Clinical Expert Series CME

Primary Dysmenorrhea

Diagnosis and Therapy

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Primary dysmenorrhea is defined as pain during the menstrual cycle in the absence of an identifiable cause. It is one of the most common causes of pelvic pain in women. Dysmenorrhea can negatively affect a woman's quality of life and interfere with daily activities. The pathophysiology of primary dysmenorrhea is likely a result of the cyclooxygenase pathway producing increased prostanoids, particularly prostaglandins (PGs). The increased PGs cause uterine contractions that restrict blood flow and lead to the production of anaerobic metabolites that stimulate pain receptors. Women with a history typical for primary dysmenorrhea can initiate empiric treatment without additional testing. Shared decision making is key to effective management of dysmenorrhea to maximize patient compliance and satisfaction. After a discussion of their risks and benefits, extremely effective empiric therapies are nonsteroidal antiinflammatory drugs and contraceptive hormonal therapy. Other treatments for primary dysmenorrhea can be employed solely or in combination with other modalities, but the literature supporting their use is not as convincing. The physician should initiate an evaluation for secondary dysmenorrhea if the patient does not report improved symptomatology after being compliant with their medical regimen.

(Obstet Gynecol 2020;136:1047–58)
DOI: 10.1097/AOG.0000000000004096

Dysmenorrhea, defined as painful menstruation, is the most common gynecologic condition affecting women. Reported prevalence varies widely, ranging from 17% to as high as 90%.[1,2] Some women experience relatively minimal pain, whereas others are significantly limited in their ability to function during their menses. Of all menstrual-related symptoms, lower abdominal and back pain are the symptoms most strongly associated with absences from or decreased efficacy at work and school. Up to 15% of women with dysmenorrhea experience symptoms of sufficient severity to cause absenteeism from work, school, and other activities.[2,3] Flexibility in hours or the ability to work from home may mitigate this problem, but, even for those women who do not miss work or school for menstrual-related symptoms, the reduced focus and productivity associated with those symptoms negatively affect performance.[4] An estimated 600 million hours or $2 billion annually is lost in the United States secondary to missed work or reduced functional abilities due to menstrual pain and associated symptomatology.[5] Lack of access to menstrual hygiene products may also contribute to absenteeism and reduced efficacy at work or school. However, the role of access to needed resources has not been explicitly explored in available literature on the effect of menstruation on performance. Future research to distinguish between absences based on menstrual symptoms and absences based on unmet product needs would further help to guide policy.[6] Dysmenorrhea is often underreported and undertreated, and adequate management of dysmenorrhea will improve overall quality of life as well as alleviate financial and academic burdens for many women.[7]

Dysmenorrhea is classified as primary or secondary based on whether or not an underlying etiology is

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Each author has confirmed compliance with the journal's requirements for authorship.

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Financial Disclosure
The authors did not report any potential conflicts of interest.

ISSN: 0029-7844/20

identified.[8] Primary dysmenorrhea is pain with menses for which there is no underlying abnormality, whereas secondary dysmenorrhea is pain associated with conditions such as endometriosis, pelvic inflammatory disease, leiomyomas, and interstitial cystitis.[9] Treatment of secondary dysmenorrhea focuses on the causative pelvic pathology or medical condition. Primary dysmenorrhea accounts for the majority of painful menses in ovulatory women. This review will focus on the pathophysiology and treatment options for primary dysmenorrhea.

DIAGNOSIS

Primary dysmenorrhea presents at the onset of ovulatory cycles, which is usually within 6–12 months of menarche but can be as long as 2 years after menarche in some adolescents. Its prevalence decreases with increasing age in a large percentage of sufferers.[3,8] Patients describe pain that is crampy and of fluctuating intensity, with the onset of pain shortly before or at the onset of bleeding and lasting up to 72 hours. The pain is located in the suprapubic region and can radiate to the upper thigh or back or both. Pain intensity usually peaks at 24–36 hours from the onset of menses, and the duration is rarely longer than a few days.[1] Additional symptoms include nausea, vomiting, bloating, and diarrhea. Risk factors for dysmenorrhea, which is typically identified as primary rather than secondary in adult study participants based on history, normal examination findings, and absence of other known causes for menstrual pain, include the following: age younger than 30 years, body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) less than 20, smoking, menarche at younger than 12 years, longer menstrual cycles or duration of bleeding, irregular or heavy menstrual flow, a history of sexual assault, and a family history of dysmenorrhea.[8,9] The prevalence of moderate to severe primary dysmenorrhea generally decreases as women age, and childbirth is associated with a reduction in the prevalence and severity of primary dysmenorrhea. Improvements are not seen in women who experienced pregnancies that ended in miscarriage or abortion.[10]

