Dysmenorrhea and Endometriosis: Diagnosis and Management in Adolescents

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Abstract: Dysmenorrhea is common in adolescents. Most have primary dysmenorrhea and respond to empiric treatment with nonsteroidal anti-inflammatory drugs and/or hormonal therapies. Infrequently, patients have persistent symptoms requiring further evaluation including a pelvic examination, ultrasonography, and/or diagnostic laparoscopy. The most common cause of secondary dysmenorrhea in adolescents is endometriosis. Endometriosis is an estrogen-dependent, inflammatory condition with no surgical or medical cure. Treatment is individualized and typically includes surgical diagnosis with resection and/or ablation limited to visible lesions followed by hormonal suppressive therapy in an attempt to relieve symptoms, limit disease progression, and protect fertility. Multidisciplinary attention to comorbidities and pain management as well as patient education and support are important.

Key words: dysmenorrhea, endometriosis, adolescent, laparoscopy, hormonal suppression

Dysmenorrhea

Dysmenorrhea, or menstrual pain, is the most common gynecologic complaint among adolescents and young women, and the leading cause of recurrent short-term school or work absenteeism. Prevalence rates vary depending on the demographics of the populations studied and the severity of symptoms. Dysmenorrhea impacts between 60% and 93% of adolescents and up to 42% of adolescents report severe symptoms. Despite the high prevalence of dysmenorrhea and documented negative impact quality of life, many patients do not seek care, underreport their symptoms, and/or are undertreated. Adolescents may not perceive benefit or interest from encounters with health care professionals regarding menstrual concerns.

Because of these dynamics, inserting questions into routine adolescent health care encounters about menstrual-related...
Symptoms and Conditions Associated With Dysmenorrhea

Lower abdominal cramping pain is easily recognized as a symptom of dysmenorrhea. However, clinical recognition of the wide range of symptoms associated with dysmenorrhea increases identification of patients who may benefit from therapeutic interventions. Generalized abdominal pain, vomiting, loss of appetite, dyschezia, and diarrhea are common gastroenterologic symptoms. Patients may also report associated generalized aching, weakness, leg aches, low back pain, headaches. Additional symptoms attributable to dysmenorrhea include sleeplessness, dizziness, depression, irritability, and nervousness. Patients with dysmenorrhea are more likely to be diagnosed with depression and/or anxiety as well as premenstrual syndrome.

Primary Versus Secondary Dysmenorrhea

Dysmenorrhea may be either primary or secondary. About 90% of impacted patients have primary dysmenorrhea, defined as dysmenorrhea in the absence of pelvic pathology. Primary dysmenorrhea is a result of pathophysiologic changes occurring throughout the menstrual cycle, including excess synthesis of prostaglandins and secretion of prostaglandins into the endometrial fluid in girls and women who experience significant dysmenorrhea. Secondary dysmenorrhea, in contrast, is due to varying underlying gynecologic etiologies, most commonly endometriosis, and obstructive Mullerian anomalies.

Understanding the pathophysiology of primary dysmenorrhea aids in appreciating therapeutic options. Primary dysmenorrhea is the result of cyclic prostaglandin and leukotriene production by the uterus during ovulatory cycles. Following progesterone withdrawal premenstrually, phospholipids are released from the cell membrane, including omega-6 fatty acids. A cascade follows where the enzyme phospholipase A2 converts the fatty acids to arachidonic acid, cyclooxygenase converts the arachidonic acid to prostaglandins, and lipoxygenase converts the prostaglandins to leukotrienes. An inflammatory response, mediated by these prostaglandins and leukotrienes, produces both the menstrual cramps and systemic symptoms. Prostaglandin F2alpha causes potent vasoconstriction and myometrial contractions, leading to uterine ischemia and pain. The intensity of the menstrual cramps and dysmenorrhea-associated symptoms are directly proportional to the amount of prostaglandin F2alpha released. Urinary leukotriene levels are increased in adolescent girls with dysmenorrhea.

