



NCC Pediatrics Continuity Clinic Curriculum: **Adolescent II** *Faculty Guide*

Overall Goal:

Identify key adolescent health issues and become comfortable interviewing an adolescent.

Overall Outline:

Adolescent I:

HEADSS-plus (review)
Contraception
Confidentiality

Adolescent II:

Dysmenorrhea
Amenorrhea

Adolescent III:

Acne
STIs

Pre-Meeting Preparation:

- Review of Menstrual Cycle
- Dysmenorrhea (PIR, 2006)
- Secondary Amenorrhea (AAFP, 2006)

Conference Agenda:

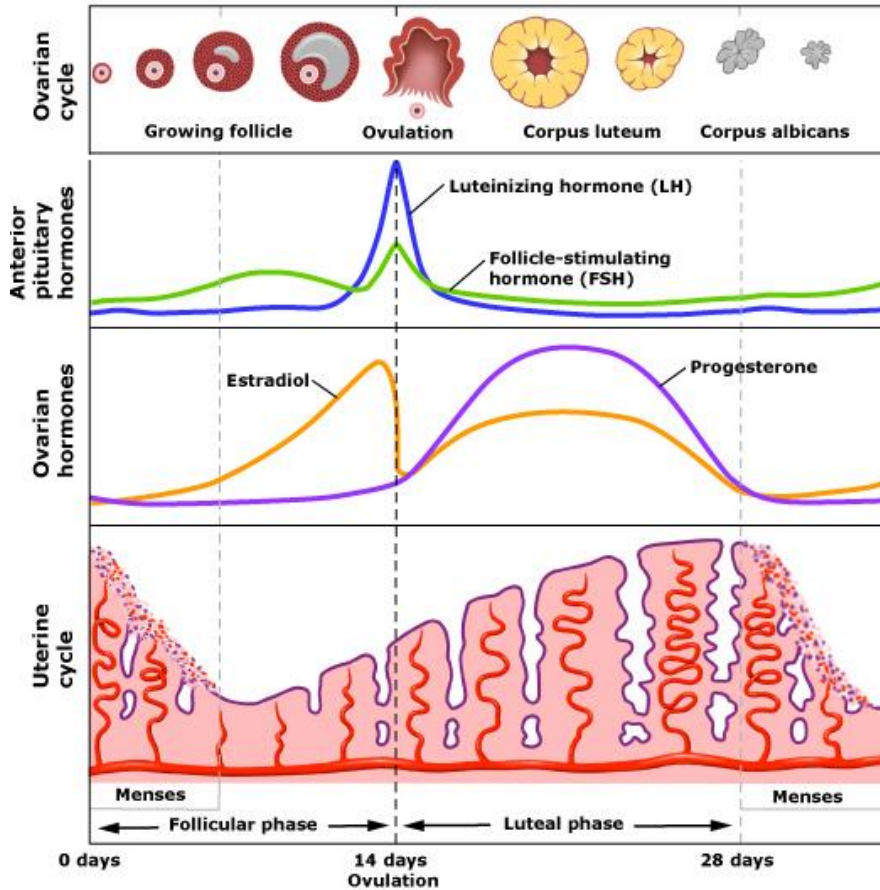
- Complete Adolescent II Quiz & Case Studies

Post-Conference: *Board Review Q&A*

Extra Credit:

- [Pathophysiology of Amenorrhea in the Adolescent](#) (Annals of NYAS, 2008)

A Brief Review of the Normal Menstrual Cycle



A. Three phases:

- (1) **Follicular (proliferative):**
 * Begins w/onset of menstrual flow and ends w/ovulation (7-22d).
 * Begins w/ pulsatile release of **GnRH** from hypothalamus, which leads to **LH** & **FSH** from pituitary.
 * FSH induces maturation of follicles, which produce \uparrow **E2**
 * **E2** causes endometrial thickening

(2) Ovulation:

- * Occurs mid-cycle, after peaking **E2** levels lead to a surge in **LH**.
 * Ruptured ovarian follicle develops into a functioning corpus luteum.

(3) Luteal (secretory):

- * Begins after ovulation and ends w/menstrual flow (12-16d).
 * **P4**, produced by corpus luteum, creates a secretory endometrium.
 * If no fertilization, the CL involutes, leading to \downarrow **E2** & **P4**.
 * This causes endometrial sloughing and **GnRH** release to restart cycle.

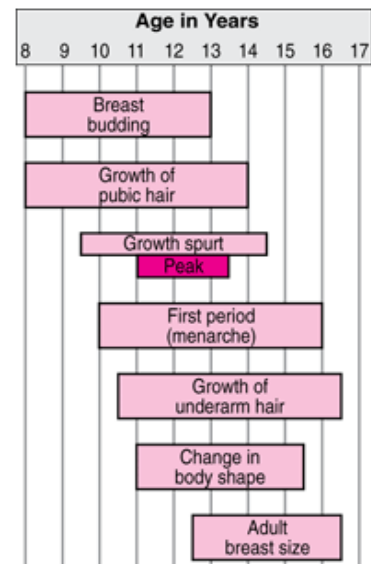
B. Characteristics:

- Length of cycle: 21-35 days
- Duration of flow: 2-8 days
- Cumulative blood loss: 30-80 ml

** Cycles are usually irregular for 1-2 years after menarche because of the lack of consistent ovulation (**anovulatory cycles**).

A Very Brief Review of Normal Female Puberty

- (1) **Adrenarche:** Ages 6-8. Increase in **adrenal androgens** (DHEA, DHEAS) before physical changes are manifest.
- (2) **Gonadarche:** Ages 8-9. Activation of **GnRH** pulse generator and pulsatile **LH**, prior to any physical changes.
- (3) **Thelarche:** Avg age 10-11 (Caucasian); age 9 (AA). Breast development (**E2-dep**). 1st sign in 85% of girls.
- (4) **Pubarche:** 6-12mo post-thelarche. Pubic hair.
- (5) **Growth spurt:** Ages 11-12. Peak GV at SMR 2-3; usually 6mo pre-menarche. Grow ~2in (2-4cm) after menarche.
- (6) **Menarche:** Avg Age 12.5 [9-16yrs]. Onset of menses. At least SMR 4; usually 2-3 yrs s/p thelarche.





CONSULTATION WITH THE SPECIALIST

Author Disclosure

Dr Adams Hillard did not disclose any financial relationships relevant to this article.

Dysmenorrhea

Paula J. Adams Hillard, MD*

Objectives After completing this article, readers should be able to:

1. Recognize the prevalence of dysmenorrhea in adolescents and its common results.
2. Describe a menstrual history that is most consistent with primary dysmenorrhea.
3. List the mediators of uterine pain and contractions believed to be involved in the pathophysiology of primary dysmenorrhea.
4. Recommend the appropriate evaluation and management of primary dysmenorrhea, including the appropriate choice and dosing of both over-the-counter and prescription medications.
5. Recognize patients who should be referred for evaluation of possible causes of secondary dysmenorrhea.

Case

A 15½-year-old girl came to the office with complaints of the recent onset of painful menstrual periods. She experienced her first menstrual period at the age of 13 years and except for an occasional mildly uncomfortable menstrual period, had not experienced significant pain until recently. She reported regular monthly menses, although she did not write down the dates. She described additional symptoms that also had not been present previously, including headache, loose stools, and breast tenderness. She has tried several over-the-counter medications, including acetaminophen, without significant relief. She has missed 3 days of school in the last 6 weeks because of these complaints. She is otherwise healthy, having no major illnesses, no history of surgeries, and no other genitourinary complaints. There is no family history of endometriosis; severe dysmenorrhea; menorrhagia; irregular periods; infertility; uterine fibroids; or breast, ovarian, colon, or uterine cancer. Her mother recalled

that she had been prescribed oral contraceptives at the age of 16 years to alleviate her severe menstrual cramps. When spoken with privately, having been assured confidentiality, the girl denied sexual activity or abuse. She was doing well in school, making As and Bs, and felt that the relationship with her parents and one sister were good. She reported that she experienced crampy midline lower abdominal pain that began with the onset of vaginal bleeding and lasted 1 to 2 days. She rated the pain as being 8 on a scale of 10 and reported that she had to go to bed and sleep to cope with the pain.

This patient has a classic history of dysmenorrhea with minimal symptoms—other painful or uncomfortable symptoms associated with ovulatory menses, including breast tenderness, bloating, nausea, and headaches. She has no history of significant gynecologic or family medical problems. Given her previous inadequate trial of nonsteroidal anti-inflammatory drugs (NSAIDs), she was encouraged to chart her menstrual periods to allow her to predict their onset and to take an adequate dose and scheduled frequency (not prn) of

*Professor, Department of Obstetrics & Gynecology and of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio.

Table 1. Conditions Related to Dysmenorrhea

Conditions That May Cause Secondary Dysmenorrhea

- Endometriosis
- Uterine fibroids
- Obstructive vaginal or uterine congenital anomalies
- Adenomyosis

Conditions That May Mimic Dysmenorrhea or Chronic Pelvic Pain

- Pelvic inflammatory disease
- Pelvic adhesions
- Ovarian cysts
- Inflammatory bowel disease
- Irritable bowel syndrome
- Interstitial cystitis

NSAIDs beginning prior to the onset of bleeding and continuing through the first 2 days of menstrual flow. It was the clinician's judgment that a pelvic examination was not indicated, given the classic symptoms of primary dysmenorrhea. A follow-up visit in 3 months was scheduled.

On return, the patient reported that she had experienced some relief of her pain and now rated her cramps as being 5 on a scale of 10, but she had missed 2 additional days of school over the 3 months. She and her mother both were interested in additional therapy; she reported that one of her girlfriends took oral contraceptives to help her periods. The family history was reviewed to confirm that there was no history of early cardiovascular events, including venous thromboembolism. No relatives had had gynecologic malignancies, including breast cancer. The clinician indicated that a pelvic ultrasonographic examination would provide information to help rule out structural causes of pelvic pain (Table 1), but a pelvic examination still was not be-

lieved to be required. Findings from pelvic ultrasonography were normal. The patient was prescribed combination oral contraceptives; told the potential risks, benefits, and adverse effects; and given specific guidelines to maximize compliance.

After 3 months, the patient returned, stating that she still had not experienced complete relief of her dysmenorrhea. She continued to rate her pain as being 5 on a 10-point scale when on oral contraceptives and NSAIDs. A bimanual examination was performed to assess for uterine tenderness that might suggest pelvic infection or endometriosis. No localized areas of tenderness were palpated posterior to the uterus or in the adnexal regions, as might be present with pelvic endometriosis. However, given the persistence of her symptoms, she was referred to the local medical center for consultation with an adolescent gynecologist and consideration of a diagnostic laparoscopy.