A physical examination revealing a normal-sized, mobile, nontender uterus and the absence of mucopurulent discharge, uterosacral nodularity, or an adnexal mass is consistent with primary dysmenorrhea.[9] No specific test is available to make the diagnosis, but patients with the classic presentation (Box 1) are candidates for empiric therapy. A pelvic examination is not necessary to initiate treatment in an adolescent with a classic history of primary dysmenorrhea.[8] As such, initial treatment is amenable to telehealth platforms and does not need to be delayed if a face-to-face visit is inconvenient for the patient or otherwise impossible to arrange (eg, during periods of reduced office hours related to contagion-containment strategies). An atypical presentation, abnormal physical examination findings, or lack of improvement with medical therapy should prompt evaluation for causes of secondary amenorrhea. A pelvic examination and radiologic testing, such as abdominal or transvaginal ultrasound scan, should be performed for a patient whose symptoms do not respond to empiric therapy. Surgical evaluation may be warranted based on the findings or clinical suspicion.

PATHOPHYSIOLOGY

Primary dysmenorrhea appears to be the result of increased prostanoid secretion by way of the cyclooxygenase pathway.[3] The prostanoid class include prostaglandins (PGs), thromboxanes, and prostacyclins. Ovulatory progesterone levels stabilize cellular lysosomes, but, at the end of the luteal phase when progesterone levels decline, lysosomes break down and release phospholipase A2.[3] This explains why the pain of dysmenorrhea begins with ovulatory cycles and not with anovulatory early menses. This enzyme starts the cyclooxygenase pathway with resultant prostanoid production (Fig. 1). Prostaglandins are a group of lipid compounds that are involved in multiple physiologic and pathologic conditions in the body. There are nine classes of PGs, but $PGF_{2\alpha}$ and PGE_2 are the major culprits involved with primary dysmenorrhea.[3] Not only does $PGF_{2\alpha}$ cause uterine contractions that restrict blood flow, but it is also directly involved in arcuate vessel constriction. Both mechanisms of action produce hypoxia that leads to the accumulation of anaerobic metabolites that

Box 1. Classic Symptoms of Primary Dysmenorrhea

1. Menstrual pain began within a few months or within 2 y of menarche
2. Pain starts right before menstruation or at onset of menstruation
3. Pain is lower abdominal and can radiate to back, inner thighs, or both
4. Pain seldom lasts more than 72 h
5. Pain is episodic and crampy in nature
6. Pain is similar from one menstrual cycle to the next
7. Additional symptoms: nausea and vomiting, fatigue, headaches, dizziness, and sleep disturbances