Evaluation of Dysmenorrhea

The evaluation of an adolescent with dysmenorrhea begins with a history including menstrual, sexual, gynecologic, medical, surgical, psychosocial, and family history. “Alone time” between the provider and the patient as well as an explanation of confidentiality practices should be explained and incorporated into the evaluation. While taking the history, the clinician assesses the likelihood of primary versus secondary amenorrhea by learning about duration, timing, and severity of menstrual cramps and other associated symptoms; impact symptoms have on the quality of life and level of functioning; response to previous therapies; and family history of endometriosis. Primary dysmenorrhea is more likely that secondary dysmenorrhea to being just before or concurrent with the onset of menstrual bleeding, and to be worst on the first or second day of flow, with subsequent improvement. Clues that raise concern for secondary dysmenorrhea include failure to respond to first-line treatments, symptoms presenting shortly after menarche, associated heavy menstrual bleeding and/or...
acyclic pain, sexual activity, family history of endometriosis, or a known renal anomaly. In patients with a history suggesting primary dysmenorrhea who have never been sexually active, a pelvic examination is not necessary, and empiric treatment should be initiated (Fig. 1). Response to therapy reinforces the diagnosis of primary dysmenorrhea. Suspicion of secondary dysmenorrhea may require further evaluation, but the initiation of therapy should not be delayed.

Patients who have been sexually active require a pelvic examination to rule out pelvic inflammatory disease. Anytime the patient’s history reveals clues suggesting secondary dysmenorrhea, a pelvic examination should be considered.

**TABLE 1. Clinical Findings Raising Suspicion of Secondary Dysmenorrhea**

<table>
<thead>
<tr>
<th>Symptoms occurring with the onset of or shortly after menarche</th>
<th>Associated heavy menstrual bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of acyclic pelvic pain</td>
<td>Presence of a renal anomaly</td>
</tr>
<tr>
<td>Family history of endometriosis</td>
<td>Symptoms unresponsive to nonsteroidal anti-inflammatory drugs and/or hormonal medications</td>
</tr>
</tbody>
</table>

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**FIGURE 1.** Approach to the evaluation and management of an adolescent with dysmenorrhea. With permission from American College of Obstetricians and Gynecologists.
be attempted. With education and support adolescents who have never been sexually active are often able to tolerate a pelvic examination.\(^5\) Endometriosis is the most common etiology of secondary dysmenorrhea and most affected adolescents have early-stage disease.\(^5\) Therefore, while a bimanual examination may elicit pelvic tenderness (particularly in the cul-de-sac posterior to the uterus) suggesting endometriosis, uterosacral, or cul-de-sac nodularity, uterine fixed retroversion, or endometriomas are rarely identified.\(^3\) Pelvic examination may also help identify obstructive Mullerian anomalies associated with dysmenorrhea such as uterine didelphys with obstructing hemivagina or a noncommunicating functional uterine horn.

Pelvic imaging with pelvic ultrasound (transabdominal or transvaginal) is indicated when patients do not respond to standard therapies for primary dysmenorrhea or have symptoms and/or physical findings suggestive of secondary dysmenorrhea. A normal study does not rule out superficial endometriosis, but pelvic imaging can identify structural abnormalities associated with dysmenorrhea such as obstructive Mullerian anomalies, ovarian cysts or endometriomas, and uterine polyps or leiomyomata. Pelvic ultrasound is the first-line imaging tool for dysmenorrhea; pelvic magnetic resonance imaging (MRI) may be required to further delineate obstructive Mullerian anomalies. MRI is not cost-effective as a first-line screening tool; like ultrasound, MRI is unable to identify early-stage endometriosis.\(^5\)

Diagnostic laparoscopy may be required to confirm some etiologies of secondary dysmenorrhea such as endometriosis, pelvic inflammatory disease, adhesions, and/or obstructive Mullerian anomalies.\(^7\) Laparoscopy is reserved for patients with suspected anatomic abnormalities suspected on pelvic examination and/or radiologic studies or patients who have failed standard medical therapies.

