.⁹ Normal menstruation also tends to be consistent in the amount of blood that is lost. The usual volume of menstrual blood loss is 30 ml; a menstrual flow greater than 80 ml is considered abnormal.^{9,10} The frequency and duration of menstrual flow are mostly stable during a woman's reproductive years, but they

commonly vary at the beginning and end of the reproductive years.¹¹ By age 25, more than 40% of cycles are 25 to 28 days in length; between the ages of 25 and 35, more than 60% of cycles are 25 to 28 days in length.⁹ The cycles begin to lengthen again when women enter their 40s, as perimenopause approaches.

Characteristics of Menorrhagia

Menorrhagia and menometrorrhagia are most commonly associated with perimenopause. Patients with the condition have lost cyclic endometrial stimulation that arises from the ovulatory cycle.³ As a result, these patients have constant, noncycling estrogen levels that stimulate endometrial growth. Proliferation without periodic shedding causes the endometrium to outgrow its blood supply. The tissue breaks down and sloughs from the uterus. Subsequent healing of the endometrium is irregular and dysynchronous. Chronic stimulation from high levels of estrogen leads to episodes of frequent, often irregular, heavy bleeding. In women with menorrhagia, menses may continue for more than 7 days, or blood loss of more than 60 to 80 ml in one menstrual cycle can occur, particularly in the presence of anatomic disruption of the endometrium, as with the presence of a polyp or a fibroid.^{1,9}

Single episodes of anovulatory bleeding generally carry a good prognosis.³ However, patients who experience repetitive episodes may experience significant consequences. For example, frequent uterine bleeding increases the risk for iron-deficiency anemia, with menorrhagia being the most common cause of anemia in perimenopausal women.¹² Menstrual bleeding can be so copious that patients require hospitalization for fluid management, transfusion or intravenous hormone therapy.

Diagnosis and Evaluation of Menorrhagia

Thorough evaluation is needed to identify the cause of abnormal uterine bleeding.

Definition of Terms

Menometrorrhagia: irregular or excessive bleeding during menstruation and between menstrual periods

Menorrhagia: excessive menstrual bleeding during menstrual periods

Metrorrhagia: irregular or excessive menstrual bleeding between menstrual periods

For women of all ages, it is crucial to rule out pregnancy as the cause of bleeding.

Among women of reproductive age, evaluation of abnormal uterine bleeding requires documentation of the severity and duration of the bleeding, its effects on the patient, contributing medical conditions and ascertainment of pregnancy status.¹ The cause of the bleeding often may be determined on the basis of history and physical examination. Hormonal assays should be directed toward specific disorders after a differential diagnosis has been established. Complications of pregnancy, including ectopic pregnancy, are common causes of bleeding in this age group.

Although organic causes of menometrorrhagia are possible, anovulation is the most common explanation. As a woman nears menopause, her cycles become increasingly anovulatory. In this age group, endometrial sampling is recommended on a routine basis. When anovulation cannot be clearly established as the cause of bleeding, diagnostic techniques, such as hysteroscopy or transvaginal ultrasonography, may be of benefit.

Endometrial sampling is often important in determining the diagnosis. Hysteroscopy is being used in the office with increasing frequency to diagnose polyps and submucous fibroids, whereas operative hysteroscopy with anesthesia often provides a means for therapeutic intervention.

Clinical Assessment of Bleeding

Clinical assessment of bleeding is essential, because subjective assessment of blood loss reported by the patient is often not an accurate reflection of measured menstrual loss.¹² Because only 38% of women with subjective complaints of menorrhagia actually suffer from excessive blood loss (defined as more than 80 ml per menstrual cycle), a careful history concerning the clinical features of menstrual flow and restriction of daily activities must be reviewed for each patient.¹³

Since it is essentially impossible to

determine the amount of blood loss in practice, the investigation of excessive uterine bleeding should include many avenues. The reported usage of more than 10 pads or tampons per day is considered abnormal, and although this is often inaccurate, it is generally an easy method for documenting the bleeding history. A clue to excessive bleeding is the passage of blood clots, as excessive volume of bleeding overwhelms the fibrinolytic mechanisms that normally function in the uterine cavity. A complete blood count can indicate anemia by showing abnormally low serum hemoglobin and ferritin levels,¹⁴ thus confirming heavy bleeding. In addition to bleeding history, a complete medication and contraceptive history should be taken, including self-reported use of hormonal contraceptives, intrauterine devices, hormonal medications, anticoagulants and aspirin, since these therapies can be associated with abnormal bleeding.¹⁵

