Endometriosis in Adolescents

**ABSTRACT:** Historically thought of as a disease that affects adult women, endometriosis increasingly is being diagnosed in the adolescent population. This disorder, which was originally described more than a century ago, still represents a vague and perplexing entity that frequently results in chronic pelvic pain, adhesive disease, and infertility. The purpose of this Committee Opinion is to highlight the differences in adolescent and adult types of endometriosis. Early diagnosis and treatment during adolescence may decrease disease progression and prevent subsequent infertility.

**Incidence**

It has been difficult to establish accurate prevalence rates of endometriosis in adult and adolescent women. Documented rates in adolescent patients undergoing laparoscopy for chronic pelvic pain range from 19% to 73%. Goldstein et al (1) reported a 47% prevalence of endometriosis found at laparoscopy in a prospective study of adolescent females with pelvic pain. Other studies have shown that 25–38% of adolescents with chronic pelvic pain have endometriosis (2, 3). In addition, it has been shown that 50–70% of adolescents with pelvic pain not responding to combination hormone therapy (such as oral contraceptive pills [OCPs]) and nonsteroidal antiinflammatory drugs (NSAIDs) have endometriosis at the time of laparoscopy (4, 5).

Endometriosis also has been identified in premenarcheal girls who have started puberty and have some breast development (6, 7). The occurrence of endometriosis before menarche contributes to the argument that one etiology for endometriosis lies in the theory of embryonic müllerian rests or coelomic metaplasia as opposed to retrograde menses. Based on the occurrence of early endometriosis, some authors have argued that “thelarche be recognized as a developmental benchmark, after which endometriosis is included in the differential diagnosis of chronic pelvic pain” (6).

It is common for adult women who have endometriosis to bring in their adolescent daughters for evaluation and early diagnosis. Data from the Endometriosis Association indicate that 66% of adult women reported the onset of pelvic symptoms before age 20 years. Forty-seven percent of these women reported they had to see a doctor five times or more before receiving the diagnosis of endometriosis or referral. As the age of the onset of symp-
toms decreases, the number of doctors having to be seen to reach a diagnosis increases. Specifically, an average of 4.2 doctors were seen for patients whose symptoms began before age 15 years compared with an average of 2.64 doctors for patients whose symptoms began between the ages of 30 years and 34 years. There are, on average, 9.28 years from the onset of symptoms to the diagnosis (8). Endometriosis is believed to be a progressive disease because the prevalence and severity of the stage of the disease significantly increase with age (9, 10). With early diagnosis and treatment, it is hoped that disease progression and infertility can be limited, but this remains to be proved with prospective research.

**Presentation and Characteristics**

The typical presentation of an adolescent with endometriosis may be different from that of an adult. One significant difference is that adolescents primarily seek medical attention because of pain rather than a concern for infertility. The most common symptom noted among published reviews is acquired or progressive dysmenorrhea, which was encountered in 64–94% of patients (4, 11). Other common symptoms included acyclic pain (36–91%), dyspareunia (14–25%), and gastrointestinal complaints (2–46%) (11). Adolescents found to have endometriosis most commonly present with both cyclic and acyclic pain (62.6%), as opposed to acyclic pain alone (28.1%), or cyclic pain alone (9.4%) (11).

In young women, pelvic pain associated with endometriosis often interferes with school attendance as well as physical and social activities. Prompt diagnosis and adequate therapy, therefore, may return normal psychosocial development and self-esteem, improve scholastic performance, and lead to a return to normal daily activities.

**Diagnosis**

**History and Physical Examination**

A thorough review of history and physical examination are necessary to assess a variety of differential diagnoses of pelvic pain such as appendicitis, pelvic inflammatory disease, müllerian anomalies or outflow obstruction, bowel disease, hernias, musculo–skeletal disorders, and psychosocial complaints. Pelvic examination may be difficult, especially in patients who have not had vaginal intercourse.