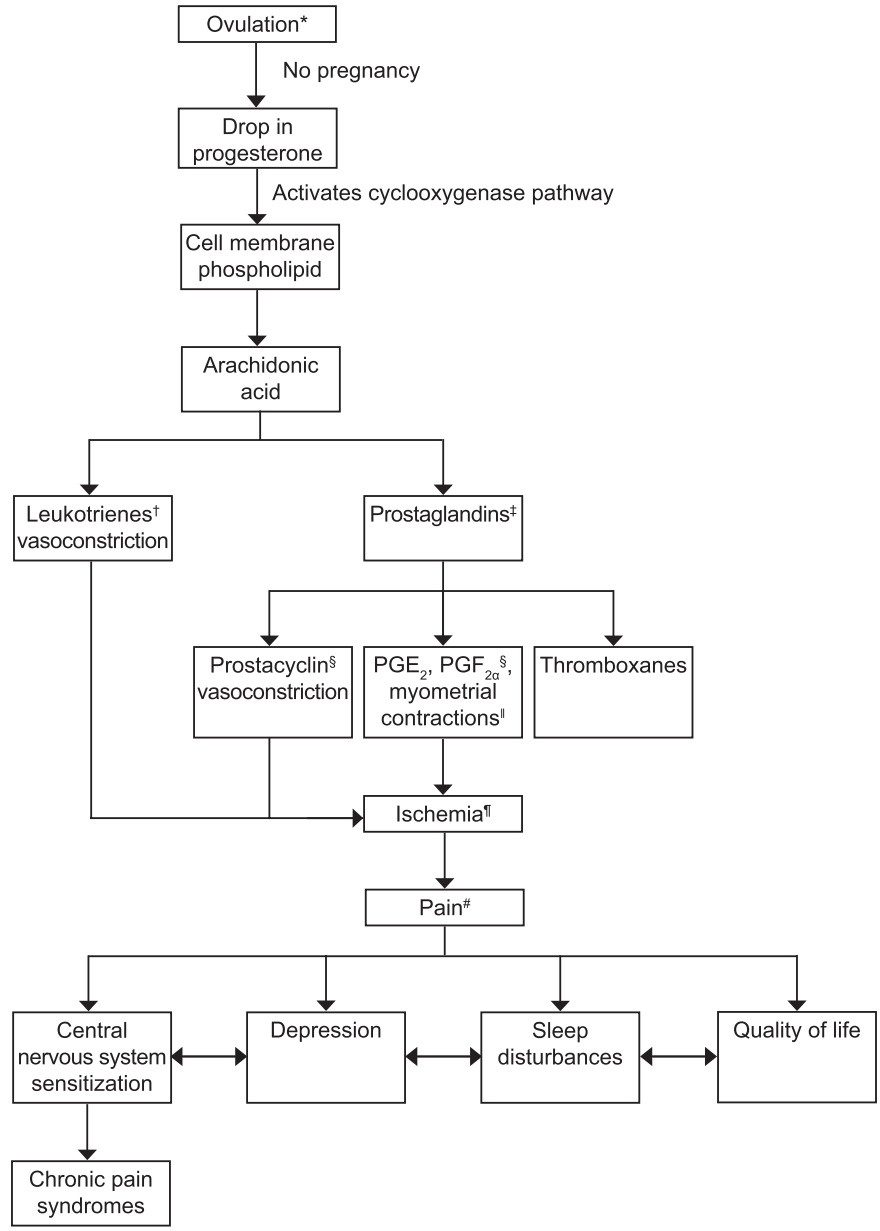

Fig. 1. Pain pathways in primary dysmenorrhea and pharmacologic interventions. *Hormonal contraception. †Meclofenamate, magnesium, ginger, acupressure, acupuncture. ‡Nonsteroidal antiinflammatory drugs (NSAIDs), vitamin E, ginger, acupuncture, acupressure. §Vitamin E, high-frequency transcutaneous electrical nerve stimulator (hfTENS), exercise. ‖Nitric oxide, magnesium, calcium channel blocker, exercise. ¶Heat. #hfTENS, NSAIDs.

Ferries-Rowe. Primary Dysmenorrhea: Diagnosis and Therapy. Obstet Gynecol 2020.

stimulate pain receptors. Prostaglandin $F_{2\alpha}$ also lowers the threshold for pain perception by sensitizing these same nerve receptors. Prostaglandin E_2 has dual mechanisms of action depending on receptor interaction, causing either myometrial contraction or relaxation and uterine vessel constriction or dilation.[7] The peak hours of menstrual pain correlate with the highest levels of PGs.[5] Accompanying gastrointestinal symptoms are also a recognized consequence of PGs.

Elevated concentrations of $PGF_{2\alpha}$ have been found in the menstrual fluid of women with primary dysmenorrhea when compared with women who are eumenorrheic. In addition, the intensity of the pain appears to be proportional to the amount of $PGF_{2\alpha}$ present.[3] Certain leukotrienes, specifically leukotrienes C4 and D4, are also found to be elevated in women with primary dysmenorrhea compared with women who are eumenorrheic and are believed to contribute to this abnormally increased uterine contractility.[3] Additionally, Akerlund reported his findings that elevated serum vasopressin results in vasoconstriction and pathologic uterine contractions. His work also found that the concentration of vasopressin $V_{1\alpha}$ receptors is highest in the premenstrual period.[11] Although not available in the United States, Atosiban is a medication that blocks these receptors

and has been found to reduce the pain of primary dysmenorrhea. Reduction in pain caused by blocking the effect of vasopressin implicates vasopressin as one mediator of pain in primary dysmenorrhea.[11] However, these results were not reproduced in another study, and the role of vasopressin in primary dysmenorrhea remains controversial.[12]

In studies assessing uterine basal tone, contraction pressures, and contraction patterns during menses in women with and without dysmenorrhea, women with primary dysmenorrhea have increased basal tone, increased active pressure during menstrual contractions, and more frequent and more poorly coordinated uterine contractions. Contractions of the uterus are associated with temporary lack of perfusion; increased basal tone and poorly coordinated contractions are hypothesized to reduce uterine reperfusion in symptomatic as compared with asymptomatic women. This combination results in hypoxia and associated pain.[13]