Evaluation for Hormonal Perimenopause

Anovulation resulting from altered neuroendocrine and/or ovarian hormonal events is the main cause of dysfunctional uterine bleeding (DUB). During perimenopause, the variability of intermenstrual interval is increased, and on average, the length of the menstrual cycle is significantly shorter.¹⁶ With the decreased progesterone secretion and the duration of the luteal phase combined with an erratic secretion of estradiol apparent in the perimenopause, DUB can result. Perimenopause is associated with low levels of estradiol but may be followed intermittently by extremely high levels. Overgrowth of the endometrium caused by estrogen stimulation without the antiproliferation may lead to erratic shedding and heavy bleeding with menses. Anovulation also may be associated with thyroid or prolactin disorders, and age is directly related to the incidence of hypothyroidism. The sensitivity of the tests plays a large role in establishing the diagnosis of

hypothyroidism.¹⁷ High-sensitivity thyrotropin-releasing hormone (TRH) measurement is usually diagnostic. Thyroid replacement therapy is a common treatment, and the abnormal bleeding usually resolves in 3 to 6 months.¹⁸

Evaluation for perimenopause is vital, although it is often unreliable and difficult. The evaluation is done through a combination of age, history and menopausal symptoms. According to a study of several hundred women who had kept accurate records of their menstrual flow, the median age at entry into the menopausal transition is approximately 45.5 years.¹⁹ Symptoms include frequent hot flashes, sleep disturbances, decrease in sex drive, depression or mood changes, and migraines.²⁰ In addition, during perimenopause, unusual hormone patterns can be seen. Elevated follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels have been evident in perimenopausal women, particularly early in the cycle. Furthermore, although not consistently reliable, a FSH level greater than 30 mIU/ml taken between days 3 and 5 of the menstrual cycle will confirm early changes of menopause. Testing between days 3 and 5 is commonly done in infertility evaluations; however, false negatives are common.

Evaluation for Structural Abnormalities

As mentioned above, menorrhagia may also result from structural abnormalities in the uterus. In women with uterine fibroids, the most common cause of increased uterine bleeding,²¹ it is important to perform an endometrial biopsy to rule out hyperplasia or precancerous changes of the endometrium. Structural abnormalities such as fibroids, hyperplasia and polyps can be evaluated with a pelvic sonogram. Adenomyosis also may cause bleeding, usually accompanied by dysmenorrhea, and may necessitate an MRI as well as a sonogram. An endometrial biopsy involves a simple office procedure in which a thin instrument is placed into the uterine cavity through the cervix, and

a small sample of endometrium is obtained for analysis. However, in the event of inconclusive or inadequate sampling, D&C may be necessary.

Because there are many possible causes of abnormal uterine bleeding, selective diagnostic laboratory tests may be used in addition to the physical exam to help determine the cause and objectively assess severity. A pelvic sonogram done with a vaginal probe may be recommended to help rule in or out anatomic causes of abnormal bleeding. This exam can help identify abnormalities of the reproductive organs and provide valuable information regarding size, shape, location and consistency of problem areas.

Alternatively, sonohysterography now provides an additional tool for the evaluation of the uterus. This involves instilling a small amount of an electrolyte solution through the vagina into the uterus via a thin catheter while simultaneously performing transvaginal ultrasound.²² In addition to ultrasound, MRI, with its superior definition of soft-tissue structures, can be an added valuable tool for the evaluation of uterine bleeding.^{23,24}

Treatment of Menorrhagia

The goals of menorrhagia treatment are to enable the patient to have a normal lifestyle, maintain an adequate hemoglobin level, relieve symptoms until the onset of menopause, control acute bleeding, prevent future abnormal bleeding and minimize the risk of endometrial cancer, which is increased in association with long-term anovulation.²⁵ In choosing the appropriate treatment for an individual patient, the cause of the bleeding, the patient's desired outcome and the desire to maintain fertility, if so desired, should be considered.

Guidelines issued by the American College of Obstetricians and Gynecologists (ACOG) recommend a treatment path for menorrhagia that begins with the least invasive therapy.¹ If there is no evidence of neoplasia, nonsurgical therapy should be the first step in management. If medical therapy is ineffective or inappro-

priate, treatment options progress to endometrial ablation or surgical removal of the uterus via hysterectomy.²⁶ The widespread availability of office endometrial sampling, office hysteroscopy and surgical hysteroscopy has markedly decreased the indications for D&C. Because menorrhagia associated with perimenopause often has an endocrine basis, D&C is rarely effective as a therapeutic procedure.

Hormone Therapy

If anovulation is the reason for menorrhagia, cyclic estrogen-progestin medications or cyclic progestin therapy may decrease the amount of menstrual flow.

