

The adolescent with irregular menses

By Beth A. Kutler, FNP-C

When is intervention necessary?



The NP learns that most of NM's periods are light, with no cramping. On occasion, she has a heavy period that requires a super tampon change every hour and that is associated with moderate cramps. She says she can predict a heavy period because she has breast tenderness and feels moody right before it starts.

NM and her boyfriend started to have sex 6 months ago and have been consistently using condoms. She has never been pregnant but has never been tested for a sexually transmitted infection (STI). She has not noticed any unusual vaginal discharge or pelvic pain. She has completed the HPV vaccination series.

NM does not smoke, drink alcohol, or use illicit drugs. She denies food binging or food-restricting behaviors. Her exercise is limited to participating in gym class twice a week. She sleeps 7-8 hours each night without problem. She has no major stressors at school, at home, or with peers.

The patient takes no medications other than occasional over-the-counter (OTC) pain remedies for menstrual cramps or headaches. NM reports that the headaches occur only prior to her heavy periods, are sometimes severe enough to keep her from her usual activities, and are relieved by rest and OTC

NM is a 16-year-old female who presents to the clinic with concerns about irregular periods. She tells the nurse practitioner (NP) that she had her first period when she was 14 and that her cycles have never been regular, ranging from 1 to 3 months. Her last menstrual period was about 2 months ago and she

thinks that she has had only four or five periods over the past year. In addition, NM is interested in discussing contraception.

What else is helpful to know about NM?

Because NM has come to the clinic for the first time, the NP takes a comprehensive health history. Given NM's report of irregular periods, the NP obtains a thorough gynecologic, sexual, endocrine, medication, and lifestyle history. The NP also takes a family history to discern any relevant endocrine disorders.

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medications. The headaches are not preceded by an aura or other neurologic signs or symptoms (S/S). NM relates an additional concern—acne—which has been worsening over the past 4-6 months. OTC acne medications have provided only minimal improvement.

In a review of systems, the NP further explores any S/S that might suggest that an endocrine disorder is causing or contributing to NM's menstrual irregularity. NM denies hair loss, unusual hair growth, weight changes, heat or cold intolerance, fatigue, change in headaches, visual changes, breast nipple discharge, or bowel function changes. Her family history is positive for hypothyroidism and type 2 diabetes in her mother and infertility in an older sister.

The combination of menstrual irregularity and acne alerts the NP to possible hyperandrogenism associated with PCOS.

Which differential diagnoses are you considering at this point?

NM is experiencing infrequent periods that are most likely anovulatory. Ovulatory cycles are typically characterized by regular intervals (28-32 days) and cramping and are often preceded by minimal symptoms such as breast tenderness and moodiness. Menstrual irregularities in adolescents are usually related to aberrations in the

hypothalamic–ovarian–pituitary axis and fall into one of two distinct categories, hypothalamic menstrual disorders or endocrinopathies. Hypothalamic menstrual disorders are usually associated with alterations in stress, diet, exercise, and/or body weight. Endocrinopathies associated with menstrual irregularities include thyroid disorders, hyperprolactinemia, hyperandrogenic anovulation or polycystic ovary syndrome (PCOS), adult-onset congenital adrenal hyperplasia (CAH), and Cushing syndrome.¹

Based on NM's history, her menstrual irregularity cannot be ascribed to changes in stress, diet, exercise, or body weight. She has no S/S of a thyroid disorder or hyperprolactinemia other than the menstrual irregularity. The combination of menstrual irregularity and acne, albeit common in adolescents, alerts the NP to possible hyperandrogenism associated with PCOS. As such, the NP will look for physical examination findings and choose laboratory tests in consideration of possible hyperandrogenism. Adrenal disorders such as CAH and Cushing syndrome are uncommon but will be explored if indicated.

Which elements do you include in your physical examination?

NM's blood pressure is 128/78 mm Hg and her body mass index (BMI) is 26.3 kg/m². A urine hCG is negative. She has moderate inflammatory acne with a combination of comedones, papules, pustules, and some faint scars along the jaw line and upper back. Scalp and body hair distribution is normal. She has no signs of hirsutism. The thyroid is normal sized with no tenderness or nodularity. Breasts

are Tanner stage 5. Palpation of the abdomen indicates no tenderness, masses, or hepatosplenomegaly. An external genital exam shows no clitoromegaly or lesions. Pubic hair distribution is Tanner stage 5, with no expanded escutcheon. No speculum or bimanual exam is indicated.² A self-collected vaginal swab specimen is obtained for chlamydia and gonorrhea testing.³

Based on the history and physical examination findings, what are your working diagnoses?