In addition to local inflammatory abnormalities that cause pathologic changes in uterine pressure and vasoconstriction, there appears to be altered pain sensitivity in women with primary dysmenorrhea.[5] In 1944, the first study was published that implicated hyperresponsiveness to pain in women suffering from primary dysmenorrhea.[5] Though additional studies have not consistently revealed this abnormality, overall it appears that this condition should be included in central sensitization syndrome.[5] These syndromes are associated with pain hypersensitivity without recognized tissue injury, inflammation, or nervous system lesion.[7] Central sensitization syndrome is characterized by both allodynia and hyperalgesia. Central sensitization syndrome includes multiple disorders such as irritable bowel syndrome, low back pain, and tension headaches and occurs when the central nervous system amplifies sensory input so the patient has more pain with less provocation. The hyperalgesia associated with primary dysmenorrhea can contribute to "viscero-visceral hyperalgesia," a condition in which painful input from one visceral domain increases the excitability of convergent visceral neurons in the spinal cord and increases the likelihood of pain in other visceral locations (eg, urinary tract, bowels, or abdominal and lumbar musculature). Central sensitization syndrome is also associated with a history of childhood sexual abuse, which likely explains the recognized association between a history of sexual abuse and dysmenorrhea.[14,15] Because central sensitization syndrome can increase the risk of developing a chronic pain syndrome, it behooves the practitioner to aggressively diagnose and adequately treat primary dysmenorrhea to prevent further medical sequelae.[5]

TREATMENT OPTIONS

Treatment options for primary dysmenorrhea aim to interfere with the production of PGs, reduce uterine tone, or inhibit the perception of pain through direct analgesic effect. Shared decision making between the patient, the health care professional, and potentially the patient's family (eg, for adolescents) that incorporates the anticipated efficacy of treatment, potential side effects, ease of use, and patient preference will be key to successful therapy and compliance. Because primary dysmenorrhea presents in adolescents and often continues well into adulthood, various treatment options may be more or less appropriate for a given patient based on stage of life. These considerations should also be included in the process of shared decision making.

Hormonal

- Combined hormonal contraceptives are effective for the treatment of dysmenorrhea in approximately 70–80% of women.[16] Inhibiting ovulation and preventing endometrial proliferation will decrease PG, progesterone, and vasopressin production. There is evidence of improvement in dysmenorrhea with the combined oral contraceptive pill (OCP), the contraceptive intravaginal ring, and the patch.[16–18] Extended-use OCPs may be more effective than cyclic use.[19] The major concern with OCPs is the risk of deep vein thrombosis (DVT). There is one additional DVT per 1,000 women when on combined OCPs, with higher risk observed in the first 6–12 months of use and in users older than 40 years.[20] On an individual level, this low risk can be decreased if the patient refrains from smoking.[21] In addition to the known thrombotic effects of estrogen, the type of progestin may affect DVT risk, though data are limited and conflicting.[22–26] The risk may be lower with a second-generation progestin (ie, norgestrel or levonorgestrel) compared with a third-generation progestin.[27] The risk with drospirenone may be even higher, though data are inconclusive[21,28,29] (Appendix 1, available online at http://links.lww.com/AOG/C64)
- Progesterone-only methods of contraception also appear to be effective treatments for primary dysmenorrhea. Croxatto et al showed that the etonogestrel (68 mg) contraceptive implant improved dysmenorrhea in 85% of users.[30] Unfortunately, data are limited for other forms of progesterone-only contraceptives, but they remain options because they inhibit ovulation and eliminate menstrual cycles. Depot medroxyprogesterone acetate

(DMPA), progesterone-only contraceptive pills, and the levonorgestrel intrauterine device (IUD) likely improve symptoms through this mechanism.[1,16] Approximately 50% of DMPA users and 20% of women with the levonorgestrel IUD are amenorrheic at 1 year of use[31,32] Additional side effects such as weight gain are commonly reported with DMPA, but the etonogestrel contraceptive implant has not been shown to cause weight changes in long-term studies.[33] Progesterone-only contraceptives also have a lower incidence of DVT when compared with combined hormonal contraceptives (Appendix 1, http://links.lww.com/AOG/C64). Although irregular bleeding is common with progesterone-only options, it is typically not associated with ovulatory cycles and thus not associated with menstrual pain in patients with primary dysmenorrhea. Depot medroxyprogesterone acetate has been associated with loss of bone mineral density, which appears to recover after discontinuation. The future fracture risk for patients using DMPA in adolescence is unknown. Shared decision making should include a discussion of this finding, but its use is not contraindicated if the benefits for primary dysmenorrhea and potentially contraception best meet a patient's needs.[34]