Definitions

Dysmenorrhea is defined as painful menstruation; the word is derived from the Greek words *dys*, meaning difficult/painful/abnormal, *meno*, meaning month, and *rrhea*, meaning flow. Primary dysmenorrhea typically begins during adolescence with ovulatory cycles and is not due to any pelvic disease; secondary dysmenorrhea is uncommon during adolescence and is due to the presence of pelvic disease. Previous attempts to categorize dysmenorrhea as "spasmodic" or "congestive" largely have been abandoned.

Epidemiology

Dysmenorrhea is the most common gynecologic condition of adolescence, occurring in 60% to 93% of adolescents. However, many do not seek medical care. One study reported that only 14% of adolescents

ages 12 to 17 years who had dysmenorrhea and only 29% of those who reported severe dysmenorrhea had seen a physician. Many teens are unaware of effective medications that are available over-the-counter, others do not know where to get gynecologic care, and many fear a pelvic examination.

Dysmenorrhea and other menstrual molimina typically are associated with ovulatory cycles. Because the hypothalamic-pituitary-ovarian axis requires time to mature, the incidence of ovulatory cycles increases with increasing gynecologic age; as many as one third of adolescents continue to experience anovulatory cycles in the fifth year after menarche. Thus, in the first several gynecologic years, dysmenorrhea often is absent or infrequent. It is not unusual for an adolescent to present to the emergency department because of pelvic cramping, experiencing her first episode of dysmenorrhea, and not recognizing that the pain is associated with her menses. Disability associated with dysmenorrhea is common; many teens report modifying their sports, work, and social activities around the time of their menses because of pain, and many miss school frequently. It has been reported that 14% of girls frequently miss work or school because of dysmenorrhea, and nearly 50% of those who have pain describe their pain as moderate or severe. One report in the mid-1980s estimated the economic loss in the United States due to dysmenorrhea among all women to be approximately \$2 billion, with more than 600 million lost work hours.

Dysmenorrhea statistically is more likely among adolescents who have early menarche, heavy menstrual flow, and a family history of dysmenorrhea. There is no association with height, body weight or body mass index, or history of abortion. Most

studies suggest that adolescents who exercise regularly or who smoke are less likely to experience dysmenorrhea. Although the cause of these associations is speculative, it may relate to relative hypoestrogenism and anovulatory cycles.

Pathogenesis

Until the early to mid-1960s, psychological factors were suggested as the major cause of primary dysmenorrhea; more recent studies suggest that emotional distress is not a major etiologic factor. In the 1970s, the pathophysiology of dysmenorrhea was elucidated and linked to the prostaglandin pathway. The physiologic basis of primary dysmenorrhea relates to cell membrane phospholipids, endomyometrial prostaglandins, and leukotrienes. After ovulation, in response to the production of progesterone, fatty acids build up in cell membrane phospholipids. Arachidonic acid and other omega-7 fatty acids are released and initiate a cascade of prostaglandins and leukotrienes in the uterus. These, in turn, mediate an inflammatory response, leading to menstrual cramps and other menstrual molimina. Prostaglandin (PG) F₂-alpha is a cyclooxygenase metabolite of arachidonic acid that causes myometrial hypertonus and vasoconstriction, with resultant ischemia and pain. Individuals who have primary dysmenorrhea produce an excess of endometrial PGs compared with those who have no pain, including, most notably, PGF₂-alpha. An abnormal PGF₂-alpha:PGE₂ ratio also has been reported in association with primary dysmenorrhea. Elevated endometrial levels of PGs have been found to correlate with the degree of pain reported. Infusion of PGF₂-alpha and PGE₂ induces dysmenorrhea. Further support for this mechanism of action is provided by the relief of symptoms

with PG synthetase (cyclooxygenase) inhibitor drugs.

It has been suggested that leukotrienes heighten the sensitivity of uterine pain fibers. High concentrations of leukotriene have been found in adult women who have dysmenorrhea; an increase in urinary leukotrienes also has been shown in adolescent girls who have dysmenorrhea. These substances are potent vasoconstrictors and inflammatory mediators, although the specifics of the mechanisms by which they are involved in causing dysmenorrhea are not well established.

Low back pain occurring in association with dysmenorrhea is due to referred pain from spinal nerves. Bloating may result from sensitivity to progesterone, a smooth muscle relaxant, produced in the second half of the cycle. Subsequent loose stools are a PG-mediated symptom. Migraine or other headaches may be triggered by declining levels of estrogen in the immediate premenstrual phase of the cycle. Mood lability or "premenstrual syndrome (PMS)" is more complex in etiology; cyclic hormonal fluctuations and hormonally mediated fluctuations in neurotransmitters likely are causative, although the specifics of these pathways are not well established. Elimination of hormonal cycling with gonadotropin-releasing hormone (GnRH) agonists has been effective in treating severe PMS and premenstrual dysphoric disorder. Their use is limited by both cost and adverse effects.

The pathologic mechanisms of pain associated with such causes of secondary dysmenorrhea as uterine fibroids, endometriosis, adenomyosis, and other pelvic pathologies may be somewhat more specific to the pathologic entity. Table 1 lists causes of secondary dysmenorrhea or conditions that may need to be considered

in adolescents who experience pelvic pain.

Endometriosis has been found to occur more frequently in first-degree relatives of women whose endometriosis has been confirmed surgically (7%) compared with first-degree relatives of their husbands (1%), suggesting a genetic component to this condition. Polygenic/multifactorial inheritance appears most likely.

Clinical Aspects

Symptoms

The defining symptom of primary dysmenorrhea is crampy midline lower abdominal pain that begins with menstrual flow or a short time before. Typically, the cramps are most intense on the first or second day of flow and resolve before the end of the menstrual flow. The pain may be referred and experienced as lower back or anterior thigh pain. Nausea or vomiting may occur in some individuals. Near-syncope or "dizziness" (not true vertigo) and complaints of "weakness" also can occur. Other premenstrual or menstrual molimina, including breast tenderness, bloating, headache, and mood changes, also may be troublesome or disabling.

Secondary dysmenorrhea is more likely to begin several days or even 1 to 2 weeks prior to the onset of bleeding and to persist through the end of menstrual flow. Associated symptoms, including heavy bleeding, may suggest uterine fibroids as a cause.

Signs

An abdominal examination is important to rule out nongynecologic causes of pain such as irritable bowel syndrome or even gastroesophageal reflux or gastritis. A periumbilical location argues for these latter conditions and against a pelvic/gynecologic etiology. Left lower quadrant full-

ness over the left colon is common with irritable bowel syndrome. The examiner must take care not to mistake the enlarged uterus associated with vaginal outlet obstruction and hematometra for obesity. Abdominal examination findings in primary dysmenorrhea include only mild suprapubic tenderness with normal bowel sounds, no upper abdominal tenderness, and no rebound tenderness.

An abdominal examination can determine abdominal wall trigger points associated with musculoskeletal pain, which is a common concomitant of dysmenorrhea. An evaluation for signs of musculoskeletal pain (Carnett sign) can be helpful. A bimanual examination during menses may reveal mild diffuse uterine tenderness without cervical motion or adnexal tenderness. Although a complete gynecologic/pelvic examination is not mandatory for evaluation of classic dysmenorrhea, inspection of the external genitalia is important to reveal an imperforate hymen or distal uterine septum. Other congenital anomalies such as a didelphic uterus with unilateral obstruction, a longitudinal vaginal septum with hemi-obstruction, cervical agenesis, cervical stenosis, or a partially obstructing uterine septum may not be elucidated completely by pelvic examination; imaging with pelvic ultrasonography or, if this is inconclusive, magnetic resonance imaging may be required.

For adolescents whose external genitalia are normal and who have classic symptoms of dysmenorrhea, a pelvic examination is not required initially. If initial therapy is ineffective, a bimanual examination can be helpful; endometriosis can be associated with mild posterior uterine/cul-de-sac tenderness. The cul-de-sac (pouch of Douglas) posterior to the uterus is the most dependent portion of the pelvis and, thus, the most likely

site for pelvic endometriosis. In adolescents, the classic findings of uterosacral nodularity are rare. The absence of posterior uterine tenderness argues against endometriosis.

Laboratory Tests

Laboratory testing typically is not required for the diagnosis of primary dysmenorrhea. If gastrointestinal (GI) disease is suspected, a rectal examination that includes testing for occult blood may be helpful. An erythrocyte sedimentation rate, while nonspecific, may be abnormal in conditions such as inflammatory bowel disease, but typically is normal with primary dysmenorrhea. Transabdominal or transvaginal ultrasonography can rule out ovarian pathology or an obstructive uterine or vaginal lesion. Transvaginal ultrasonography provides a more definitive picture of the internal pelvic organs. Adolescents who are sexually active usually tolerate this examination well, as can many appropriately informed mid- to older adolescents who have been using tampons successfully. Transvaginal ultrasonography should not be attempted in a virginal younger teen without an assessment of her ability to tolerate this approach and a discussion of what should be expected with the examination.

Diagnosis

The diagnosis of primary dysmenorrhea rests on a classic pain history, with attention to the timing and onset of symptoms (typically a few hours before onset of bleeding and lasting for 1 to 3 d), the nature and location of the complaints (crampy pelvic pain), the presence of menses, the presence of minimal symptoms associated with ovulation, and the lack of other signs or symptoms that suggest a secondary cause. The pain of secondary dysmenorrhea often begins 1 to 2 weeks

prior to menses, may be more constant, and often persists throughout the duration of menstrual flow. A bimanual examination is indicated if signs or symptoms suggest secondary dysmenorrhea. Findings on examination that suggest endometriosis or uterine fibroids may prompt further study, including pelvic ultrasonography or laparoscopy.

Management NSAIDs

The management of primary dysmenorrhea involves the use of NSAIDs, which are cyclooxygenase inhibitors that reduce the production of PGs. Some NSAIDs, in particular meclizolene, inhibit both cyclooxygenase and lipoxygenase pathways, inhibiting the production of leukotrienes as well. This theoretical advantage has not been shown to result in a clear-cut advantage of one NSAID over another. Cyclooxygenase type 2 (COX-2) inhibitors are approved by the United States Food and Drug Administration (FDA) for the treatment of primary dysmenorrhea in adults; pediatric use has not been evaluated. The FDA defines the adolescent subpopulation of pediatrics as including ages 13 to 21 years. Until recently raised questions of the safety of the COX-2 inhibitors have been answered satisfactorily, their use is not recommended for first-line therapy of dysmenorrhea.

Over-the-counter pain medications frequently are used for dysmenorrhea; such use has been reported in 30% to 70% of adolescents. However, many adolescents are unaware of the differences in the mechanism of action of over-the-counter analgesics and often do not distinguish between those that have effective components and those that do not. Several medications that are marketed heavily for dysmenorrhea in teens do not contain components that have any

proven efficacy. In addition, so many different formulations of these over-the-counter drugs exist (Table 2) that even when some of the formulations contain NSAIDs, it is difficult for teens to decipher this from merely knowing the names of the drugs.