Infrequent menses, or oligomenorrhea, is defined as cycles longer than 38 days. Irregular menses is defined as a variation of cycle length greater than 20 days.⁴ Many adolescents have menses that meet these criteria in the first 1-2 years postmenarche. About 75% of adolescents have an average menstrual cycle of 21-45 days within 1 year postmenarche and about 90% are in this range within 4 years postmenarche.⁵ NM reached menarche 2 years ago. Her cycles range from 1 to 3 months. Most adolescents become ovulatory over time, but half of girls with infrequent menses or secondary amenorrhea have a permanent ovulatory disorder.⁶

Moderate to severe acne affects 15%-20% of 15- to 17-year-olds.⁷ The exact cause of acne is unknown. Genetic influences may determine acne susceptibility and severity. Main contributory factors are excessive sebum production, hyperkeratinization of pilosebaceous follicles causing blockage and mixing dead skin cells with sebum, and proliferation of the bacterium *Propionibacterium acnes*. Inflammatory acne develops when the wall of these follicles ruptures and sebum enters

the surrounding dermis. Pustules form when inflammation is close to the surface, and papules and cystic nodules form when inflammation is deeper, causing mild to severe scarring.⁸ Although most cases of acne regress spontaneously during later adolescence, some may persist into adulthood.

Production of adrenal androgen increases in early puberty in girls, contributing not only to pubic and axillary hair growth but also to increased sebum production and acne. However, acne in adolescent girls should be evaluated not in

isolation but, rather, in the context of each patient's family history and menstrual history and in the absence or presence of hirsutism.

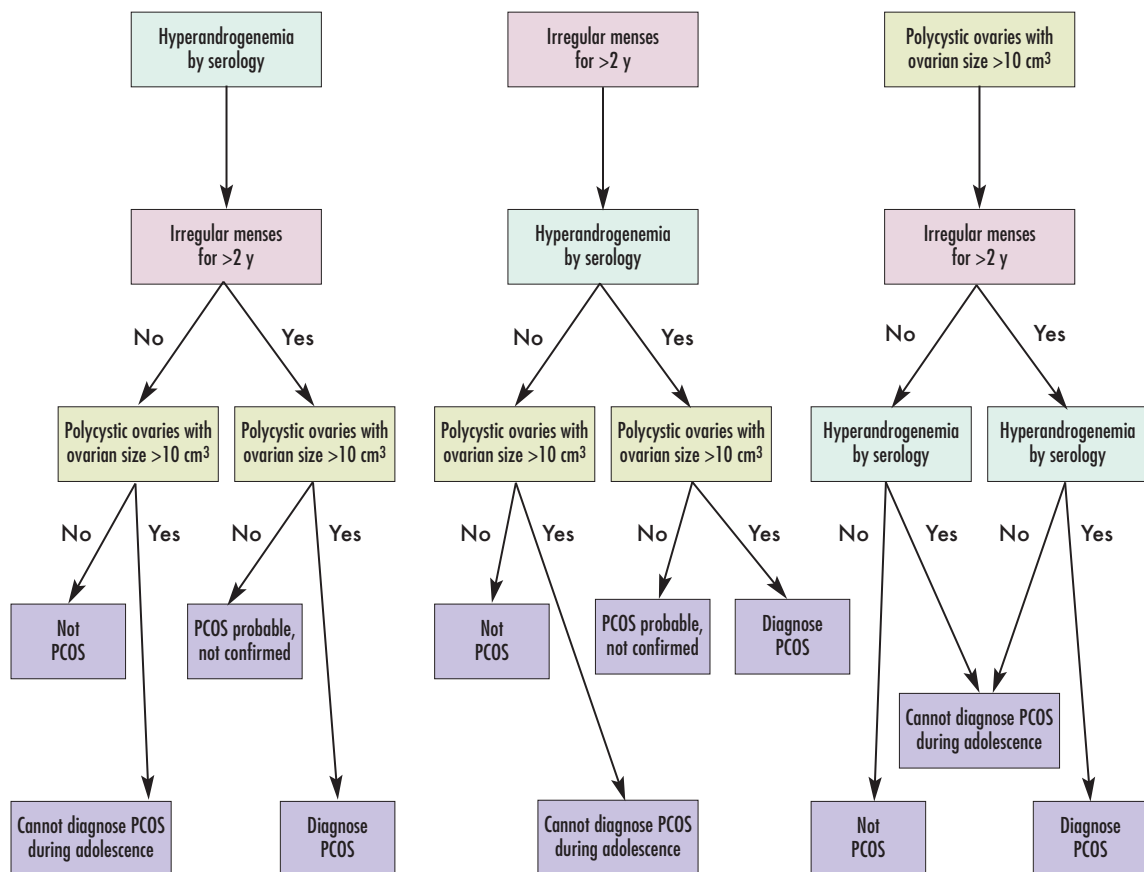
Which laboratory tests are indicated?