Nonhormonal

- Nonsteroidal antiinflammatory drugs (NSAIDs) are considered first-line treatment for primary dysmenorrhea, and they provide effective pain relief for the vast majority of women.[1,35] They work by two mechanisms. They interrupt cyclooxygenase activity and suppress PG production. Reduced levels of endometrial PGs are associated with a return to normal uterine contractility patterns and improvement in menstrual pain.[1] Nonsteroidal antiinflammatory drugs have the additional benefit of direct analgesic activity at the level of the central nervous system. Side effects, which may include gastrointestinal symptoms, nephrotoxicity, hematologic abnormalities, and edema, are infrequent in healthy young women using short courses of NSAIDs (72 hours or less) for treatment of dysmenorrhea. There is limited evidence that any one NSAID is superior to another, so cost considerations, side-effect profiles, and dosing regimen are reasonable considerations when deciding which medication to use.[36,37] A network meta-analysis of 70 studies that ranked NSAIDs by their relative efficacy as well as their side-effect and safety profiles in women with dysmenorrhea reported that flurbiprofen and tiaprofenic acid were the most optimal NSAIDs, though the latter medication is not available in the United States.[36] The more expensive COX-2 inhibitor celecoxib should be reserved for those women who have a history of peptic ulcer disease, coagulation abnormalities, and gastrointestinal side effects with other NSAIDs.[38]
- Nonsteroidal antiinflammatory drugs should not be taken on an as-needed basis but should be on a scheduled dosing regimen and can even be started 1–2 days before menses onset[39] (Table 1). Women report improved pain scores when they follow a regimen of a higher loading NSAID dose and then use a lower scheduled amount over a traditional same-dose regimen.[38] The prescriber should emphasize the dosing regimen, because studies have shown that only one third of young women take the recommended daily dosage and wait an average of 30 minutes from the onset of pain to take their medication.[40] Patients might require a note for the school nurse to ensure that they do not miss any medication while in class.

Note that standard formulations or dosing regimens do not exist for the following non-NSAID treatment options, and their use as treatment for dysmenorrhea is off-label.

- Because nitric oxide produces smooth muscle relaxation, medications that increase levels of nitric oxide may reduce the pathologic uterine contractions responsible for dysmenorrhea.[35] In addition, there is reduced nitric oxide production when progesterone levels decrease.[36] Glyceryl trinitrate patches (0.1 mg) have produced improvement in menstrual pain for as many as 90% of women and are significantly more effective than placebo.[41–43] However, up to a quarter of patients treated with glyceryl trinitrate experienced treatment-limiting headaches, so this medication is typically not a first-line treatment option for menstrual pain.[43]
- Magnesium reduces menstrual fluid $PGF_{2\alpha}$, is a muscle relaxant, and causes vasodilation. Several studies have shown that magnesium provides pain relief superior to placebo, but formulations and dosages varied widely among the studies. Inadequate information is currently available to solely recommend magnesium therapy.[44]
- Calcium channel blockers produce muscle relaxation. Nifedipine (20–40 mg) relieves the pain of primary dysmenorrhea, likely through reduction of uterine contractions. Nifedipine was also shown to decrease uterine PG production in a rodent model.[45] Side effects included transient flushing and increased heart rate (on average 20 beats

Table 1. Scheduled Use of Nonsteroidal Antiinflammatory Drugs: Loading Doses and Dosing Regimen

Drug	Dosage	Cost*
COX-1 and COX-2 inhibitors		
Flurbiprofen	100 mg every 12 h or 50 mg every 8 h	$$
Tiaprofenic acid†	200 mg every 4 h	
Piroxicam	20–40 mg daily for 2 d, then 20 mg daily	$$
Mefenamic acid	500 mg, then 250 mg every 6 h	$$$$
Ibuprofen	800 mg, then 400–800 mg every 8 h	$
Naproxen sodium	440–550 mg, then 220–550 mg every 12 h‡	$
Meclofenamate	100 mg every 8 h	$$$$
Diclofenac	50 mg every 8 h	$$$
COX-2 inhibitors		
Celecoxib§	400 mg initially, then 200 mg every 12 h	$$$

* Medication expense depends on insurers formularies and patient out-of-pocket costs.
† Not available in the United States.
‡ Naproxen sodium 220 mg available over the counter.
§ U.S. Food and Drug Administration–approved for primary dysmenorrhea only in women older than 18 years.

per minute), and the higher dose (30–40 mg) was associated with a slight headache.