Teens commonly take medications for dysmenorrhea that are ineffective. In addition, most lay persons do not understand pharmacology, that is, concepts of loading dose, duration of action, half-life, and sustained serum levels of drugs. They rarely take NSAIDs prophylactically, often take subtherapeutic doses at random intervals, and even may expect a single dose of 200 mg of over-the-counter ibuprofen to last throughout the duration of their cramps. Effective relief of primary dysmenorrhea can be obtained with NSAIDs in up to 80% of teens when taken in appropriate doses and frequency. A Cochrane systematic review concluded that “NSAIDs are an effective treatment for dysmenorrhoea, although women using them need to be aware of the significant risk of adverse effects” and that “there is insufficient evidence to determine which (if any) individual NSAID is the most safe and effective for the treatment of dysmenorrhoea.”

Nonpharmacologic Therapies

Some nonpharmacologic therapies have been shown in small series to be effective for dysmenorrhea. Two of these therapies, transcutaneous electrical nerve stimulation (TENS) and spinal manipulation, have been included in a Cochrane systematic review of efficacy with conclusions of efficacy for primary dysmenorrhea. (1)(2) TENS appears to work by blocking efferent pain stimuli. Topical heat, in the form of either a hot water bottle or heating pad or newer chemical heat-producing adherent

Table 2. Over-the-counter Analgesics Marketed for Dysmenorrhea*

Multicomponent Formulations

- Midol® (Bayer Healthcare LLC)
 - “Menstrual Complete”—500 mg acetaminophen, 60 mg caffeine, 15 mg pyrilamine
 - “Premenstrual Syndrome”—500 mg acetaminophen, 25 mg pamabrom, 15 mg pyrilamine
 - “Teen Formula”—500 mg acetaminophen, 25 mg pamabrom
 - “Cramps and body aches”—ibuprofen 200 mg
 - “Maximum strength extended relief”—naproxen sodium 200 mg (approved by FDA)
- Pamprin® (Chattem, Inc)
 - “Multi-symptom”—500 mg acetaminophen, 25 mg pamabrom, 25 mg pyrilamine (similar to Midol Premenstrual except 15 mg pyrilamine)
 - “All Day”—220 mg naproxen sodium
 - “Cramp”—250 mg acetaminophen, 250 mg magnesium salicylate, 25 mg pamabrom

NSAIDs

- Ibuprofen
 - Motrin® (McNeil Consumer & Specialty Pharmaceuticals)—200 mg q 4 to 6 h; two if no relief; not more than six in 24 h
 - Advil® (Wyeth Consumer Healthcare)—200 mg
 - Nuprin® (McNeil Consumer & Specialty Pharmaceuticals)—200 mg
- Naproxen sodium
 - Aleve® (Bayer Corporation)—220 mg q 8 to 12 h; two as initial dose; not more than three per 24 h
- Ketoprofen
 - Orudis KT® (Whitehall–Robins Healthcare)—12.5 mg

*Note that the only components of the multicomponent formulations that have proven efficacy for dysmenorrhea are naproxen and ibuprofen; thus, the use of the other multicomponent formulations without proven efficacy should be discouraged.

pads, may be effective and is associated with minimal risks. A Cochrane systematic review concluded that spinal manipulation therapy for primary dysmenorrhea was no more effective than sham manipulation. Herbal preparations such as black cohosh, oil of fennel, and evening primrose oil have been suggested, but the data to support their use and safety are sparse.

Oral Contraceptives

Combination oral contraceptives have been prescribed widely in the last 40 years for dysmenorrhea in those who have not experienced sufficient relief with NSAIDs or who also require contraception. Oral con-

traceptives reduce PG release by inhibiting ovulation and, thus, decreasing the progesterone-induced increase in PG synthesis. Decreases in both PGs and leukotrienes have been noted in the menstrual fluid of women taking oral contraceptives compared with controls.

Oral contraceptives are well tolerated in adolescents and provide additional noncontraceptive benefits, such as improvement in acne. Adolescents who experience relief of dysmenorrhea are more likely to use oral contraceptives consistently and correctly. Combination oral contraceptives for management of dysmenorrhea are an appropriate therapy if no

significant medical or family history precludes their use. Some clinicians or parents may be reluctant to begin oral contraceptives for the management of dysmenorrhea in the mistaken belief that they will promote the earlier initiation of sexual intercourse.

Oral contraceptives should be considered for adolescents who have not experienced sufficient relief of dysmenorrhea with NSAIDs. The literature and a Cochrane systematic review support the use of older medium-dose oral contraceptives; clinical practice suggests the efficacy for newer lower-dose oral contraceptives. The Cochrane review states that no clear conclusions can be drawn about the use of newer ultra low-dose oral contraceptives for dysmenorrhea. (3) Thus, a 30- or 35-mcg ethinyl estradiol-containing pill may be preferable to a 20-mcg formulation.

The FDA supports deferring the pelvic examination prior to initiating oral contraceptives in selected adolescents. However, adolescents who have a history of sexual intercourse should undergo sexually transmitted disease testing (which may be performed by using urine-based nucleic acid amplification tests) and may be candidates for cervical cytology testing (depending on the age of initiation of sexual intercourse, as recommended by American Cancer Society guidelines).

One alternative therapy for adolescents who do not have endometriosis but who have persistent dysmenorrhea in spite of oral contraceptives and NSAIDs is the extended cycling of oral contraceptives. A recently marketed combination oral contraceptive has been formulated with 84 days of hormonally active pills followed by 7 days of placebo, rather than the traditional but arbitrary 21/7 formulation. Significant dys-

menorrhea represents an excellent indication for use of oral contraceptives in this manner because menstrual periods and, thus, dysmenorrhea occur less frequently. The packaging of this oral contraceptive makes insurance coverage, compliance, and successful use more likely. Girls using oral contraceptives in this formulation must be cautioned that breakthrough or unscheduled bleeding is not uncommon, particularly in the early 84/7 cycles. Other traditional 21/7 oral contraceptive formulations are equally efficacious and can be used in an extended or continuous fashion by discarding placebos.

Potential Endometriosis

Referrals for possible laparoscopy should be considered to determine the possibility of endometriosis in adolescents: 1) who have persistent dysmenorrhea in spite of adequate doses and frequency of NSAIDs and combination oral contraceptives, 2) who have a first-degree relative who has endometriosis, 3) who have pelvic findings of posterior uterine or cul-de-sac tenderness on pelvic examination, 4) who have a history of significant disability due to pain, 5) who have had costly previous medical evaluations (hospitalizations or GI endoscopy), 6) whose mother or family needs surgical confirmation, 7) who have a high level of anxiety, 8) who are suspected of having psychopathology and will not accept recommendations for counseling without surgical confirmation or refutation, and 9) who are undergoing other surgical procedures such as appendectomy or GI endoscopy.

Although the American College of Obstetricians and Gynecologists *Practice Bulletin on Chronic Pelvic Pain* suggests that empiric treatment with GnRH agonists without laparoscopy be considered as an accept-

able approach to treatment in adults, this author contends that differences between adults and adolescents are sufficient that surgical confirmation is preferable in adolescents. The prospect of condemning an adolescent to a diagnosis of endometriosis carries more potential implications for teens, given their longer prospective reproductive lifetimes. In addition, many adolescents are very concerned about their future infertility and may be less able than adults to understand the implications of endometriosis on fertility. Finally, the potential risks to bone density of therapy with GnRH agonists during a time of adolescent bone growth and accretion are of concern. One small study examined the impact of GnRH agonist therapy for endometriosis on adolescent bone density and found no significant age-related effect on absolute bone mineral density (BMD) loss with a single 6-month course, but the authors urged caution in the use of such therapy prior to the patient achieving peak BMD (mid- to late twenties). In adults, recovery of BMD has been shown and is greater with higher calcium intake. However, nearly 90% of teens do not have an adequate calcium intake, and adolescent basal calcium requirements are higher than adult requirements.

Thus, such therapy may be indicated, but should be determined by a gynecologist who has experience in managing chronic pelvic pain and dysmenorrhea in adolescents and in diagnosing endometriosis surgically. The early lesions of endometriosis may not have the classic “powderburn” appearance that they have in adults; instead, they may appear as clear, vesicular, white, or red lesions that are atypical. If endometriosis is not seen and confirmed by laparoscopic biopsy, the teen and her family should be assured that this informa-

tion is “good news” and that the clinician will continue to work with the family to provide adequate pain relief.

Conclusion

The use of generic NSAIDS with appropriate dosing, frequency, and duration is cost-effective for the relief of primary dysmenorrhea. When NSAIDS provide insufficient relief of dysmenorrhea and secondary causes are not suspected, generic oral contraceptives can provide cost savings and are likely to maintain efficacy. When quality of life is factored into an analysis, the costs of missed hours of school and work due to dysmenorrhea can be considerable. Insurance coverage for oral contraceptives is variable. Some policies do not cover oral contraceptives, even when prescribed for noncontraceptive indications; others may provide coverage for dysmenorrhea if a letter of medical necessity is provided by the clinician. Even when these medications are not covered by prescription benefits, many families conclude that preventive measures such as NSAIDS and

combination oral contraceptives provide a benefit that is worth the cost.

References

1. Proctor ML, Smith CA, Farquhar CM, Stones RW. Transcutaneous electrical nerve stimulation and acupuncture for primary dysmenorrhoea. *Cochrane Database of Systematic Reviews*. 2005. Issue 4. Available at: <http://cochrane.org/reviews/en/ab002123.html>
2. Proctor ML, Hing W, Johnson TC, Murphy PA. Spinal manipulation for primary and secondary dysmenorrhoea. *Cochrane Database of Systematic Reviews*. 2005. Issue 4. Available at: <http://cochrane.org/reviews/en/ab002119.html>
3. Proctor ML, Roberts H, Farquhar CM. Combined oral contraceptive pill (OCP) as treatment for primary dysmenorrhoea. *Cochrane Database of Systematic Reviews*. 2005. Issue 4. Available at: <http://cochrane.org/reviews/en/ab002120.html>

Suggested Reading

- Davis AR, Westhoff CL. Primary dysmenorrhea in adolescent girls and treatment with oral contraceptives. *J Pediatr Adolesc Gynecol*. 2001;14:3–8
- Freeman EW, Rickels K, Sondheimer SJ. Premenstrual symptoms and dysmenorrhea in relation to emotional distress factors in adolescents. *J Psychosom Obstet Gynaecol*. 1993;14:41–50

Golomb LM, Solidum AA, Warren MP. Primary dysmenorrhea and physical activity. *Med Sci Sports Exerc*. 1998;30:906–909

Harel Z. A contemporary approach to dysmenorrhea in adolescents. *Pediatr Drugs*. 2002;4:797–805

Marjoribanks J, Proctor ML, Farquhar C. Nonsteroidal anti-inflammatory drugs for primary dysmenorrhoea. *Cochrane Database of Systematic Reviews*. 2005. Issue 4. Available at: <http://cochrane.org/reviews/en/ab001751.html>