When evaluating an adolescent for suspected endometriosis or dysmenorrhea, the clinician should aim to rule out a pelvic mass or a congenital anomaly of the reproductive tract. A bimanual examination may not be necessary to evaluate pelvic pain, especially in adolescents who are virgins. If a bimanual examination cannot be performed or is declined, a rectal–abdominal examination in the dorsal lithotomy position may be helpful to determine if a pelvic mass is present, and a cotton-tipped swab can be inserted into the vagina to evaluate for the presence of a transverse vaginal septum, vaginal agenesis, or agenesis of the lower vagina. If a bimanual examination is performed, the clinician should check for the existence of both diffuse and focal pelvic tenderness, and evaluate the pelvis for a displaced uterus or an adnexal mass. An ultrasound examination may be helpful in evaluating the pelvis of a young adolescent who declines a bimanual or rectal–abdominal examination.

**Imaging Studies and Serum Markers**

Ultrasonography and magnetic resonance imaging are helpful in evaluating anatomical structures, but are not specific for diagnosing endometriosis. An adolescent will rarely have a pelvic mass from an endometrioma or uterosacral nodularity. CA 125, although very sensitive, is not specific and, thus, is not helpful in the diagnosis of adolescent endometriosis. No data exist regarding the use of CA 125 to monitor the clinical progression or regression of disease in adolescents with endometriosis.

**Empiric Therapy**

If an adolescent younger than 18 years has persistent pain while taking combination hormone therapy and NSAIDs, endometriosis should be suspected and she should be offered a laparoscopic evaluation (discussion follows in section on “Surgical Diagnosis”). If, however, she is older than 18 years and had a negative assessment for an ovarian mass or tumor, she can be offered an empiric trial of gonadotropin-releasing hormone (GnRH) agonist therapy (12, 13). If the pain subsides with the use of GnRH agonist, then a diagnosis of endometriosis can be made. An empiric trial of GnRH agonist is not routinely offered to patients younger than 18 years because the effects of these medications on bone formation and long-term bone density have not been adequately studied. For patients younger than 18 years or who decline empiric therapy, diagnostic and ther-
apeutic laparoscopy can be initiated. An algorithm for therapy is provided in Figure 1 (14).

**Surgical Diagnosis**

After a comprehensive preoperative evaluation and trial of combination hormone therapy and NSAIDs to treat dysmenorrhea, laparoscopy should be recommended for diagnosing and treating presumed endometriosis in an adolescent. Laparoscopy can be safely performed in adolescents. At the time of surgical diagnosis, most adolescents have Stage I disease as classified by the American Society for Reproductive Medicine classification system (15). Goldstein et al commented that almost 60% of the

![Image of protocol for evaluation and treatment of adolescent pelvic pain and endometriosis](image)

**Fig. 1.** Protocol for evaluation and treatment of adolescent pelvic pain and endometriosis. (Modified with permission from Bandera CA, Brown LR, Laufer MR. Adolescents and endometriosis. Clin Consult Obstet Gynecol 1995;7:206.)
patients in their cohort had Stage I disease (1), whereas 80% of the cases reported by other researchers had minimal to mild disease (4). Gynecologic surgeons who perform laparoscopy in adolescents with pelvic pain should be familiar with the typical lesions of endometriosis in adolescents, which tend to be red, clear, or white (15) as opposed to the powder-burn lesions seen commonly in adults who have endometriosis. The use of a liquid medium in the pelvis may facilitate the identification of clear lesions, which are very common in adolescents (11).

Müllerian Anomalies and Endometriosis
The development of endometriosis in adolescent patients has been associated with müllerian anomalies with outflow tract obstruction. The published incidence of anomalies of the reproductive system and associated endometriosis has been reported to be as high as 40%, but most studies quote a rate of 5–6%. The clinical outcome in patients with outflow tract obstructions has been reported to differ from those without such obstruction because regression of disease usually has been observed once surgical correction of the anomaly has been accomplished (16).

Treatment
The premise for treating the symptomatic adolescent is based on the concept that endometriosis has been shown to be a progressive disease without a known cure. A physician treating an adolescent with endometriosis should adopt a multidimensional approach and consider the use of the following components: surgery, hormonal manipulation, pain medications, mental health support, complementary and alternative therapies, and education. Patients younger than 18 years with persistent pelvic pain while taking combination hormone therapy should routinely be offered a laparoscopic procedure for diagnosis and surgical management of endometriosis. The gynecologic surgeon must be familiar with the appearance of endometriosis in adolescents and should remove or destroy all visible lesions of endometriosis. Only procedures that preserve fertility options should be applied; oophorectomy or hysterectomy should not be offered to adolescents.