Oral contraceptive pills containing estrogen and progestin have been advocated for nonsmoking patients with menorrhagia who desire contraception.³ Oral contraceptives suppress endometrial development, re-establish predictable bleeding patterns, decrease menstrual flow and lower the risk of iron-deficiency anemia. Acute episodes of heavy bleeding suggest an environment of prolonged estrogenic exposure and build-up of the endometrial lining. Bleeding usually is controlled within the first 24 hours, as the overgrown endometrium becomes pseudo-decidualized. An alternate diagnosis should be sought if flow fails to abate in 24 hours.

Estrogen alone, in high doses, is indicated in certain clinical situations. Estrogens are very effective in controlling acute, profuse bleeding. Estrogen exerts a vasospastic action on capillary bleeding by affecting the level of fibrinogen, factor IV and factor X in blood, as well as platelet aggregation and capillary permeability. Estrogen also induces the formation of progesterone receptors, making subsequent treatment with progestins more effective. However, estrogen therapy only controls bleeding acutely and does not treat the underlying cause.

Progestins are commonly administered for the treatment of menorrhagia.²⁷ They may be administered cyclically (usually

on a monthly schedule), continuously or locally through progestin-impregnated IUDs. Occasional anovulatory bleeding that is not profuse or prolonged can be treated with progestins.³ Synthetic progestins have an antimitotic effect, allowing the endometrium to become atrophic if administered continuously. Some perimenopausal patients will not respond well to progestin therapy because of an inherent estrogen deficiency. Also, patients in whom thinning and denuding of the endometrium occurs after several days of chronic bleeding might require induction of new endometrial proliferation by estrogen therapy first.

Minimally Invasive Options

Since the 1970s, treatment of menorrhagia with hysteroscopic endometrial ablation (the destruction of the lining of the uterus) has been reported as a viable alternative to hysterectomy in terms of cost-effectiveness and patient acceptance.^{1,3,28} Ablation procedures are more conservative than hysterectomy and result in a shorter recovery time for the patient.

The early techniques of endometrial ablation used a hysteroscope with an attachment to destroy the tissue.²⁹ These techniques require specialized training and surgical expertise and involve a significant learning curve. The first hysteroscope ablative techniques employed the Nd:YAG laser. In clinical practice, however, electrosurgical techniques of hysteroscopic endometrial ablation have superseded the laser technique. Electrosurgical techniques include rollerball coagulation, resection with a loop electrode and electrosurgical vaporization.

Traditional hysteroscopic endometrial ablation techniques that utilize electrosurgical or laser ablative sources can effectively control abnormal bleeding in 85 to 90% of menorrhagia cases.^{1,6}

A newer hysteroscopic technique, known as hydrothermablation, involves the use of heated free fluid. The procedure requires that the hysteroscope be inserted to visualize the endometrial cav-

ity during the procedure. One such device, the Hydro ThermAblator® (BEI Medical Systems, Inc.), is approved by the U.S. Food and Drug Administration (FDA) for clinical use. It delivers hot saline solution into the uterus through a tube inserted into the cervix. The hot water destroys the uterine lining in about 10 minutes. Initial 2-year follow-up data presented at the 30th annual American Association of Gynecological Laparoscopists' Global Congress of Gynecologic Endoscopy in November 2001 indicated that 91.8% of patients treated with the Hydro ThermAblator had normal or no bleeding after the procedure.

In recent years, nonhysteroscopic techniques for endometrial ablation have been approved by the Food and Drug Administration. They are easy for physicians to perform and do not require intensive, specialized training. In 1997, the FDA approved the GYNECARE THERMA-CHOICE Uterine Balloon Therapy System (ETHICON), the first nonhysteroscopic ablation device to treat menorrhagia resulting from benign causes. Because uterine balloon therapy obviates the need for hysteroscopy, it requires less training and poses less risk of intraoperative complications.^{6,28} It also can be performed under local anesthesia and in less time than traditional hysteroscopic ablation techniques. A balloon catheter is inserted into the uterus. The balloon is inflated with a small amount of sterile fluid that is heated for 8 minutes to break down the uterine lining. When the treatment cycle is completed, the heated fluid is withdrawn from the balloon back into the catheter, and the catheter is removed from the uterus. The uterine lining sloughs off over the next 7 to 10 days. Women typically return to normal activity the day after treatment.

More than 100,000 women worldwide have been treated with uterine balloon therapy. Studies performed to date suggest that uterine balloon therapy is as effective as commonly employed rollerball ablation and may be safer.