Proctor ML, Latthe PM, Farquhar CM, Khan KS, Johnson NP. Surgical interruption of pelvic nerve pathways for primary and secondary dysmenorrhoea. *Cochrane Database of Systematic Reviews*. 2005. Issue 4. Available at: <http://cochrane.org/reviews/en/ab001896.html>

Proctor ML, Murphy PA. Herbal and dietary therapies for primary and secondary dysmenorrhoea. *Cochrane Database of Systematic Reviews*. 2005. Issue 4. Available at: <http://cochrane.org/reviews/en/ab002124.html>

Schroeder B, Sanfilippo JS. Dysmenorrhea and pelvic pain in adolescents. *Pediatr Clin North Am*. 1999;46:555–571

Slap GB. Menstrual disorders in adolescence. *Best Pract Res Clin Obstet Gynaecol*. 2003;17:75–92

Weissman AM, Hartz AJ, Hansen MD, Johnson SR. The natural history of primary dysmenorrhoea: a longitudinal study. *BJOG*. 2004;111:345–352

Amenorrhea: Evaluation and Treatment

TARANNUM MASTER-HUNTER, M.D., *University of Michigan Medical School, Ann Arbor, Michigan*
DIANA L. HEIMAN, M.D., *University of Connecticut School of Medicine, Hartford, Connecticut*

A thorough history and physical examination as well as laboratory testing can help narrow the differential diagnosis of amenorrhea. In patients with primary amenorrhea, the presence or absence of sexual development should direct the evaluation. Constitutional delay of growth and puberty commonly causes primary amenorrhea in patients with no sexual development. If the patient has normal pubertal development and a uterus, the most common etiology is congenital outflow tract obstruction with a transverse vaginal septum or imperforate hymen. If the patient has abnormal uterine development, müllerian agenesis is the likely cause and a karyotype analysis should confirm that the patient is 46,XX. If a patient has secondary amenorrhea, pregnancy should be ruled out. The treatment of primary and secondary amenorrhea is based on the causative factor. Treatment goals include prevention of complications such as osteoporosis, endometrial hyperplasia, and heart disease; preservation of fertility; and, in primary amenorrhea, progression of normal pubertal development. (*Am Fam Physician* 2006;73:1374-82, 1387. Copyright © 2006 American Academy of Family Physicians.)



ILLUSTRATION BY JOAN BECK

► **Patient information:** A handout on amenorrhea, written by the authors of this article, is provided on page 1387.

Primary amenorrhea can be diagnosed if a patient has normal secondary sexual characteristics but no menarche by 16 years of age. If a patient has no secondary sexual characteristics and no menarche, primary amenorrhea can be diagnosed as early as 14 years of age. Secondary amenorrhea is the absence of menses for three months in women with previously normal menstruation and for nine months in women with previous oligomenorrhea. Secondary amenorrhea is more common than primary amenorrhea.¹⁻³

Pubertal changes typically occur over a three-year period and can be measured using Tanner staging.⁴ The normal progression of female puberty is illustrated in *Table 1*.^{4,5} The normal menstrual cycle involves a complex interaction between the hypothalamic-pituitary-ovarian axis and the outflow tract. Any disruption in this interaction can cause amenorrhea.

Evaluation

Physicians should conduct a comprehensive patient history and a thorough physical exam-

ination of patients with amenorrhea (*Table 2*,⁶⁻⁸). Many algorithms exist for the evaluation of primary amenorrhea; *Figure 1*^{1,7,9,10} is one example. Laboratory tests and radiography, if indicated, should be performed to evaluate for suspected systemic disease. If secondary sexual characteristics are present, pregnancy should be ruled out. Routine radiography is not recommended, however.⁷





Figure 2^{1-3,6} is an algorithm for the evaluation of secondary amenorrhea. The most common cause of secondary amenorrhea is pregnancy. After pregnancy is ruled out, the initial work-up should be based on patient history and physical examination findings. Prolactin levels should be checked in most patients. The risk of amenorrhea is lower with subclinical hypothyroidism than with overt disease. However, the effects of subclinical hypothyroidism on menstruation and fertility are unclear, and abnormal thyroid hormone levels can affect prolactin levels; therefore, physicians should consider measuring thyroid-stimulating hormone (TSH) levels.^{3,11,12} A study¹³ of 127 women with adult-onset amenorrhea showed that

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
A female patient with primary amenorrhea and sexual development, including pubic hair, should be evaluated for the presence of a uterus and vagina.	C	1, 18
Women with secondary amenorrhea should receive pregnancy tests.	C	1-3, 6
Women with polycystic ovary syndrome should be tested for glucose intolerance.	C	21

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1313 or <http://www.aafp.org/afpsort.xml>.

TABLE 1
Normal Female Pubertal Development

<i>Developmental stage (age in years)</i>	<i>Anatomic drawing</i>	<i>Tanner stage</i>	
		<i>Breast development</i>	<i>Pubic hair development</i>
Initial growth acceleration (8 to 10)	Elevation of papilla only; no pubic hair	1	1
Thelarche (9 to 11)	See adrenarche for stage 2 development	2	1
Adrenarche (9 to 11)		2	2
Peak growth (11 to 13)		3	3
Menarche (12 to 14)		4	4
Adult characteristics (13 to 16)		5	5

Illustrations by Renee Cannon.

Information from references 4 and 5.

Amenorrhea

7.5 percent of participants had abnormal prolactin levels and 4.2 percent had abnormal TSH levels.

If TSH and prolactin levels are normal, a progestogen challenge test (Table 3^{3,14}) can help evaluate for a patent outflow tract and detect endogenous estrogen that is affecting the endometrium. A withdrawal bleed usually occurs two to seven days after the challenge test.³ A nega-

tive progestogen challenge test signifies an outflow tract abnormality or inadequate estrogenization. An estrogen/progestogen challenge test (Table 3^{3,14}) can differentiate the two diagnoses. A negative estrogen/progestogen challenge test typically indicates an outflow tract obstruction. A positive test indicates an abnormality within the hypothalamic-pituitary axis or the ovaries.

TABLE 2
History and Physical Examination Findings Associated with Amenorrhea

<i>Findings</i>	<i>Associations</i>
Patient history	
Exercise, weight loss, current or previous chronic illness, illicit drug use	Hypothalamic amenorrhea
Menarche and menstrual history	Primary versus secondary amenorrhea
Prescription drug use	Multiple, depending on medication
Previous central nervous system chemotherapy or radiation	Hypothalamic amenorrhea
Previous pelvic radiation	Premature ovarian failure
Psychosocial stressors; nutritional and exercise history	Anorexia or bulimia nervosa
Sexual activity	Pregnancy
Family history	
Genetic defects	Multiple causes of primary amenorrhea
Pubic hair pattern	Androgen insensitivity syndrome
Infertility	Multiple
Menarche and menstrual history (mother and sisters)	Constitutional delay of growth and puberty
Pubertal history (e.g., growth delay)	Constitutional delay of growth and puberty
Physical examination	
Anthropomorphic measurements; growth chart	Constitutional delay of growth and puberty
Body mass index	Polycystic ovary syndrome
Dysmorphic features (e.g., webbed neck, short stature, widely spaced nipples)	Turner's syndrome
Rudimentary or absent uterus; pubic hair	Müllerian agenesis
Striae, buffalo hump, significant central obesity, easy bruising, hypertension, or proximal muscle weakness	Cushing's disease
Tanner staging (Table 1)	Primary versus secondary amenorrhea
Thyroid examination	Thyroid disease
Transverse vaginal septum; imperforate hymen	Outflow tract obstruction
Undescended testes; external genital appearance; pubic hair	Androgen insensitivity syndrome
Virilization; clitoral hypertrophy	Androgen-secreting tumor
Review of systems	
Anosmia	Kallmann syndrome
Cyclic abdominal pain; breast changes	Outflow tract obstruction or müllerian agenesis
Galactorrhea; headache and visual disturbances	Pituitary tumor
Hirsutism or acne	Polycystic ovary syndrome
Signs and symptoms of hypothyroidism or hyperthyroidism	Thyroid disease
Vasomotor symptoms	Premature ovarian failure

Information from references 2 and 6 through 8.

Evaluation of Secondary Amenorrhea

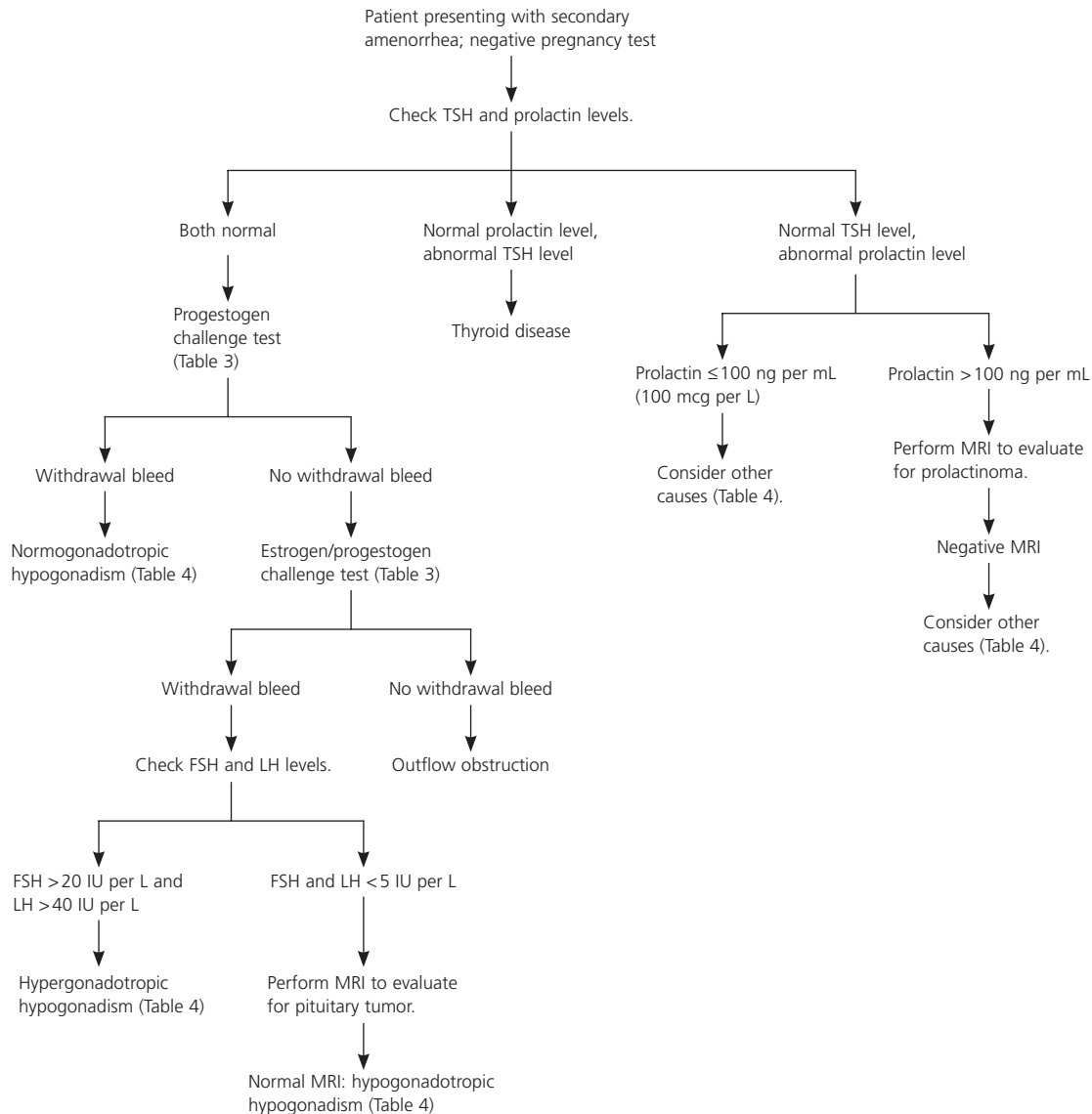


Figure 2. Algorithm for the evaluation of secondary amenorrhea. (TSH = thyroid-stimulating hormone; MRI = magnetic resonance imaging; FSH = follicle-stimulating hormone; LH = luteinizing hormone.)