Long-term follow-up studies of treatments for adolescent endometriosis have not been performed. Current treatments for adolescents have been extrapolated and adapted from the literature of adult cases of endometriosis. The goal of therapy for adolescent endometriosis should be suppression of pain, suppression of disease progression, and preservation of fertility. Consequently, after surgery, all adolescents who have endometriosis should be treated with medical therapy until they have completed child bearing to suppress pain, progression of disease, and resulting potential infertility.

First-line treatment modalities should involve the use of NSAIDs and hormone therapy. Because red lesions have been shown to be active producers of prostaglandins, and adolescents with endometriosis typically report severe dysmenorrhea, NSAIDs may be used in conjunction with hormonal menstrual suppressive therapy to provide sufficient relief. Most pharmacologic agents bring about relief by inducing an anovulatory or a hypoestrogenic state or both. Continuous combination hormone therapy (OCPs, combination hormonal contraceptive patch, or vaginal ring) for menstrual suppression can be used to create a “pseudopregnancy” state, which was described more than 40 years ago (17). This method routinely has been promoted for adolescents who have endometriosis. Although this method may provide effective relief, the Cochrane Database Review 2003 provided data suggesting that further studies are needed to prove long-term benefits (18). Most clinicians advocate continuous use of combination hormone therapy to induce amenorrhea, but this modality can result in significant breakthrough bleeding. One randomized controlled trial compared a 28-day regimen with continuous combination oral contraceptives and found no increase in spotting days after 9 months of therapy, with fewer total bleeding days in the group taking continuous combination oral contraceptives (19). Thus, continuous use of combination hormone therapy is believed to be both safe and effective for adolescents with endometriosis-related pain and, thus, is the first-line hormone therapy for adolescents younger than 16 years with endometriosis. Gonadotropin-releasing hormone agonists are not offered as first-line therapy for adolescents in this age range.

Progestin-only protocols have been used for the treatment of adult endometriosis with mixed results. In a recent critical review, progestins were shown to be as effective as danazol or GnRH agonists (20). Common side effects include irregular bleeding and weight gain. Some studies suggest that these side effects are well tolerated (20), however in a data set of 3,751 women who have endometriosis, treatment
with medroxyprogesterone acetate or depot medroxyprogesterone acetate was the least well tolerated and was the least effective in treating pain compared with combination OCPs, GnRH agonists, and pain medications (8). Furthermore, depot medroxyprogesterone acetate used for longer than 2 years has been shown to decrease bone density in adolescents (21, 22, 23). The U.S. Food and Drug Administration has warned against the long-term use of depot medroxyprogesterone acetate because of adverse affects on bone density (24).

Danazol, an androgenic and antiestrogenic agent, is extremely effective in treating symptomatic endometriosis in adults. Doses of 400–800 mg daily have been advocated for 6 months followed by continuous OCP use for maintenance suppression of the hypothalamic–pituitary ovarian axis. This choice of pharmacotherapy was more common in the 1980s, but the androgenic side effects have made this a poor option for adolescents.

Gonadotropin-releasing hormone agonists create a hypoestrogenic state by downregulating the hypothalamic–pituitary axis. Whereas these agents are greatly effective in the treatment of endometriosis-related pain in adolescents, their use alone (without add-back therapy described in the following paragraph) usually is limited to 6 months because of the resultant profound hypoestrogenic state and its subsequent effect on bone mineralization. This is a major issue for an adolescent who is accruing peak bone mineral density. Therefore, it has been suggested that this therapy not be offered as a first-line treatment for adolescents younger than 16 years (14). At 6 months, GnRH agonist induces a 5% loss in trabecular bone mineral density and a 2% loss in femoral neck bone mineral density in adult women. In a cross-sectional study, researchers collected bone mineral density test results of 265 females, aged 8–50 years (25). They determined that the majority of bone mass growth is achieved by age 20 years and that after the age 18 years, no significant differences in bone mass or bone mineral density were noted at most skeletal sites. This emphasizes that a drug-induced hypoestrogenic state could significantly affect peak bone mineralization that occurs during adolescence, particularly in females younger than 16 years.