A recent long-term study demonstrated that uterine balloon therapy is a successful method for treating menorrhagia, avoiding hysterectomy, decreasing dysmenorrhea and premenstrual symptoms, and improving quality of life.⁴ The 3-year study followed 214 women who underwent treatment with either the THERMACHOICE Uterine Balloon Therapy System or the older rollerball ablation method. The comparable results in the two treatment groups demonstrated that balloon therapy is as effective as rollerball ablation. Women treated with the balloon therapy experienced a significant improvement in their condition at 3-year follow-up: 86% reported normal or no bleeding without additional treatment; more than 95% remained satisfied with treatment; and fewer than 2% said bleeding still had a major impact on their lives.

Cryotherapeutic endometrial ablative techniques are currently undergoing investigation. One device, the Her Option™ Uterine Cryoablation Therapy™ System (CryoGen, Inc.), was approved by the FDA for clinical use in April 2001. It uses a probe capable of producing temperatures of minus 148° F at the tip. This extreme cold is applied to the tissue for 10 minutes to freeze and destroy the uterine lining. Ultrasound is used to guide and monitor the procedure. Initial clinical data presented at the time of FDA approval suggest that 74% of patients treated with cryoablation had normal or no bleeding following the procedure.³⁰

Other approaches to endometrial ablation currently under investigation include using other energy sources, such as ultrahigh radiofrequency alternating current, electrodes, microwave energy, lasers and photosensitizing agents.^{1,28}

Approaches to Structural Abnormalities

Hysteroscopic treatment offers a minimally invasive option for dealing with structural abnormalities.³¹ The morcellation of fibroids and polyps can be accomplished during operative hysteroscopy.

This procedure involves a hysteroscope that has channels through which very thin instruments can be inserted. These instruments can be used to perform a variety of procedures, including the removal of polyps or severing of adhesions. In a recent study comparing pre- and postmenopausal women, hysteroscopic surgery was found to be an effective and safe therapeutic option for intrauterine lesions regardless of menopausal status.³² Additionally, hysteroscopic treatment of fibroids appears to be safe, efficacious and cost-effective.³³

Treatment of uterine fibroids and other structural abnormalities has progressed in the past decade so that a hysterectomy is not the only option. A growing number of reports indicate that uterine fibroids can be effectively treated with uterine artery embolization (UAE). This is a radiologic procedure that uses angiography for visualization of the blood circulation.³⁴ Essentially, the flow through the uterine arteries is stopped, cutting off blood supply to the tissue and causing the tissue to break down and be reabsorbed by the body. Recent studies have shown high success rates using UAE in the treatment of symptomatic uterine fibroids, and major complications are rare.³⁵

As with any medical procedure, there are some expected minor discomforts to the patient. For example, most patients experience moderate to severe pain and cramping in the first several hours following the procedure, and some experience nausea and/or fever. Medications are usually effective in treating these symptoms, and most patients are substantially improved by the next morning. In a few cases, pain and cramping may last for several days or more. Possible serious complications include injury to the uterus from decreased blood supply or infection. Serious complications are uncommon, however, and the procedure is generally considered very safe.

Considerations Regarding Hysterectomy

Abdominal or vaginal hysterectomy may

be necessary in patients who have failed or declined hormonal therapy, have symptomatic anemia or have experienced a disruption in their quality of life from persistent, unscheduled bleeding.³

The economic implications of hysterectomy are significant. Recent studies have shown that in the United States, the average cost per surgery for all types of hysterectomies is \$9,223.²⁷ This translates to an annual cost of more than \$5.5 billion. Hysterectomy poses a greater cost burden than ablation therapy to payers, providers and patients, because a hysterectomy requires approximately 4 days of hospitalization, higher rates of surgical risks, potential complications and a 3- to 6-week recovery period.³⁴ In contrast, ablation procedures require an average length of stay of less than 1 day, and recovery can take as little as 1 day.²⁶ When endometrial ablation is performed instead of hysterectomy for menorrhagia, when appropriate, an average per-case cost savings of approximately \$4,300 is possible.

Conclusions

Although menorrhagia is a very common condition, many women are unaware that heavy periods represent a treatable medical condition. Others are too embarrassed to seek treatment. Open dialogue between physicians and patients about excessive menstrual bleeding and other perimenopausal changes is essential, because it can lead to an appropriate diagnosis, and ensure that patients receive proper treatment.

With abnormal bleeding, desired outcomes vary. Some women desire no period, some want a predictable period, some want to slow the bleeding, some want to maintain fertility and some are more concerned about reducing pain than reducing volume of flow.²⁸ Women with menorrhagia need to be made aware that several minimally invasive treatments are available and that these treatments are associated with fewer side effects and complications, faster recovery and less ex-

pense than hysterectomy. While hysterectomy may be the best choice for some women, endometrial ablation may be more appropriate for many others. ■

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