Information from references 1 through 3 and 6.

physician should continue an evaluation similar to that for secondary amenorrhea (Figure 2^{1-3,6}).¹

ABSENCE OF SECONDARY SEXUAL CHARACTERISTICS

Diagnosis of patients with amenorrhea and no secondary sexual characteristics is based on laboratory test results and karyotype analysis. The most common cause of hypogonadotropic hypogonadism (low FSH and LH levels) in primary amenorrhea is constitutional delay of growth and puberty.^{16,17} A detailed family history also may help detect this etiology, because it often is familial. Hypogonadotropic hypogonadism associated with con-

stitutional delay of growth and puberty is indistinguishable from that associated with hypothalamic or pituitary failure.¹⁰ Watchful waiting is appropriate for constitutional delay of growth and puberty. Kallmann syndrome, which is associated with anosmia, also can cause hypogonadotropic hypogonadism.¹⁸

Hypergonadotropic hypogonadism (elevated FSH and LH levels) in patients with primary amenorrhea is caused by gonadal dysgenesis or premature ovarian failure. Turner's syndrome (45,XO karyotype) is the most common form of female gonadal dysgenesis. Characteristic physical findings include webbing of the neck, widely

TABLE 3

Guidelines for Progestogen and Estrogen/Progestogen Challenge Tests

<i>Drug</i>	<i>Dosing</i>	<i>Duration</i>
Progestogen challenge test		
Medroxyprogesterone acetate (Provera)	10 mg orally once per day	Seven to 10 days
Norethindrone (Aygestin)	5 mg orally once per day	Seven to 10 days
Progesterone	200 mg parenterally once per day	Single dose
Progesterone micronized	400 mg orally once per day	Seven to 10 days
Progesterone micronized gel (4 or 8%)	Intravaginally every other day	Six applications
Estrogen/progestogen challenge test		
Conjugated equine estrogen (Premarin) or	1.25 mg orally once per day	21 days
Estradiol (Estrace) followed by	2 mg orally once per day	21 days
Progestational agent	As noted above	As noted above

Information from references 3 and 14.

spaced nipples, and short stature. Mosaicism occurs in approximately 25 percent of patients with Turner's syndrome.¹⁹ These patients often have a more normal phenotype with spontaneous onset of puberty and menarche. Other rare causes of pure gonadal dysgenesis can occur with a 46,XY or XX karyotype.⁷

Differential Diagnosis of Secondary Amenorrhea

After pregnancy, thyroid disease, and hyperprolactinemia are eliminated as potential diagnoses, the remaining causes of secondary amenorrhea are classified as normogonadotropic amenorrhea, hypogonadotropic hypogonadism, and hypergonadotropic hypogonadism; each is associated with specific etiologies (Table 4^{3,6,15}).

HYPOTHYROIDISM

Other clinical signs of thyroid disease are usually noted before amenorrhea presents. Mild hypothyroidism is more often associated with hypermenorrhea or oligomenorrhea than with amenorrhea. Treatment of hypothyroidism should restore menses, but this may take several months.¹²

HYPERPROLACTINEMIA

A patient with markedly elevated prolactin levels, galactorrhea, headaches, or visual disturbances should receive imaging tests to rule out a pituitary tumor. Adenomas are the most common cause of anterior pituitary dysfunction.¹⁵ A prolactin level more than 100 ng per mL (100 mcg per L) suggests a prolactinoma, and MRI should be performed. If tumor is excluded as the cause, medications (e.g., oral contraceptive pills, antipsychotics, antidepressants, antihypertensives, histamine H₂ blockers, opiates) are the next most common cause of hyper-

prolactinemia. Medications usually raise prolactin levels to less than 100 ng per mL.¹⁵ When hyperprolactinemia is not related to tumor, physicians should identify and treat or eliminate the underlying cause. Table 4^{3,6,15} lists common etiologies of hyperprolactinemia.

If asymptomatic microadenomas (smaller than 10 mm) are found on MRI, repeat prolactin measurements and imaging should be performed to monitor for progression. Microadenomas are slow growing and rarely malignant. Treatment of microadenomas should focus on management of infertility, galactorrhea, and breast discomfort. A dopamine agonist can help improve symptoms and fertility. Bromocriptine (Parlodel) is effective, but cabergoline (Dostinex) has been shown to be superior in effectiveness and tolerability.²⁰ Macroadenomas may be treated with dopamine agonists or removed with transsphenoidal resection or craniotomy, if necessary.

NORMOGONADOTROPIC AMENORRHEA

Two common causes of normogonadotropic amenorrhea are outflow tract obstruction and hyperandrogenic chronic anovulation. The most common cause of outflow obstruction in secondary amenorrhea is Asherman's syndrome (intrauterine synechiae and scarring, usually from curettage or infection).³ Hysterosalpingography, hysteroscopy, or sonohysterography can help diagnose Asherman's syndrome. Other causes of outflow tract obstruction include cervical stenosis and obstructive fibroids or polyps.

Polycystic ovary syndrome (PCOS) is the most common cause of hyperandrogenic chronic anovulation. The National Institutes of Health diagnostic criterion for PCOS²¹ is chronic anovulation and hyperandrogenism

TABLE 4

Causes of Amenorrhea

Hyperprolactinemia	Hypergonadotropic hypogonadism	Hypogonadotropic hypogonadism (continued)
Prolactin \leq 100 ng per mL (100 mcg per L)	Gonadal dysgenesis	Excessive exercise
Altered metabolism	Turner's syndrome*	Excessive weight loss or malnutrition
Liver failure	Other*	Hypothalamic or pituitary destruction
Renal failure	Postmenopausal ovarian failure	Kallmann syndrome*
Ectopic production	Premature ovarian failure	Sheehan's syndrome
Bronchogenic (e.g., carcinoma)	Autoimmune	Normogonadotropic
Gonadoblastoma	Chemotherapy	Congenital
Hypopharynx	Galactosemia	Androgen insensitivity syndrome*
Ovarian dermoid cyst	Genetic	Müllerian agenesis*
Renal cell carcinoma	17-hydroxylase deficiency syndrome	Hyperandrogenic anovulation
Teratoma	Idiopathic	Acromegaly
Breastfeeding	Mumps	Androgen-secreting tumor (ovarian or adrenal)
Breast stimulation	Pelvic radiation	Cushing's disease
Hypothyroidism	Hypogonadotropic hypogonadism	Exogenous androgens
Medications	Anorexia or bulimia nervosa	Nonclassic congenital adrenal hyperplasia
Oral contraceptive pills	Central nervous system tumor	Polycystic ovary syndrome
Antipsychotics	Constitutional delay of growth and puberty*	Thyroid disease
Antidepressants	Chronic illness	Outflow tract obstruction
Antihypertensives	Chronic liver disease	Asherman's syndrome
Histamine H ₂ receptor blockers	Chronic renal insufficiency	Cervical stenosis
Opiates, cocaine	Diabetes	Imperforate hymen*
Prolactin > 100 ng per mL	Immunodeficiency	Transverse vaginal septum*
Empty sella syndrome	Inflammatory bowel disease	Other
Pituitary adenoma	Thyroid disease	Pregnancy
	Severe depression or psychosocial stressors	Thyroid disease
	Cranial radiation	

*—Causes of primary amenorrhea only.

Information from references 3, 6, and 15.

with no other identified secondary cause. The primary etiology of PCOS is unknown, but resistance to insulin is thought to be a fundamental component.²¹

The diagnosis of PCOS is primarily clinical, although laboratory studies may be needed to rule out other causes of hyperandrogenism (Table 5^{6,21}). Significantly elevated testosterone or dehydroepiandrosterone sulfate levels indicate a possible androgen-secreting tumor (ovarian or adrenal). Levels of 17-hydroxyprogesterone can help diagnose adult-onset congenital adrenal hyperplasia. Cushing's disease is rare; therefore, patients should only be screened when characteristic signs and symptoms (e.g., striae, buffalo hump, significant central obesity, easy bruising, hypertension, proximal muscle weakness) are present.^{21,22}

Patients with PCOS have excess unopposed circulating estrogen, increasing their risk of endometrial cancer threefold.²¹ The insulin resistance associated with PCOS increases a patient's risk of diabetes mellitus two- to

fivefold; therefore, testing for glucose intolerance should be considered.²¹⁻²⁴

The primary treatment for PCOS is weight loss through diet and exercise. Modest weight loss can lower androgen levels, improve hirsutism, normalize menses, and decrease insulin resistance. It may take months to see these results, however.²¹ Use of oral contraceptive pills or cyclic progestational agents can help maintain a normal endometrium. The optimal cyclic progestin regimen to prevent endometrial cancer is unknown, but a monthly 10- to 14-day regimen is recommended.²¹ Insulin sensitizing agents such as metformin (Glucophage) can reduce insulin resistance and improve ovulatory function.^{21,25,26}

HYPERGONADOTROPIC HYPOGONADISM

Ovarian failure can cause menopause or can occur prematurely. On average, menopause occurs at 50 years of age and is caused by ovarian follicle depletion. Premature

TABLE 5
Laboratory Evaluation of Hyperandrogenism

<i>Findings</i>	<i>Indications</i>
Serum testosterone (normal: 20 to 80 ng per dL [0.7 to 2.8 nmol per L]) ≤200 ng per dL (6.9 nmol per L) >200 ng per dL	Consider hyperandrogenic chronic anovulation* Evaluate for androgen-secreting tumor
Serum dehydroepiandrosterone sulfate (normal: 250 to 300 ng per dL [0.7 to 0.8 μmol per L]) ≤700 ng per dL (1.9 μmol per L) >700 ng per dL	Consider hyperandrogenic chronic anovulation* Evaluate for adrenal or ovarian tumor
Serum 17-hydroxyprogesterone (normal: <2 ng per mL [6.1 nmol per L])† >4 ng per mL (12.1 nmol per L)	Consider adrenocorticotrophic stimulation test to diagnose congenital adrenal hyperplasia
Dexamethasone suppression test (if clinically indicated)†† Morning cortisol level > 5 μg per dL (138 nmol per L)§	Evaluate for Cushing's disease

*— These values are not specific for diagnosis of hyperandrogenic chronic anovulation.