### Treatment of Primary Dysmenorrhea

Treatment options including nonhormonal medications, hormonal therapies, and complementary and alternative regimens may be used alone or in combination. Patient’s desire for contraception and gynecologic comorbidities, such as heavy menstrual bleeding, often influence prioritization and choice of interventions.

### Nonhormonal Medications

Nonsteroidal anti-inflammatory drugs (NSAIDs) interrupt the cyclooxygenase-mediated prostaglandin production and are considered first-line treatment for dysmenorrhea.\(^5\) NSAIDs are more effective than placebo in relieving pain associated with primary dysmenorrhea. No one individual NSAID has a better efficacy or safety profile in treating primary dysmenorrhea.\(^5\) If the initial NSAID does not provide relief, patients should be encouraged to try an alternative agent.

A common reason adolescents do not respond to NSAIDs is delayed initiation of use in the cycle and subtherapeutic dosing. Educating the patient and potentially her family about the correct use of the medications is critical; parents and physicians may need to work with school personnel to authorize patients to self-medicate while at school, although an NSAID with a longer half-life, such as naproxen (12 to 17 h), may obviate the need to redose during school hours.\(^5\) NSAIDs are most effective when initiated 1 to 2 days before the onset of menses and taken as weight-specific doses on a routine schedule (not PRN) through the first 2 to 3 days of bleeding.\(^5\) Some patients do not respond to NSAIDs despite adequate adherence due to either molecular etiologies or the presence of underlying secondary causes of dysmenorrhea.\(^9\)

Acetaminophen, acetaminophen with caffeine, and acetaminophen and pamabrom in
combination have all been shown superior to placebo in treating dysmenorrhea. Acetaminophen has fewer gastrointestinal side effects and can be used in addition to NSAIDs. Opioids should not be used to treat dysmenorrhea because of risks of physical dependence, addiction, and hyperalgesia.

Hormonal Therapies
Hormonal therapies, either alone or in combination with nonhormonal medications and/or alternative and complementary agents, are another first-line option to treat primary dysmenorrhea. All hormonal contraceptives are beneficial in alleviating dysmenorrhea; the most likely mechanism is decreasing prostaglandin and leukotriene production by either limiting endometrial proliferation and/or ovulation. Evidence supports the use of combination estrogen and progestin methods such as the pill, patch, or ring as well as progestin-only methods such as depot medroxyprogesterone acetate, the contraceptive implant, and levonorgestrel intrauterine systems.

There is no strong evidence that one single hormonal therapy is most effective, and therefore, patient preference after counseling about all methods should drive decision making. If the first method chosen is not acceptable due to adherence, side effects, or lack of improvement in symptoms, another method should be tried. Using combination methods in an extended cycle regimen may lead to an earlier alleviation of symptoms, but cyclic use is as beneficial long term. One study did show levonorgestrel intrauterine system compared with combination oral contraceptive pills to be more effective in treating dysmenorrhea. Noncontraceptive hormonal therapies can be helpful for patients and/or families who are reluctant to use a contraceptive method to treat dysmenorrhea. Norethindrone acetate, 5 mg daily, is as effective as cyclic combination hormonal contraceptive pills to treat dysmenorrhea in young women. Empiric use of gonadotropin-releasing hormone agonists (GnRHa) or antagonists are not recommended to treat primary dysmenorrhea in adolescents due to concerns about bone mineralization.

Alternative and Complimentary Agents
A wide range of alternative and complimentary agents have been suggested as a treatment for primary dysmenorrhea and patients’ use of and response to these agents should be elicited. Unfortunately, there is a paucity of high-quality research about many of the suggested modalities. Many alternative or complimentary options have undergone Cochrane review without the quality of evidence to endorse the recommendation. Currently, the strongest evidence supports the use of local heat and exercise to improve dysmenorrhea symptoms. Given the low cost and safety record of both exercise and heat, as well as the additional health benefits of exercise, both should be routinely recommended. With only limited (and sometimes conflicting) evidence of benefit, dietary supplements, transcutaneous electrical nerve stimulation, behavioral interventions, high dose vitamin D, yoga, herbal supplements, and acupuncture are not currently recommended as a first-line alternative or complimentary modalities to treat primary dysmenorrhea.