- Vitamin E may have beneficial effects in the treatment of primary dysmenorrhea.[46] Several small studies have found that vitamin E (200–400 international units) significantly reduced dysmenorrhea.[47] A Cochrane Review, however, did not find any high-quality evidence for its efficacy and concluded that additional studies are needed.[48] Mice studies exploring the efficacy of vitamin E suggest that production of prostanoid vasodilators is increased and cyclooxygenase activity is inhibited, with subsequent reduction in PG production.[49] The combination of increased vasodilator production and decreased PG production results in increased oxygen delivery to myometrial cells. This increased oxygenation is believed to be responsible for menstrual pain improvement.[3]
- Ginger has been used for multiple diseases over the past 2,500 years and inhibits cyclooxygenase as well as lipoxygenase activity.[50] A study involving 50 women with moderate to severe primary dysmenorrhea showed further improved pain scores when one dose of 500 mg of ginger was added to a standard regimen of mefenamic acid 250 mg twice a day.[50] Additional studies evaluating ginger alone have used 750–2,000 mg daily doses and have shown menstrual pain improvement at the same level as NSAIDs.[40] Because ginger also works as an antiemetic, working both peripherally on gastric emptying and centrally by altering neurotransmitter release, this would provide additional benefit to women suffering from associated gastrointestinal symptomatology.
- A variety of herbal and nonmedical remedies have been proposed to treat dysmenorrhea, including rose tea, sweet fennel seed extract, fish oil, krill oil, increased dairy intake, and a low-fat vegetarian diet.[1,35] The omega-3 fatty acids found in fish and krill oil have shown some benefit for primary dysmenorrhea pain and have been associated with a reduced need for ibuprofen.[51] A Cochrane Review exploring dietary supplements for treatment of dysmenorrhea found no high-quality data for any dietary supplement. However, there was limited and low-quality evidence for fenugreek, valerian, zataria, zinc sulphate, fish oil, and vitamin B1 to potentially improve dysmenorrhea.[48] Even though data are insufficient to support recommending the use of these agents, the associated side effects are minimal, and we do not believe it is necessary to discourage patients from using these therapies if they find them helpful. More high-quality studies are needed.[52]

Nonpharmacologic

- Transcutaneous electrical nerve stimulation is hypothesized to relieve primary dysmenorrhea in three ways. First, it sends electrical impulses through the sensory fibers of the nerve root, such that the threshold for reception of pain signals is elevated and the pain sensation is not perceived. Two electrodes should be placed suprapubically, approximately 10–15 cm apart. At these locations, preganglionic fibers are stimulated, which causes the nerve cells of the dorsal horn to be saturated. This, in turn, blocks the fibers from emitting further pain impulses.[53,54] Second, transcutaneous electrical nerve stimulation stimulates the release of endogenous endorphins, which are associated with reduction in pain. Third, transcutaneous electrical nerve stimulation reduces uterine muscle hypoxia by increasing local vasodilation. There is insufficient evidence to recommend

low-frequency transcutaneous electrical nerve stimulation, but a meta-analysis of high-frequency transcutaneous electrical nerve stimulation has shown it to be superior to placebo.[55,56] High-frequency transcutaneous electrical nerve stimulation alone is helpful in 30% of cycles in women with severe dysmenorrhea, and lower doses of NSAIDs are required to manage pain in the remaining cycles.[3] The high-frequency transcutaneous electrical nerve stimulation unit consists of reusable patches connected to a hand-sized device, and the patient controls both the intensity and duration of the treatment. The use of high-frequency transcutaneous electrical nerve stimulation does not require a person to be sedentary, so it does not interfere with work or school.