†—Morning level during follicular phase of menstrual cycle.

††—For an overnight dexamethasone suppression test, the physician should administer a 1-mg dose of dexamethasone orally between 11 p.m. and midnight and draw a single blood sample for serum cortisol testing at 8 a.m. the following day.

§—Morning cortisol level in a healthy patient with an intact hypothalamic-pituitary axis. There is some variability in the cutoff values that can affect sensitivity and specificity of the test. Patients should receive further testing to confirm Cushing's disease.

Information from references 6 and 21.

ovarian failure is characterized by amenorrhea, hypoes-trogenism, and increased gonadotropin levels occurring before 40 years of age and is not always irreversible²⁷ (0.1 percent of women are affected by 30 years of age and one percent by 40 years of age).²⁸ Approximately 50 percent of women with premature ovarian failure have intermittent ovarian functioning²⁹ with a 5 to 10 percent chance of achieving natural conception.

Women with premature ovarian failure have an increased risk of osteoporosis and heart disease.²⁹⁻³¹ The condition also can be associated with autoimmune endocrine disorders such as hypothyroidism, Addison's disease, and diabetes mellitus.^{27,29} Therefore, fasting glucose, thyroid-stimulating hormone (TSH), and, if clinically appropriate, morning cortisol levels should be measured. Other laboratory testing should be determined based on the individual patient.³² Approximately 20 to 40 percent of women with premature ovarian failure will develop another autoimmune disorder; therefore, if initial laboratory tests are normal, periodic screening should be considered. Patients younger than 30 years should receive a karyotype analysis to rule out the presence of a Y chromosome and the need for removal of gonadal tissue.²⁹ Ovarian biopsy and anti-ovarian antibody testing have not been shown to have clinical benefit.^{27,29}

HYPOGONADOTROPIC HYPOGONADISM

Hypothalamic amenorrhea is associated with abnormalities in gonadotropin-releasing hormone (GnRH)

secretion and disruption of the hypothalamic-pituitary-ovarian axis. The condition often is caused by excessive weight loss, exercise, or stress. Other causes are listed in *Table 4*.^{3,6,15} The mechanism of how stress or weight loss affects GnRH secretion is unknown.³³⁻³⁵ Treatment of hypothalamic amenorrhea depends on the etiology. Women with excessive weight loss should be screened for eating disorders and treated if anorexia nervosa or bulimia nervosa is diagnosed. Menses usually will return after a healthy body weight is achieved.³⁵

Young athletes may develop a combination of health conditions called the female athlete triad that includes an eating disorder, amenorrhea, and osteoporosis. Menses may return after a modest increase in caloric intake or a decrease in athletic training. Similar to patients with eating disorders, athletes with continued amenorrhea are at risk of bone loss. In adolescent athletes, the bone loss occurs during peak bone mass development and may not be reversible.^{36,37} Weight-bearing exercise may partially protect against bone loss.³⁸

In patients with amenorrhea caused by eating disorders or excessive exercise, the use of oral contraceptive pills or menopausal hormone therapy may decrease bone turnover and partially reverse bone loss; however, neither therapy has been shown to significantly increase bone mass.³⁸ Bisphosphonates, traditionally used to treat postmenopausal osteoporosis, are possible teratogens and have not been studied as a therapy in women of reproductive age. Adequate calcium and vitamin D intake are recommended for these patients.

Adolescent Quiz—Part II:

1. Based on the average age ranges for “normal female puberty,” how would you define **precocious puberty**? Any physical signs of puberty before age 8 (newer criteria suggest cutoffs of 7 for Caucasian girls and 6 for African American girls, but this is controversial). How would you define **delayed puberty**? No physical signs of puberty by age 13.
2. Clang associations: Match the following H&P findings with appropriate cause of amenorrhea:

(A) Hirsutism or acne	<u>PCOS (normogonadotropic/hyperandrogenic)</u>
(B) Short stature	<u>Turner’s Syndrome (hypergonadotropic)</u>
(C) Psychosocial stressors	<u>Hypothalamic or ED (hypogonadotropic)</u>
(D) Galactorrhea	<u>Hyperprolactinemia (multiple causes)</u>
(E) Striae & central obesity	<u>Cushing’s disease (normogonadotropic)</u>

Which of these is a cause of primary amenorrhea *only*? Turner’s Syndrome
3. What is the female athlete triad? Eating disorder, amenorrhea, & osteoporosis.
4. What is the primary treatment for PCOS? Weight loss (can lower androgen levels, improve hirsutism, normalize menses, and decrease insulin resistance). Use of OCPs can help maintain a normal endometrium and metformin can reduce insulin resistance.
5. Why is primary dysmenorrhea often absent during the 1st several years of menstruation? Because dysmenorrhea is typically associated with ovulatory cycles, and many adolescents experience anovulatory cycles during the 1st several years as the H-P-O axis matures.
6. Which of the following are risk factors for dysmenorrhea?
 - (A) BMI at 90th %ile
 - (B) Menarche at age 9
 - (C) Menstrual flow requiring q2hr pad or tampon changes
 - (D) Smoking (studies show may be *less* likely to experience dysmenorrhea)
 - (E) Mother and grandmother with h/o dysmenorrhea
7. What are the 2 mainstays of treatment for dysmenorrhea and how do they work?
 - (A) OCPs: Inhibit ovulation→ inhibit progesterone release→ inhibit prostaglandin synthesis→ decrease prostaglandin/leukotriene inflammatory cascade.
 - (B) NSAIDs: Inhibit cyclooxygenase→ reduce prostaglandin production→ reduce infl’y cascade

Adolescent Cases—Part II:

Case 1:

A 16 year old female comes to your clinic complaining of “painful periods”. She has had increasingly severe pain that begins less than 1 day before menstrual flow and typically is worst on the first 2 days of flow. She reports moderate bleeding (she has to change her pad every 3-4 hours during the day). She is sexually active with her boyfriend only and “tries to remember” to use condoms for contraception. Vitals are normal for age, except for her weight which is 87% of her ideal body weight.

What additional history would you want to elicit?

- How bad is the **pain** on a scale of 1-10? Where is it located? What is its quality? How does the pain affect her life? (school, work, social)
- Are there any **“molliminal”/ PMS symptoms**? Breast tenderness, bloating, nausea, headache?
- **ROS** which might suggest a non-GYN disorder – IBD, IBS, muscle pain; a dysmenorrhea “mimic”—PID, ovarian cyst; or a cause for secondary dysmenorrhea—congenital anomaly?
- Has she tried any **OTC medications** for pain? If so, when does she take them in relation to her cycle? Is she taking the appropriate dosage? Is she taking them scheduled or PRN?
- **Nutrition history**? Body image?

Is the patient’s history more consistent with primary or secondary dysmenorrhea?

Primary—pain begins a short time before menstrual flow, is most intense on the 1st or 2nd day of flow, and resolves before the end of menstrual flow. (*Secondary*—pain begins several days to 1-2 weeks prior to onset of bleeding and may persist through end of menstrual flow; due to organic disease).

Would you complete a bimanual pelvic examination on this patient? Why or why not?

Arguments can be made both for and against doing a pelvic exam:

PRO: Sexually active patient with unreliable contraception history presenting with pelvic pain.

Do pelvic exam to r/o PID (+ cervical motion tenderness)

CON: Classic sx’s of primary dysmenorrhea. If external genitalia are normal, a pelvic exam is not required initially. If initial therapy is ineffective, a bimanual exam may be helpful (i.e. to r/o endometriosis or other causes of chronic pelvic pain).

The following additional information becomes available: Bimanual examination reveals no tenderness of the uterus, posterior cul-de-sac, or adnexae; her Tanner staging and genital examination is normal. Other physical findings include pale conjunctiva, poor dentition, and 4-5 closed comedones on her chin and forehead.

What is the most likely diagnosis or diagnoses? Why?

- **Pelvic pain:** Consider primary dysmenorrhea, fibroids, ovarian cyst, endometriosis
- **Other:** Consider anemia (excessive bleeding?); an eating disorder (ED-NOS?: poor dentition, weight nearly meets AN criteria-- <85% of IBW); acne vulgaris (*see Adol III*).

What labs, if any, will you obtain?

No labs related to likely diagnosis of primary dysmenorrhea. BUT . . .

- May consider laboratory evaluation for **STDs**, given admission of unprotected sex (e.g. Gonorrhea and Chlamydia urine NAAT; RPR for Syphilis; Hep B surface Ag, HIV . . . *discussed in more detail in Adolescent III module*).
- May consider laboratory evaluation for **ED**, depending on results of history-taking (e.g. CBC, BMP, U/A, TFTs . . . *see Nutrition II module*).
- Also consider checking **hCG** to r/o pregnancy.

How will you manage this patient?

Start with **combination OCPs**, given need for dysmenorrhea relief, contraception, AND acne treatment. The Cochrane review suggests that a 30-35 mcg ethinyl estradiol pill may be best.

35 mcg ethinyl estradiol	1 mg norethindrone	Nortrel 1/35 ^d Necon 1/35 ^a Norinyl 1+35 ^a
35 mcg ethinyl estradiol	0.5 mg norethindrone	Brevicon ^a Nortrel 0.5/35 ^d Necon 0.5/35 ^a
35 mcg ethinyl estradiol	0.4 mg norethindrone	Ovcon-35 ^b
35 mcg ethinyl estradiol	0.25 mg norgestimate	Ortho-Cyclen ^c
35 mcg ethinyl estradiol	1 mg ethynodiol diacetate	Zovia 1/35E ^a
30 mcg ethinyl estradiol	1.5 mg norethindrone acetate	Loestrin Fe 1.5/30 ^f Mirogestin Fe 1.5/30 ^a
30 mcg ethinyl estradiol	0.3 mg norgestrel	Lo/Ovral ^c Cryselle ^d Low-Ogestrel ^a
30 mcg ethinyl estradiol	0.15 mg desogestrel	Desogen ^a Ortho-Cept ^c Apri ^d
30 mcg ethinyl estradiol	0.15 mg levonorgestrel	Nordette ^h Levlen ⁱ Levora 0.15/30 ^a Portia ^d
30 mcg ethinyl estradiol	3 mg drospirenone	Yasmin 3/0.03 ⁱ

You could also recommend **extended cycling (84/7)** of oral contraceptives (e.g. Seasonale). Finally, consider using **NSAIDs** concurrently. Ensure appropriate dosage and frequency.

How will you follow-up with this patient? When would you refer to OB-GYN?