Follow-up and Treatment Failure
Patients benefit from regularly scheduled follow-up appointments to monitor side effects, adherence, and response to therapy. A successful intervention is defined not by the complete absence of any pain or discomfort, but rather full participation in school, sports, and social functions and few, if any, trips to urgent care of emergency departments with dysmenorrhea symptoms. An adequate response to

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therapy reinforces the diagnosis of primary dysmenorrhea.

If patients continue to have pain, adherence should be assessed seeking input from both the patient and her parent or guardian. Adolescents are frequently less adherent with medication schedules and may have a conflict with parents over medication use.\(^5\) Patients should be encouraged to try alternative NSAIDs and hormonal agents if their initial choices are not helpful. As shown in Figure 1, patients experiencing pain despite adherence with NSAIDs and hormonal agents for at least 3 to 6 months require additional evaluation for potential etiologies of secondary dysmenorrhea.

**Endometriosis**

Endometriosis is the most common cause of secondary dysmenorrhea in adolescents.\(^5\) While the exact prevalence of endometriosis in adolescents is unknown, in patients undergoing laparoscopy for dysmenorrhea unresponsive to hormonal therapy and NSAIDs, approximately two thirds of patients will be diagnosed with endometriosis.\(^13\) Risk factors for adolescent endometriosis include an affected first-degree family member, an obstructive Mullerian anomaly, and increased exposure to menstruation including earlier menarche.\(^14\)

The most common symptoms of adolescent endometriosis are dysmenorrhea and chronic pelvic pain. Adolescents with endometriosis may experience dyspareunia if they are sexually active, and they are more likely than adults to experience acyclic pelvic pain.\(^14\) Similar to primary dysmenorrhea, endometriosis is an inflammatory mediated estrogen-dependent disorder, stimulated by estrogen production from both the ovaries and endometriotic implants.\(^5\)

In earlier studies, adolescent endometriosis had been primarily reported as mild or early-stage disease (revised American Society of Reproductive Medicine State, rASRM Classification Stage I or II).\(^14\) More recently there have been several case series reporting a significant proportion of adolescents with rASRM Stage III and IV disease, including deep infiltrating disease and endometriomas.\(^14\) All stages and types of endometriosis have now been reported in adolescents, and endometriosis is no longer considered only early-stage disease in this age group.

**Treatment of Endometriosis**

There is currently no clear evidence regarding the most effective treatment options for adolescent endometriosis, and therefore, treatment should be individualized with a focus on restoring function by minimizing symptoms, suppressing the progression of the disease, and preserving fertility. The mainstay of treatment is medical, including hormonal therapies combined with NSAIDs; GnRHa may benefit some older adolescents. Surgical interventions focus primarily on initial diagnosis combined with conservative treatment. Multidisciplinary care addressing both comorbidities and chronic pain management as well as patient and family education, and support play important roles in therapeutic plans.\(^5\)

**Role of Surgery**

Surgical interventions have a limited role in the management of adolescent endometriosis. Many patients with dysmenorrhea unresponsive to hormonal therapies and NSAIDs or chronic pelvic pain with is a high index of suspicion for endometriosis undergo diagnostic laparoscopy. The advantages of diagnostic laparoscopy include confirmation of any suspected pathology as well as an opportunity to treat with either ablation or excision of visible lesions. A negative diagnostic laparoscopy may reassure any patient with dysmenorrhea and/or chronic pain and particularly those with anxiety or somatization. Traditionally, early diagnosis and treatment of endometriosis has been advocated to help
minimize disease progression and protect fertility.