Investigators have determined that to reduce the symptoms and bone loss related to a hypoestrogenic state, add-back therapy with norethindrone acetate (5 mg per day) or conjugated estrogens/medroxyprogesterone acetate (0.625/2.5 mg per day) can help preserve bone density (26, 27). Add-back therapy has been shown not to influence the primary therapeutic effect and resulted in less bone loss 12 months after cessation of therapy in adult women. There is some evidence in adults to suggest that immediate add-back therapy may result in even less bone loss (28). No data exist on the long-term effects of GnRH agonist use with add-back therapy in the adolescent population and, thus, it should be reserved for adolescents refractory to continuous combination hormone therapy (14, 29). Lifestyle modifications, such as adequate physical exercise and calcium and vitamin D intake, also are essential to maintaining proper bone health when taking GnRH agonists (with or without add-back therapy).

Aside from medical management, surgery also has proved to be an effective form of treatment for adult patients with pain (30). Surgery for the management of endometriosis-related pain is an important option for adolescents, but clearly, radical procedures (oophorectomy, bilateral oophorectomy, or hysterectomy) should be avoided in this age group, even in rare cases of severe endometriosis. A double-blinded randomized controlled trial compared laser vaporization of endometriosis and laser uterosacral nerve ablation with controls in 63 adult patients with proven endometriosis. At 6 months of follow-up, 63% of patients reported significant relief compared with 23% of controls (31). Patients with more advanced disease had better outcomes in pain management compared with those with minimal disease. At 1-year follow-up, 90% of those in the treatment arm who initially responded had continued pain relief (32). Among the symptomatic controls, an even distribution of patients was noted to have progression, regression, and maintenance of disease. Both new and recurrent disease was noted at second look. In a Cochrane review of these data, adult patients were almost 5 times more likely to benefit from surgical management of endometriosis compared with controls (33). One study demonstrated, in a prospective review of 643 patients with pain, or infertility, or both, that there was a significant relationship between pain and the depth of infiltration of the endometriosis implants (9). This study also confirmed that red implants were more common in younger patients and that the depth of invasion increased with age, suggesting that endometriosis is a progressive disease. The concept that endometriosis is a progressive disease supports the recommen-
dation for long-term medical treatment for pain management of adolescent endometriosis and until a woman has completed childbearing. Long-term studies are needed to determine if medical treatment can inhibit the progression of endometriosis diagnosed in adolescents and preserve future fertility.

In addition to surgery and hormonal manipulation, complementary and alternative medicine has been used for the treatment of endometriosis. A multidisciplinary pain management service, including support groups and age-appropriate educational information, may be beneficial for an adolescent with chronic pelvic pain caused by endometriosis.

Summary

Endometriosis can be a debilitating disease that affects adolescent girls and young women. Pediatricians, adolescent health care providers, and gynecologists should recognize that thelarche and the presence of endogenous estrogen can be considered a developmental milestone and benchmark for inclusion of adolescent endometriosis in the differential diagnosis of postpubertal girls and young women with chronic pelvic pain. Adolescent patients typically present with progressive and severe dysmenorrhea, but also may present with acyclic pelvic pain. Standard therapy (combination hormone therapy and NSAIDs) for dysmenorrhea should be initiated, and if symptoms do not resolve after 3 months, further evaluation for endometriosis is indicated. Prompt evaluation and consideration of the adverse effects of endometriosis is, therefore, essential in this age group.

Findings of the physical examination of adolescents may vary from the adult population because uterosacral nodularity and endometriomas are found in more advanced disease and, thus, are uncommon in adolescents. A bimanual pelvic examination may not be necessary for further evaluation of pelvic pain and should not be a requirement before the diagnosis of endometriosis and initiation of therapy for adolescents. It is important to evaluate the vagina for a possible obstructive anomaly and the ovaries for a possible ovarian mass. This can be accomplished with an evaluation of the vagina with a cotton-tipped swab and an ultrasound examination of the pelvis.

Endometriosis in adolescents typically presents as early disease (Stage I) and clear, red, and white lesions are the most common. Treatment should focus on conservative measures with surgical and medical interventions. Only procedures that preserve fertility options should be applied. Long-term endometriosis treatment may be required for chronic pain relief. Because there is no cure for endometriosis, long-term treatment should continue until desired family size is reached or fertility no longer needs to be preserved. A multidisciplinary team approach to the adolescent who has endometriosis may be the most rewarding for the adolescent, her family, and the clinician.

Resources

Endometriosis Association
(www.endometriosisassn.org)

The Center for Young Women’s Health
(www.youngwomenshealth.org)

References