This is open for discussion. Consider following up 1-2 weeks after starting OCPs to ensure no troublesome side-effects. Then, consider following up after 1 menstrual cycle to determine effectiveness of OCPs and/or NSAIDs in alleviating abdominal/pelvic pain.

Referral to OB-GYN to r/o endometriosis (i.e. with possible laparoscopy) can be made if patient has persistent dysmenorrhea in spite of adequate doses and frequency of NSAIDs and combination OCPs. *Other criteria are listed on p.69 of PIR article.*

Flashback: What health maintenance and immunization needs does this patient have?

- Screen for TB and dyslipidemia risk factors. STI and cervical dysplasia screening.
- Ensure Tdap, Menactra, and HPV. Ensure seasonal influenza.

Case 2:

You are the clinic PGY3 and are assigned to precept one of the eager Sub-I's. At the end of the day, you review the following HPI for co-sign:

15.5 yo female presents for school physical. Parental concern for missed menses x 1 year. Menarche age 13, with regular periods for approx 6 months. Then became irregular, skipping 1-2 months at a time. Usually lasted 7 days, with three pad or tampon changes daily. No spotting or dysmenorrhea. After 1 year of 'irregular' periods, had 1 year of amenorrhea. 3 days ago, had one day of very light bleeding that she hardly could consider a period. No vaginal discharge, sexual activity, dysuria, or changes in bowel habits.

Based on the Sub-I's history, does the patient have primary or secondary dysmenorrhea?

Secondary—absence of menses for 3 months in women with previously normal menstruation and for 9 months in women with previous oligomenorrhea. (Remember, though, that the 1st 2 years of an adolescent's menstrual cycle can be irregular due to anovulatory cycles).

What additional historical information should the Sub-I have documented and why?

- **HEADSS interview:** Is she stressed? Dieting/purging? Depressed? Sexually active? – may elicit pregnancy, hypothalamic amenorrhea (e.g. due to stress), eating disorder
- **Endocrine symptoms:** Hirsutism, acne, voice deepening, acanthosis nigricans; changes in hair/nails, hot/cold intolerance— may suggest PCOS; hypothyroidism.
- **Neuro symptoms** – headache, galactorrhea, vision change— may suggest prolactinoma.

Reading further, you see the following additional history documented by the Sub-I:

ROS:

-no hirsutism, deepening of voice, or changes in acne pattern
-no headaches, changes in vision, galactorrhea
-no hot/cold intolerance, changes in skin or nails, rashes, or diarrhea/constipation.

HEADSS:

-H: lives with step mother, father, and 4 siblings; real mother lives in California; approx 16 months ago real mother initiated legislation for custody of patient; patient wants to live with her mother
-E: 9th grade, A/B student, feels safe at school and home
-A: works out 3 days per week, has good social support, enjoys hanging out with friends
-D: no depressive symptoms, sleeping 7-10 hours per night without problems, no drugs/EtoH/herbals
-S: no sexual activity, no suicidality
-Diet history: Multiple attempts to lose weight in the last year. Tries a diet for 1 week, gets bored and goes off of it for 3-5 weeks before starting a new diet. During her 'on diet' weeks, she also increases her physical activity to 4-5 days per week, 1 hr each session. She has not lost any weight in the last year.

You had previously completed your own physical exam on the patient, which showed normal vital signs, including BMI, and an unremarkable physical exam with Tanner 4 breast and pubic hair and no acne, hirsutism, or acanthosis nigricans.

What is your working diagnosis?

Consider causes of **secondary amenorrhea**:

- Pregnancy; Hypothyroidism; Hyperprolactinemia
- Normogonadotropic amenorrhea (e.g. **PCOS**)
- Hypergonadotropic hypogonadism (e.g. premature ovarian failure)
- Hypogonadotropic hypogonadism (e.g. eating disorder, chronic illness, **hypothalamic amenorrhea due to excessive weight loss, exercise, or stress**—*most common cause*)

What labs, if any, will you obtain?

See **Secondary Amenorrhea Algorithm**. (*Algorithm shows stepwise approach, but many providers obtain the labs in concert to expedite the work-up. The following is per Dr. Vogt.*)

→ **First Line Tests:**

- Pregnancy test, TSH, prolactin.
- LH/FSH: To distinguish hyper vs. hypogonadotropic hypogonadism. Can also see an elevated LH:FSH ratio in PCOS, but this is not very sensitive.
- Testosterone (free + total): To help diagnose PCOS. (Free can be elevated in PCOS even with normal total T. Also can be elevated with minimal physical signs of hyperandrogenism.)

→ **Second Line Tests:**

- Estradiol: To identify hypogonadotropic hypogonadism (assay isn't very good, though)
- DHEAS, 17OHP: If significant hirsutism or other signs of hyperandrogenism. DHEA-S can support diagnosis of PCOS or r/o adrenal tumor; 17OHP can r/o CAH.
- CBC, CMP, U/A: If clinical signs point towards chronic disease.
- Pelvic Ultrasound: If tumor is suspected.
- Progesterone withdrawal test (progestogen challenge): MPA 10mg x 10 days to test for presence of adequate estrogen exposure to build up the uterine lining. Can narrow differential, but many skip this step.

How will you manage this patient?

Treatment depends on underlying cause. Consider starting OCPs.

Flashback: What nutritional deficiencies is she at risk for and how would you address?

Adolescent females with continued amenorrhea are at risk for bone loss. Recommendation for 1000 mg calcium/day and 600 IU Vitamin D/day.

You reach the end of your Sub-I's note and see that she listed "Established patient age 12-17 school/camp physical" (V70.3) as the only ICD-9 code in her A/P. Recalling what you learned from Dr. Labow when you were a Sub-I, **how would you amend her A/P?**

Include other diagnosis made during the well-child visit using the **25 modifier** under the "Additional E&M Coding" Tab (i.e. Secondary Amenorrhea); this generates an additional +0.45 RVUs. Depending on what your Sub-I accomplished, you could add **procedure codes** for the following: med counseling (98960); urine HCG test (81025); venipuncture (36410).

Adolescent Board Review—Part II:

1. A 15-year-old girl is concerned about irregular menses and acne. Menarche was at age 11 years and 9 months, and she remembers developing pubic hair around age 7 years. On physical examination, her vital signs are normal and her body mass index is 32.3 kg/m². She has facial comedonal and papular acne as well as mild darkening of the skin of her neck and axilla. You also note hypopigmented, narrow stretch marks on her abdomen and hair in a linear distribution from her umbilicus to the pubic symphysis and on the upper inner surface of her thighs. She is at Sexual Maturity Rating 5, and clitoral diameter is 2 mm.

Of the following, the MOST likely diagnosis is

- A. Cushing syndrome
- B. hypothyroidism
- C. metabolic syndrome
- D. physiologic anovulation
- E. polycystic ovarian syndrome**

The presence of acanthosis nigricans combined with obesity (body mass index >30 kg/m²), acne, and some increase in body hair described for the girl in the vignette as well as irregular menses 3 years after menarche suggests the need for further evaluation for polycystic ovarian syndrome (PCOS). The diagnosis of PCOS, using the 2003 Rotterdam criteria, requires, in addition to exclusion of related conditions, the presence of two of the following three criteria: 1) oligo- or anovulation, 2) clinical or biochemical signs of hyperandrogenism, and 3) polycystic ovaries. Oligo- or anovulation presents as irregular menses, and hyperandrogenism may present as acne, increased body hair, and rarely, clitorimegaly (a transverse clitoral diameter greater than 3 mm). The severity of hirsutism may be assessed using the Ferriman-Gallwey Scoring system. A score ranging from 0 (no hair) to 4 (frankly virile [extensive hair growth]) is assessed for each of nine body areas most sensitive to androgens. These sites include the upper lip, chin, chest, abdomen, suprapubic region, arms, thighs, upper back, and lower back. A score of 8 or more is considered significant and suggestive of increased androgen concentrations. The severity of acne and hirsutism, however, may not correlate well with the concentrations of androgens because the response of the androgen-dependent follicle to androgen excess varies considerably between and within persons. Therefore, total and free testosterone measurement may be supportive.

A number of risk factors for PCOS have been outlined at various stages of development. One of these factors is premature adrenarche, which is the appearance of pubic hair before age 8 years without other evidence of puberty. Whether peripubertal obesity predisposes to PCOS remains to be determined. Those who have risk factors for insulin resistance such as acanthosis nigricans or a family history of type 2 diabetes and cardiovascular disease may be at increased risk for PCOS. Acanthosis nigricans is a velvety hyperpigmentation and thickening of the skin on the nape of the neck, axilla, and other body folds. It is a nonspecific sign of insulin resistance.

A number of disorders may be considered in the differential diagnosis of PCOS but are not associated with signs of androgen excess. Patients who have hypothyroidism may be overweight and have menstrual disturbances, but they typically have other symptoms, including hair loss, constipation, and dry skin. A common symptom of Cushing syndrome is sudden weight gain. In addition, affected patients have signs or symptoms of cortisol excess such as muscle weakness; facial rounding and plethora; easy bruising; and multiple wide, purplish striae on the abdomen, not the narrow hypopigmented type exhibited by the patient in the vignette. In addition to central obesity and high blood pressure, patients who have metabolic syndrome have elevated fasting glucose and triglyceride values and decreased high-density lipoprotein cholesterol values. Metabolic syndrome is common in those who have PCOS, and such patients should be screened regularly for metabolic syndrome. Physiological anovulation becomes less likely as an explanation for irregular menses 3 years after menarche.

2. A 15-year-old girl complains of significant pain with her monthly menstruation that results in her missing school for 1 day each month. The pain is worse on the first day and subsides spontaneously over the next 2 days. She has tried ibuprofen and naproxen sodium with no relief. On physical examination, you note pustular acne diffusely over her face and trunk. Other findings are normal.

Of the following, the medication that is MOST likely to be of benefit for both of this girl's problems is

- A. acetaminophen
- B. diuretic with menses
- C. isotretinoin
- D. omega-3 fatty acids

E. oral hormonal contraception

Hormonal methods of contraception are associated with health benefits beyond pregnancy prevention. An understanding of the noncontraceptive benefits of these birth control methods can increase compliance and continuation of use, thus decreasing unplanned pregnancy. The noncontraceptive benefits include a decrease in ovarian cyst formation as well as ovarian, endometrial, and colorectal cancer. They offer some protection against salpingitis and ectopic pregnancies and decrease benign breast disease and acne. They also decrease dysmenorrhea and menorrhagia, reduce iron deficiency anemia and osteoporosis, and decrease the symptoms of polycystic ovarian syndrome. Accordingly, the girl described in the vignette may experience relief of her dysmenorrhea and some improvement in her acne with oral hormonal contraception.