Endometriosis in adolescents most commonly presents in early-stage disease and with clear or red lesions as opposed to the powder burn lesions identified in older patients. Lesions suspicious for endometriosis should be biopsied for pathologic confirmation and additionally resected or coagulated. Two surgical techniques described to more readily identify adolescent endometriosis include moving the laparoscopy within millimeters of the peritoneum and filling the pelvic with saline and “diving in” with the laparoscope. There is currently no evidence in adolescents whether surgical resection or coagulation is more advantageous. The adhesive disease should be lysed at the time of laparoscopy as potential sources of pain.

In addition, diagnostic laparoscopy is an ideal time to consider the placement of a levonorgestrel intrauterine device to treat dysmenorrhea symptoms in patients regardless of whether endometriosis is identified at the time of surgery, particularly in girls who are virginal or hesitant about in-office insertion. There is no definitive surgical cure for adolescent endometriosis. After diagnosis and treatment during the initial laparoscopy, treatment turns to hormonal suppressive therapy. Repeat laparoscopies are avoided unless in attempts to treat symptomatic endometriomas or deep, infiltrating disease.

There is currently no evidence regarding “peritoneal stripping” as a treatment modality for adolescent endometriosis. The American College of Obstetricians and Gynecologists does not endorse its use in adolescents given the lack of evidence regarding both short-term and long-term outcomes, as well as concerns with the potential for adhesion formation leading to bowel obstruction, infertility, and/or chronic pain. Recent case reports and expert opinion also discourage the use of “extensive peritoneal excision” of early-stage endometriosis in adolescents due to subsequent symptomatic adhesion formation.

**Medical Therapies**

Adolescent endometriosis is a chronic condition with the potential for progression. After surgical diagnosis and conservative surgical treatment, hormonal suppressive therapy is continued or initiated to manage symptoms, decrease the likelihood of progression, and potentially protect fertility. As evidence is lacking regarding one single best agent or treatment plan, choice of hormonal suppressive therapy can be individualized based on the need for contraception, patient preference, and contraindications to combined hormonal methods. All contraceptive methods, as well as norethindrone acetate, have demonstrated benefit. Patients often benefit from trialing different hormonal therapies and extended cycle preparations.

Some adolescents with endometriosis have persistent symptoms despite conservative surgical therapy and hormonal suppression and may benefit from GnRHa treatment in combination with add-back therapy. Daily add-back therapy with conjugated equine estrogen (0.625 mg) with norethindrone acetate (5.0 mg) is superior to norethindrone acetate (5.0 mg) alone in both improving quality of life and maintaining bone mineral density in adolescents with endometriosis. GnRHa treatment is typically reserved for older adolescents with surgically proven endometriosis given concerns about the accrual of bone mineral density during adolescence. Dual-energy x-ray absorptiometry is not indicated before initiation of GnRHa therapy or after treatment of <12-month duration. Weight-bearing exercise and supplementation with calcium and vitamin D should be encouraged during GnRHa therapy. Hormonal suppression should resume after a course of GnRHa therapy.

gonadotropin-releasing hormone antagonists are a newer class of drugs being used to treat endometriosis. No trials have been done.
yet in women younger than 18 years of age and they are not Food and Drug Administration (FDA) approved for contraception. Endometrial suppression and rates of amenorrhea may be lower than with GnRHa.

NSAIDs, in conjunction with hormonal suppression, play an important role for management of both the inflammation and pain associated with adolescent endometriosis. Opioids should not be used for pain relief in adolescents with endometriosis outside of a specialized pain clinic.5

**Summary**

Dysmenorrhea is a common adolescent menstrual complaint and typically improves with NSAIDs and/or hormonal therapies. Some adolescents with dysmenorrhea are diagnosed with endometriosis and should be treated with conservative surgical intervention and hormonal suppression. More research is needed to determine the most effective hormonal agents as well as the role of both GnRH and the newer gonadotropin-releasing hormone antagonists in treating adolescent endometriosis. Additional unanswered questions include the natural course of adolescent endometriosis and the impact of the disease on future fertility.

**References**


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