Because infrequent menses or amenorrhea may be the only presenting sign in adolescents with thyroid dysfunction or hyperprolactinemia, laboratory testing for these disorders is indicated. Normal serum thyroid-stimulating hormone (TSH) and prolactin levels rule out these two conditions.

After PCOS, non-classic CAH is the second most common cause of hyperandrogenic anovulation.⁹ Non-classic CAH can be excluded with a carefully timed 17-hydroxyprogesterone measure, which is checked in the early morning, during the follicular phase or an anovulatory cycle.

Although a diagnosis of hyperandrogenism can be made clinically in typical presentations of adult PCOS, adolescents should undergo a serologic evaluation because of the prevalence of acne in teens with normal androgen levels.

Figure. Diagnostic criteria for PCOS in an adolescent



About 50% of adolescents with acne have no biochemical evidence or other clinical findings associated with hyperandrogenism.¹⁰ If a lab can assure accuracy in females, a total testosterone level, best drawn in the morning, can be checked as a cost-effective test for hyperandrogenemia. If rapid-onset or severe hirsutism is noted, the level of dehydroepiandrosterone sulfate is measured to detect adrenal hyperandrogenism caused by unusual virilizing disorders. Absence of serologic hyperandrogenism in an adolescent can exclude a diagnosis of PCOS.

NM's lab findings include TSH, 2.4 mIU/L (normal range, 0.4-4.0 mIU/L); prolactin, 16 ng/mL (normal range in nonpregnant females, 2-29 ng/mL; normal range in pregnant females, 10-209 ng/mL); and total testosterone, 84 ng/dL (normal range for girls aged 12-16 years, <7-75 ng/dL).

Which additional study or studies can help make the diagnosis?

Ultrasonography (USG) of the ovaries is needed in NM's case. The presence of clinically insignificant polycystic ovaries is high in the general adolescent population,¹¹ suggesting that multifollicular ovaries may be a normal developmental variant. Overall ovarian volume may be a stronger determinant of PCOS in adolescents than subjective qualities of the ovary, which are often limited by the transabdominal USG technique frequently used in adolescent girls.¹²

NM's USG shows bilaterally enlarged ovaries with numerous follicles, and a mean ovarian volume of 11.3 cm³. Based on the constellation of infrequent menses, serologic evidence of hyperandrogenism, absence of

Take-home messages

- Unlike the requirement to meet two of three Rotterdam criteria in women, the diagnosis of PCOS in adolescents requires all three Rotterdam criteria: hyperandrogenemia, oligoamenorrhea, and enlarged, polycystic ovaries on ultrasonography.
- Presence of acne is not a reliable marker for hyperandrogenemia in adolescent girls. Serologic testing is preferred.
- The choice of a contraceptive for an adolescent with PCOS depends on her preference and on the ease of its use, as well as on the S/S management that it offers.
- Adolescents with PCOS need long-term monitoring for development of chronic conditions and encouragement toward meeting exercise and weight-management goals.

other endocrinopathies, and the USG findings, a diagnosis of PCOS is made.

What are the official diagnostic criteria for PCOS in adolescents?

The diagnostic criteria for PCOS have not been firmly established. The National Institutes of Health calls for evidence of hyperandrogenism and oligoamenorrhea; ovarian USG is not needed to make the diagnosis.¹³ The Rotterdam criteria consider various phenotypes of PCOS based on a combination of any two of these three findings: hyperandrogenism, menstrual irregularity, and polycystic ovaries on USG.¹⁴ The Androgen Excess and the PCOS Society emphasize hyperandrogenism, with additional findings of menstrual irregularity and/or polycystic ovaries on USG being diagnostic.¹⁵

Whereas the diagnostic criteria

for PCOS may have broadened for women, inclusion of adolescents is problematic. Transitory findings of clinical hyperandrogenism (i.e., acne) and perimenarchal menstrual irregularity may lead to a premature diagnosis of PCOS in adolescents. Such a diagnosis can contribute to unnecessary treatment, psychological distress, body image concerns, and undue worry about future fertility. However, true PCOS in adolescents is a marker for future metabolic syndrome and should be treated and monitored accordingly.¹⁶

The 2012 consensus report of the two largest fertility societies, the European Society of Human Reproduction and Embryology and the American Society for Reproductive Medicine suggests that all three Rotterdam criteria, with stipulations specific to adolescents, be present to accurately diagnose PCOS in this population¹⁰:

- Hyperandrogenism, defined by serologic testing;
- Oligoamenorrhea, present for at least 2 years; and
- Polycystic ovaries by USG, with an ovarian volume >10 cm³.