Diuretics have been used for the treatment of bloating and weight gain associated with menstruation. Spironolactone, a potassium-sparing diuretic and androgen receptor blocker, has achieved the greatest popularity, largely as a result of specific properties that make this agent uniquely suited to hormonally based disorders. Other diuretics have been tried for treatment of premenstrual syndrome, with variable success in alleviating water retention symptoms. However, diuretics are not effective in the management of dysmenorrhea. Acetaminophen does not target the prostaglandins causing menstrual cramps. Early evidence suggested possible benefits of fish oil/omega-3 fatty acids for women who have dysmenorrhea, but further studies are required to confirm these findings. Isotretinoin is indicated for nodular acne or severe acne that is unresponsive to conventional therapies but would not improve dysmenorrhea.

3. The mother of a 12-year-old white girl is concerned because her daughter has not yet menstruated. Most of her daughter's classmates are menstruating. She does not remember when her daughter began breast development but states that the girl is now taller than her 13-year-old brother. The mother asks if you can estimate when her daughter is going to have her first menstrual period.

Of the following, the MOST appropriate next step to answer the mother's question is to

- A. determine bone age
- B. determine Sexual Maturity Rating**
- C. measure alkaline phosphatase
- D. obtain an endocrinology consultation
- E. order pelvic ultrasonography

The National Health and Nutrition Examination Survey (NHANES) III and the National Health Examination Survey (NHES) indicate that the median age of menarche in United States girls is 12.43 years and has not changed over the past 3 decades. Certain ethnic differences have emerged, with non-Hispanic black girls having menses earlier than white girls and menses for Hispanic girls falling between these two groups. The interval between breast development (the first sign of puberty in females) and menstruation is 2.3 ± 0.1 years, but the range is 0.5 to 5.75 years. Most adolescents (62%) menstruate when they reach Sexual Maturity Rating (SMR) stage 4, with 26% in stage 3 and 11% in stage 5. Only 1% menstruate in stage 2. Menarche occurs approximately 3.3 years after the onset of the growth spurt and 1.1 years after the peak height velocity is attained. The percentage of

body fat is critical; according to Frisch's theory, a minimum body fat value of 17% is required to initiate menses and a value of 22% is required to maintain regular cycles.

The girl described in the vignette has had a significant growth spurt, which indicates that she has entered puberty and is probably in SMR stage 2 or 3. If this is confirmed by clinical examination, no further evaluation is necessary and it is likely that the girl will begin menstruating in the next year or two. A mother's age of menstruation can be used as a guide for her daughters' menarche, but is not as useful as determination of her daughter's SMR. If a patient shows no sign of pubertal development by age 13.5 years or if there is no progression of puberty, endocrinologic consultation and performance of pelvic ultrasonography may be indicated. The bone age is a useful tool in patients who have delayed puberty because pubertal events correlate most closely with bone age and not chronologic age. Measuring serum alkaline phosphatase will not be of benefit in predicting menarche.

4. A 15-year-old girl presents for treatment of menstrual cramps. She had menarche 3 years ago, and over the last year, she has begun having pain on the first day of her cycle. She says that if she can get past the first day, the pain decreases and goes away in the next day or two. The herbal tea her mother was giving her no longer works.

Of the following, the MOST effective initial treatment for this girl's symptoms is

- A. acetaminophen
- B. calcium channel blocker
- C. combined oral contraceptive
- D. ibuprofen**
- E. omega-3 fatty acids

Dysmenorrhea or painful menstrual bleeding is the leading cause of recurrent, short-term school absenteeism and lost work time among adolescent girls. Primary dysmenorrhea refers to painful menses with normal pelvic anatomy and starts when menstrual cycles become ovulatory. A presumptive diagnosis can be based on a typical history of lower abdominal pain that begins shortly before or with the onset of menses and lasts 1 to 3 days with normal findings on physical examination. Potential associated symptoms include headaches, back pain, vomiting, and diarrhea.

The pathogenesis of primary dysmenorrhea is believed to be related to increased endometrial prostaglandin production, which causes myometrial contractility that, if excessive, leads to uterine ischemia and pain and the other associated symptoms. Elevated vasopressin concentrations also are observed in affected patients. Risk factors for primary dysmenorrhea include nulliparity, heavy menstrual flow, smoking, and poor mental health and social supports. If the history or examination findings are inconsistent with primary dysmenorrhea, further evaluation for secondary causes is necessary.

Initial therapy for dysmenorrhea includes drugs that inhibit the synthesis of prostaglandin through the prostaglandin synthetase system and antagonize their action at the cell receptor level. The most established medications are the nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen. They have been found to be significantly more effective for pain relief than placebo. Evidence is insufficient to determine which NSAID is the safest and most effective for the treatment of dysmenorrhea. However, clinical trials have shown that all NSAIDs are more effective than acetaminophen. These medications are available over the counter and, thus, should be the first line of treatment. Specific cyclooxygenase-2 inhibitors also may relieve dysmenorrhea symptoms.

In as many as 20% to 25% of patients, NSAIDs are not effective and alternate treatment such as combined hormonal contraceptives is indicated. Combined hormonal contraceptives act by suppressing ovulation and lessening the endometrial lining of the uterus. Therefore, both menstrual fluid volume and the amount of prostaglandins produced decreases, which effectively reduce dysmenorrhea by decreasing uterine motility and

uterine cramping. Other hormonal contraceptive products have been used for treatment of dysmenorrhea, including depomedroxyprogesterone acetate and levonorgestrel intrauterine device. All hormonal methods of contraception are prescription medications and require a doctor's visit. This increases their cost in time and money. Therefore, they are recommended for use only if NSAIDs are not effective. Several medications that are effective in inducing uterine relaxation have been proposed as treatment for dysmenorrhea. For example, early uncontrolled trials of calcium channel blockers have shown promise but require further investigation.

Many consumers are seeking alternatives to conventional medicine, and research into the menstrual cycle suggests that nutritional intake and metabolism may play an important role in the cause and treatment of menstrual disorders. One small trial showed fish oil (omega-3 fatty acids) to be more effective than placebo for pain relief. However, evidence is not yet strong enough to recommend the use of any herbal and dietary therapies for the treatment of primary or secondary dysmenorrhea. Pelvic nerve interruption has been suggested for recalcitrant cases of dysmenorrhea, but this procedure is not recommended in the management, regardless of cause.

5. You are seeing a 15-year-old girl for her annual health supervision visit. Her menarche occurred at age 12 years, and she had normal monthly menses over the first 2 years. In the last year, however, her periods became progressively more irregular and stopped 4 months ago. Her mother notes that the girl has been very health-conscious since she entered puberty. She has gained no weight over the last 3 years and is on the cross-country team at school. On physical examination, her body mass index is 17 kg/m², her heart rate is 55 beats/min, she has no acne or hirsutism, and she is at Sexual Maturity Rating 5 genital development. The remainder of the physical examination findings are normal.

Of the following, the MOST likely cause of this girl's amenorrhea is

- A. ergogenic agents
- B. exercise regimen**
- C. heart disease
- D. physiologic anovulation
- E. school stress

The American College of Sports Medicine coined the term "the female athlete triad" in 1992. It comprises three interrelated components: disordered eating, amenorrhea, and osteoporosis. The risk of the disorder is greatest among those participating in endurance sports. Athletes are distributed along a spectrum between health and disease, and those at the pathologic end may not exhibit all of the components simultaneously. The girl described in the vignette has amenorrhea that is related to her level of exercise and inadequate nutrition.

Nutrition issues underlie most of the pathophysiology of the female athlete triad. Energy availability is defined as dietary energy intake minus exercise energy expenditure. Exercise-induced amenorrhea can be an indicator of decreased energy availability that may be inadvertent, intentional, or psychopathological. Bone density loss results from the low estrogen environment and is concerning because 50% of adult skeletal mass is laid down during adolescence, with peak bone mass attained between ages 18 and 25 years.

The first aim of treatment for any triad component is to increase energy availability by increasing energy intake, reducing exercise energy expenditure, or both. Nutrition counseling and monitoring are sufficient for many athletes, but significantly disordered eating warrants more intensive intervention.

Education of athletes, parents, coaches, trainers, judges of competitions, and administrators is a priority for prevention and early intervention. Athletes should be assessed for the triad during preparticipation physical examination or the annual health screening examination and whenever an athlete presents with any of the triad's symptoms or signs. Sports administrators should consider rule changes to discourage unhealthy weight loss

practices. Athletes who have eating disorders should be required to meet established weight criteria to continue exercising, and their training and competition may need to be modified.

Ergogenic aids are dietary supplements used to enhance athletic performance. The most commonly used are those that have supposed anabolic effects because they mimic the effects of steroids and are legal for use. Creatine is the most widely used such supplement taken by both professional and recreational athletes. It causes weight gain from muscle hypertrophy and fluid retention. It does not alter vital signs or cause menstrual changes. The girl described in the vignette has no symptoms referable to the cardiovascular system; her low heart rate likely is a result of her inadequate nutrition and exercise. In the first 2 years following menarche, irregular menses may be the result of immaturity of the hypothalamic pituitary axis (physiologic anovulation). However, this girl's regular menses in the first 2 years make physiologic anovulation a less likely cause of the amenorrhea. Psychological stress in an adolescent may cause amenorrhea, but the history and examination findings of this girl are most consistent with amenorrhea resulting from exercise.

6. A 13-year-old girl presents with severe lower abdominal pain of 24 hours' duration. She states that the pain is sharp and constant and that she has had similar pain for several days approximately monthly over the past 4 months. She has no vomiting or diarrhea with the pain, but she is constipated frequently, having a bowel movement about every 3 to 4 days. She feels that her jeans are getting tighter around the waist, although she remains active, playing soccer daily. She has never had a menstrual period and denies ever being sexually active. On physical examination, she is afebrile, her heart rate is 85 beats/min, and her blood pressure is 110/70 mm Hg. Her weight is at the 60th percentile and her height at the 50th percentile for age. Her breasts and genitalia are at Sexual Maturity Rating 5. Abdominal examination reveals a firm and tender midline mass that is inferior to the umbilicus.

Of the following, the MOST likely diagnosis is

- A. bladder obstruction
- B. endometriosis
- C. hematocolpos**
- D. megacolon
- E. ovarian cyst

The adolescent described in the vignette has a clinical history and physical examination findings compatible with an imperforate hymen, which probably is the most common obstructive anomaly of the female reproductive tract. An adolescent patient who has an imperforate hymen may be asymptomatic or may have a history of cyclic abdominal pain that may occur for several years before the diagnosis is made. A bluish, bulging hymen may be seen on genital inspection, and a distended vagina may be palpated on rectoabdominal or abdominal examination. If the vagina becomes substantially enlarged with accumulated blood, the patient may experience back pain, pain with defecation that can result in constipation, nausea and vomiting, or difficulty in urinating.

Bladder outlet obstruction occurs rarely, and although it produces a suprapubic mass, it does not cause cyclic abdominal pain. Megacolon also is unlikely and does not cause cyclic pain, although colonic irritation may develop from the pressure produced by the mass. An ovarian cyst typically causes a right- or left-sided (not midline) mass, and endometriosis is an unlikely cause of a palpable mass, although it can cause cyclic and acyclic pain in adolescents.