

Abnormal Uterine Bleeding in the Adolescent

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Abnormal uterine bleeding is a common problem in adolescents. The differential diagnosis varies from pregnancy and infection to anovulation and coagulopathy. Careful history and examination can help elucidate the best next steps for workup and management. Heavy menstrual bleeding is particularly worrisome in this group not only when it occurs at menarche, but also anytime afterward when bleeding lasts longer than 7 days, blood loss is greater than 80 mL per cycle, or other warning signs that indicate a history of heavy bleeding such as anemia. Once conditions of pregnancy, infection, structural abnormalities, and hormonal causes have been ruled out, first-line treatment is medical management with hormonal therapy or nonhormonal options. Invasive measures are a last resort in this patient population, because maintenance of fertility is of critical importance.

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Abnormal uterine bleeding (AUB) is a common menstrual symptom among female adolescents. The American College of Obstetricians and Gynecologists has championed using the menstrual cycle as a vital sign, with abnormal menstruation patterns triggering work-up of potential health concerns.^{1,2} The average age of menarche has remained stable at approximately 12–13 years over the past 80 years in well-nourished populations in developed countries.³ Irregular cycles occur most frequently within the first 2–3 years after menarche. Although this is normal during this timeframe, cycle length still should be approximately 21–45 days, with menses lasting 2–7 days. Normal blood loss is 30 mL per cycle or three to six pads or tampons per day (Box 1).^{1,4,5} Heavy menstrual bleeding refers to cycles lasting more than 7 days or a blood loss of greater than 80 mL per men-

ses. Additionally, blood loss affecting quality of life and adolescent well-being warrants investigation.⁶ Because adolescents often do not quantify volume of menstruation very well, changing a sanitary product every 1–2 hours has been deemed excessive, especially if menses is longer than 7 days.¹

INCIDENCE

Abnormal uterine bleeding affects 3–20% of reproductive-aged females, with a higher incidence in adolescence.⁷ Heavy menstrual bleeding is the most frequent symptom. In a population-based study of 1,000 healthy Swedish adolescents, 73% reported menstrual problems and 37% reported heavy menstrual bleeding.⁸ Other population-based studies have reported that 12.1% and 17.9% of adolescents experienced heavy menstrual bleeding in Nigeria and Hong Kong, respectively.^{9,10}

PATHOPHYSIOLOGY

In an adolescent presenting with AUB, pregnancy, sexual trauma, and infection must be reliably excluded regardless of the sexual history the patient provides.¹¹ A urine pregnancy test and, if positive, serum β -hCG should be obtained; if indicated, a sensitive pelvic examination and sexually transmitted infection testing should also be performed. It is important to remember that pelvic inflammatory disease and ectopic pregnancy can present as AUB and abdominal pain, and only once these have been reasonably eliminated can the AUB PALM-COEIN (polyp; adenomyosis; leiomyoma; malignancy

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and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified) system be considered.

In 2011, the International Federation of Gynecology and Obstetrics published the PALM-COEIN system for classifying AUB in hopes of eliminating the confusing and poorly defined terminology, including dysfunctional uterine bleeding, menorrhagia, and metrorrhagia.¹² In 2018, revisions to this system further clarified the parameters defining AUB.⁷ Abnormal uterine bleeding describes any aberration of menstrual volume, frequency, or duration in a non-pregnant female. The system further separates the causes of AUB into structural and nonstructural etiologies. Structural causes (polyps, adenomyosis, leiomyomas, malignancies [PALM]) are rare in adolescents, constituting only about 1.3% of AUB in this population.¹³

Nonstructural causes (coagulopathies, ovulatory disorders, endometrial disorders, iatrogenic, not yet classified [COEIN]) are more prevalent in the adolescent population, with ovulatory dysfunction being the most prevalent. Ovulatory dysfunction due to an immature hypothalamic-pituitary-ovarian axis occurs in up to 95% of adolescents with AUB.¹⁴ Another consideration is polycystic ovarian syndrome (PCOS); studies show that up to 59% of adolescents with AUB when followed longitudinally will meet criteria for PCOS.¹⁵

Among adolescents presenting with heavy menstrual bleeding, up to 20% may be found to have an underlying bleeding disorder. Von Willebrand disease is the most common of bleeding disorders, occurring in 1% of the population, and heavy menstrual bleeding in adolescents is often the first presenting symptom in otherwise healthy teens.^{2,6} In addition to a von Willebrand panel (von Willebrand-ristocetin cofactor activity, von Willebrand factor antigen, and factor VIII activity), a complete blood cell count with platelets, prothrombin time, and partial thromboplastin time should be performed in patients with a suspicious presentation.^{2,16}

Iatrogenic causes include anticoagulation medication, hormonal contraceptives, or any other medication known to interfere with ovulation, such as antipsychotics. Abnormal uterine bleeding that does not fit into any of the other structural or nonstructural causes is classified as AUB-N, or not yet classified.