The *Figure* provides an algorithm designed by the author that is based on these diagnostic criteria.

What are NM's treatment options?

Treatment of PCOS is judged appropriate in NM's case. Goals of her treatment include S/S management and prevention and detection of subsequent chronic conditions for which she is at higher risk. These conditions include metabolic syndrome, infertility, and endometrial cancer. NM should have an annual assessment of her lipid levels, HbA_{1c} or glu-

cose tolerance, BMI, and BP.

The NP and NM discuss treatment options related to NM's goals. NM wants to have regular periods—or no periods—and reduced acne, and she wants to start using an effective contraceptive. She may be able to reach all these goals with one pharmacologic agent, a combined hormonal contraceptive (CHC). No contraceptive method is specifically contraindicated in patients with PCOS.¹⁷ Correction of NM's hyperandrogenism through use of a CHC, specifically a combined oral contraceptive (COC), may be the most effective treatment for her acne, while offering reliable contraception and endometrial cancer protection at the same time. By suppressing ovarian production of testosterone, COCs reduce free or circulating androgens. All COCs can help improve acne.¹⁸ Little research is available on the effectiveness of transdermal or vaginal CHCs in this regard.¹⁹ COCs containing drospirenone (DRSP), relative to those containing other progestins, may have superior efficacy against acne because of DRSP's antiandrogenic, spironolactone-like effect.

For many women, the spironolactone equivalent of 25 mg of DRSP contained in COCs is not a high enough dose to adequately control acne. One study found that adding 100 mg of spironolactone to a DRSP-containing COC was well tolerated and resulted in near-resolution of acne in 85% of subjects.²⁰ Although DRSP has androgen-blocking potential, NPs must be cautious in prescribing DRSP-containing COCs for obese women because of a potentially increased risk for venous thromboembolism.²¹

Long-acting reversible contra-

ceptives (LARC) such as intrauterine devices (IUDs) and implantable progestin rods are first-line contraceptive choices for adolescents.²² Although both the levonorgestrel-containing intrauterine system (LNG-IUS) and the progestin implant offer endometrial cancer protection, neither produces reliable androgen suppression. Some studies of the LNG-IUS and the progestin implant show improvement of baseline acne, whereas others show onset or worsening of acne.²³⁻²⁵ If a LARC method is deemed the most acceptable contraceptive for a given patient, it can be paired with spironolactone to treat hyperandrogenic acne. Because of its potentially teratogenic effects, spironolactone is contraindicated in sexually active women who are not using a reliable contraceptive. LNG-IUS and progestin implant users may experience irregular bleeding during the first several months of use and possibly amenorrhea after 6 months to 2 years of use.²⁶

NM decides to take a COC in a continuous regimen so as to avoid having her period and perhaps her menstrual headaches as well. The NP encourages NM to continue condom use along with the COC for STI risk reduction. In addition, because COCs can take 3-6 months to control acne,²⁷ NM is started on a regimen of topical clindamycin and tretinoin. Topical tretinoin is a vitamin A derivative that act by normalizing keratinocyte development, decreasing sebum production, and reducing inflammation. Their use in combination with topical antibiotics such as clindamycin is more effective for moderate acne than either agent used alone.²⁸

The NP refers NM to an **online**

guide about PCOS for teens^B

provided by the Center for Young Women's Health of Boston Children's Hospital.²⁹ She gives NM a prescription for regular exercise and nutrition counseling, with a goal of keeping her BMI below 26.

Conclusion

Irregular menses and acne are common findings in adolescent girls; NPs need to use evidence-based guidelines to aid these girls by distinguishing PCOS from normal physiologic variants. In NM's case, the findings of oligomenorrhea, serologic hyperandrogenism, and polycystic, enlarged ovaries confirm a diagnosis of PCOS. Once the diagnosis is made, treatment is focused on the adolescent's goals and need for S/S management. Long-term monitoring for associated chronic diseases is included in the ongoing plan of care. With appropriate monitoring and lifestyle modifications, PCOS can be effectively managed with minimal long-term complications. ●

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For a list of references, see <https://npwomenshealthcare.com/?p=5088>

Web resources

A. npwomenshealthcare.com/author-guidelines/

B. youngwomenshealth.org/wp-content/uploads/2014/10/PCOS-Resources-for-a-Healthier-You.pdf