- Acupuncture and acupressure are both methods to stimulate designated anatomic locations in a way that relieves pain. Various points on the auricle and along the medial calf, specifically three thumb breadths above the medial malleolus posterior to the border of the tibia (SP6 point) and three thumb breadths below the medial condyle of the tibia along the line connecting the medial condyle to the medial malleolus (SP9 point), have been identified as potentially beneficial for menstrual pain.[57,58] Acupuncture uses thin needles at these points, whereas acupressure uses firm massage. Possible mechanisms of pain relief include alterations in pain modulation, increase in uterine blood flow from the ovarian sympathetic nerve reflex, and a decrease in PG levels.[59] A recent Cochrane Review concluded that there is insufficient evidence to determine whether acupuncture or acupressure improve symptoms of primary dysmenorrhea because there are no well-designed randomized controlled trials.[59] However, systematic reviews and a meta-analysis of small trials have suggested that acupuncture may be superior to placebo, pharmacologic, and herbal treatments for the pain of primary dysmenorrhea.[60–62] Also, small studies of acupressure suggest therapeutic efficacy comparable with ibuprofen.[63] There is insufficient evidence to recommend a particular acupuncture schedule, and treatments have ranged from once per menstrual cycle to daily for 7 days.[64] Recommendations were to use acupressure for 1 minute at least twice daily or up to five times per day. Because acupressure is free and has limited time constraints, it should work well in a patient's schedule. Further large randomized controlled trials are necessary to better understand the potential benefit of both acupuncture and acupressure, but they can be used in addition to conventional pharmacotherapy.
- Continuous heat applied to the suprapubic region provides relief of pain for some women, but additional high-quality trials are needed to confirm its efficacy.[16,55] Local heat increases blood flow, improves tissue oxygenation, and has a dilutional effect on intravascular PGs. There are various methods for heat delivery, but ThermaCare HeatWraps have a patented technology involving iron's interaction with oxygen and water so heat can be released over an 8-hour period.[65] ThermaCare HeatWrap application over the quadriceps muscle resulted in more than a 100% increase in skin blood flow and an almost 150% increase in underlying muscle blood flow. Heat patches are thin enough to wear under clothes, easily accessible, inexpensive, and can also be used in combination with other treatment modalities.
- Exercise and yoga may also provide relief of dysmenorrhea symptoms through multiple pathways, including increased blood flow and endorphin release and lowering stress and anxiety.[66,67] A Cochrane Review exploring the effect of exercise on primary dysmenorrhea found only a single randomized controlled trial of limited quality.[66] This study did show that exercise decreased symptoms of dysmenorrhea and that this improvement was sustained over the observed three menstrual cycles.[68] Other studies with small numbers of participants have shown improvements in dysmenorrhea with aerobic or stretching exercises as well as yoga for 30–60 minutes per day for at least 3 days per week, but there is concern that the evidence is only moderate quality.[69,70] It is well recognized that physical exercise provides multiple health benefits, and both the American Medical Association and the U.S. Department of Health and Human Services have released guidelines to encourage physicians to recommend exercise to all of their patients (Box 2). Studies have shown that physician advice has a positive effect on patient behavior, including increasing the amount, duration, frequency, and intensity of a patient's exercise regimen.[71] In addition, adolescence and young adulthood is the period when lifestyle behaviors emerge and can become routine; thus, it behooves physicians to try to have a significant effect at a critical juncture that can have lifelong benefits.[71]
- Hysteroscopic endometrial ablation may have some benefit when dysmenorrhea is associated with heavy menstrual bleeding. For patients who experience both heavy menstrual bleeding and dysmenorrhea, rates of dysmenorrhea have improved postoperatively in proportion to

decreases in menstrual bleeding. In a study by Wyatt et al,[72] approximately 50% of women had resolution of their dysmenorrhea after ablation. However, endometrial ablation was not evaluated as a treatment for primary dysmenorrhea in the absence of heavy menstrual bleeding. Additionally, it is not an appropriate therapy for patients desiring future fertility. There is also a twofold increased risk of treatment failure when the patient is younger than 45 years.[73]

- Other surgical options for primary dysmenorrhea include uterosacral nerve ablation and presacral neurectomy.[1] These procedures are designed to interrupt sensory pain fibers in the pelvis and can be performed using both laparoscopic and open techniques. There is evidence of improvement in pain after these interventions, but the relief is likely temporary. Pain typically returns when nerve regeneration occurs. Adverse effects of the procedure may include constipation and urinary dysfunction. Uterine nerve ablation when performed along with the transection of the uterosacral ligaments carries an additional risk of pelvic organ prolapse.[74,75] Given the potential for complications, the invasive nature of the procedure, and the anticipated temporary benefit, these surgical interventions for primary dysmenorrhea are not recommended.
- Hysterectomy is an option for patients with primary dysmenorrhea who have satisfied parity and for whom other options are ineffective or unacceptable. It is estimated that up to 20% of premenopausal women will regret losing childbearing potential, which makes this procedure problematic in younger women–especially given divorce rates up to 50%. Meta-analysis of available data demonstrated no increase in anxiety and a potential decrease in depression for women undergoing hysterectomy for benign conditions,[76] and the first study to estimate the prevalence of regret in women who had a hysterectomy when they were younger than 35 years reported reassuring data if the patients were properly counseled.[77] The role of bilateral oophorectomy in the treatment of primary dysmenorrhea is unclear. Informed consent would require discussion of the potential for increased morbidity and mortality with premenopausal oophorectomy as compared with the risk of future pelvic surgery for persistent pain or adnexal masses with retained ovaries.
- Insufficient data exist to support spinal manipulation as more effective than sham treatment in the treatment of primary dysmenorrhea.[78]

Box 2. Physical Activity Guidelines for Americans

Guidelines for Adolescents

- Young people should participate in enjoyable physical activities that are appropriate for their age and that offer variety.
- Adolescents up to 17 years of age should do at least 1 h of moderate-to-vigorous physical activity daily.
- Aerobic: Most of the 60 min should be either moderate- or vigorous-intensity aerobic physical activity.

Guidelines for Adults

- Adults should do at least 2.5 h/wk of moderate-intensity or 1.5 h/wk of vigorous-intensity aerobic physical activity. Preferably, aerobic activity should be spread through the week.

Modified from U.S. Department of Health and Human Services. Physical activity guidelines for Americans (2nd edition); U.S. Department of Health and Human Services: 2018. Available at: https://health.gov/sites/default/files/2019-09/Physical_Activity_Guidelines_2nd_edition.pdf. Retrieved July 7, 2020.

MANAGEMENT APPROACH

In patients with presentation and physical examination typical for primary dysmenorrhea, empiric therapy is appropriate. There are multiple options for treatment, many of which have reasonable efficacy and safety profiles. As such, there is no "one-size-fits-all" algorithm for treatment of dysmenorrhea. Considerations such as desire for contraception, cost, ease of use, contraindications, potential side effects, and patient (and possibly family) preference all help to guide the choice of initial therapy.

Effective treatment of dysmenorrhea requires a discussion of risks, benefits, and alternatives, with a particular focus on finding a treatment modality that meets patient goals within the context of her lifestyle and other medical conditions. Often this is fairly straightforward, starting with treatment options demonstrated to be most likely to improve symptoms. In some cases, though, less effective modalities may meet the patient's needs, and more than one therapy can be initiated to improve efficacy. Shared decision making encourages the health care professional and patient to work together to balance the opportunity to improve symptoms with avoidance of harm and to incorporate patient autonomy in her disease management. Within this framework, the following discussion describes potential approaches to the treatment of primary dysmenorrhea.

Generally, hormonal contraception and NSAIDs are considered first-line therapy for primary dysmenorrhea. For patients desiring contraception, it is

reasonable to initiate therapy with hormonal medication. Given that both combined oral contraceptive and progesterone-only options that produce reduction or cessation of menses are effective in reducing the symptoms of primary dysmenorrhea, the choice of hormonal agent should incorporate patient preference regarding route of administration, contraceptive efficacy, and the potential for abnormal bleeding. Personal medical history also influences the choice of a hormonal agent. Patients with a history of venous thromboembolism or migraine with aura, for example, would not be candidates for estrogen-containing therapy but may benefit from progesterone-only options. The U.S. Medical Eligibility for Contraceptive Use is a useful resource to guide hormonal contraceptive choice in patients with concomitant medical conditions.[79] Even for patients desiring contraception, other considerations may lead them to decline hormonal contraception for dysmenorrhea. For example, some patients may find the need for a daily medication to improve pain that occurs only with menses unacceptable and may prefer other options.

For patients not desiring contraception or for whom hormonal contraception is contraindicated or otherwise undesirable, NSAIDs would be an appropriate initial choice. Ibuprofen and naproxen are generally affordable and well tolerated, and both can be titrated to balance efficacy with side effects. Contraindications to the therapy, frequency of administration, or prohibitive side effects may render this option unacceptable.

Although hormonal contraception and NSAIDs are typically prescribed as initial therapy based on efficacy considerations, patient preference or contraindications may lead to the selection of another option. Some patients, for example, may desire a treatment that permits self-control of administration and may prefer high-frequency transcutaneous electrical nerve stimulation or acupressure. Other patients may prefer nonpharmacologic treatment options and may choose to start with herbal remedies. Counseling for patients who prefer to try nontraditional therapies first would include a discussion of the fact that these options may have an increased risk of treatment failure and may be less likely to be covered by insurance. In the absence of contraindications, patients should also be informed that hormonal contraception and NSAIDs remain available if nontraditional approaches fail to adequately relieve pain.

Additionally, multiple modalities may be used in concert to provide additive benefit. Contraceptive therapy with NSAID administration during menses is commonly employed, and complementary treatment with heat or acupuncture is reasonable. One study demonstrated that the placement of a levonorgestrel-containing IUD after endometrial ablation for heavy menstrual bleeding reduces the risk of residual dysmenorrhea postoperatively.[80] Owing to a greater risk of harm, invasive options such as presacral neurectomy, uterosacral nerve ablation, or hysterectomy would be reserved for particularly refractory cases in which potential causes of secondary dysmenorrhea have been excluded.

Follow-up is important after initiating any therapy for primary dysmenorrhea. If treatment does not improve symptoms–particularly if either hormonal contraception or NSAID therapy is ineffective–further evaluation for secondary causes of dysmenorrhea is indicated. Transvaginal or abdominal ultrasound scan works well for a large number of patients, and diagnostic laparoscopy may be considered to identify endometriosis. Additional treatments for pain would then be directed at any identified underlying etiology.

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PEER REVIEW HISTORY

Received April 24, 2020. Received in revised form July 5, 2020. Accepted July 9, 2020. Peer reviews and author correspondence are available at http://links.lww.com/AOG/C65.

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