CLINICAL PRESENTATION

Abnormal uterine bleeding in the adolescent often presents with “skipped periods” or “too much bleeding.” Because of frequent anovulatory cycles, adoles-

cents may have heavier blood loss and may present with acute anemia requiring emergency treatment and hematologic evaluation. A patient presenting with heavy menstrual bleeding should first be assessed for medical stability and triaged to emergency care if necessary. Management of AUB-heavy menstrual bleeding is detailed below.

A detailed history regarding menarche, intervals between menses, duration of bleeding, amount of bleeding, and signs and symptoms of anemia should be obtained. Family history of bleeding disorders should be obtained, in addition to assessing for easy bruising or gum bleeding. Up to 20% of adolescents with heavy menstrual bleeding have subsequently been found to have a bleeding disorder.¹⁷ Screening tools such as the Pictorial Blood Assessment Chart and questionnaires such as the one in Box 2 have been found to be useful in determining which adolescents to screen for bleeding disorders.²

Patients with obesity, hirsutism, and acanthosis nigricans should be evaluated for PCOS.⁶ The diagnosis of PCOS in the adolescent can be challenging, because irregular menses and acne are common in adolescence. Laboratory tests should include total or free testosterone and a 17-OH-progesterone to rule out nonclassical congenital adrenal hyperplasia, which can present similarly to PCOS.¹⁸ Androstenedione, dehydroepiandrosterone sulfate, luteinizing hormone, follicle-stimulating hormone, and estradiol, can also be considered. In a patient found to be at risk for PCOS, annual metabolic laboratory tests (complete metabolic panel, hemoglobin A_{1c}) can be checked, given the risk of comorbidities.

Thyroid dysfunction can be evaluated by asking about a history of heat or cold intolerance; palpitations; fatigue; hair, skin, or nail changes; and weight gain or loss. Thyroid-stimulating hormone levels should be evaluated, because both hyperthyroidism and hypothyroidism can cause AUB. Additionally, a prolactin level should be checked to evaluate for hyperprolactinemia. Medications such as antipsychotics can cause elevated prolactin levels. Prolactinomas are usually suggested by values greater than 100 ng/mL and can present with headaches, vision field obstructions, and galactorrhea.¹⁴ For the patient with slightly elevated prolactin levels, a fasting level should be obtained to verify elevation.

Although the incidence of endometrial cancer in women younger than 20 years is low, in patients for whom medical treatments have failed and who have risk factors such as genetic conditions, morbid obesity, and prolonged history of anovulatory cycles, evaluation of the endometrium may be warranted.¹¹



MEDICAL MANAGEMENT FOR ABNORMAL UTERINE BLEEDING

It is important to understand the cause of AUB to direct therapy. When pregnancy, infections, structural causes, and thyroid conditions have been ruled out, tailored medical management can be discussed, taking into account the patient's preferences and underlying health conditions.⁷ Management of acute or chronic bleeding can be approached with either hormonal or nonhormonal options. Among patients found to have a bleeding disorder, management should be coordinated with a hematologist in the event other factors or blood products need to be administered concurrently. For patients who are anticoagulated, working with a hematologist regarding the options for reversibility of anticoagulant therapy to control AUB is also important.¹⁹

ACUTE ABNORMAL UTERINE BLEEDING

Hormonal Options

In the acute setting of blood loss, the first priority is to stabilize the patient. Determination for admission will be based on whether the patient has symptomatic anemia requiring a blood transfusion. Should the patient require admission, stabilizing with blood products is important, in addition to initiating medical therapy.^{6,20} When starting hormonal therapy, iron therapy should also be administered, whether intravenously or orally. Depending on the patient's medical history and ability to tolerate oral intake, estrogen-containing options may be considered. The first-line options in this acute setting include intravenous conjugated estrogen and oral contraceptive tapers. A number of regimens have been studied previously with the goal of bleeding cessation within the first 24–48 hours (Table 1).^{6,20} In the event that bleeding does not cease within this timeframe, additional aug-

mentation agents may be considered, including tranexamic acid or aminocaproic acid (discussed in more detail below).⁶

After immediate stabilization with intravenous conjugated estrogen, patients can be transitioned to an oral contraceptive taper with the goal to titrate down eventually to one pill per day. For the patient who is not a candidate for estrogen therapy, progesterone-only pills can be considered. High-dose progesterone can be delivered orally, with most pill tapers focusing on norethindrone-acetate, medroxyprogesterone, or norethindrone alone (Table 1). For patients with limited intestinal absorption, injectable depot medroxyprogesterone acetate (150 mg intramuscularly or 104 mg subcutaneously) can be administered, with plans for additional backup use of antifibrinolytics or oral progesterone-only pills.⁶ For patients who are already anticoagulated but found to have supertherapeutic international normalized ratio levels, acute heavy menstrual bleeding may be a concern. In one study at a single institution, 68 adolescent females were receiving antithrombotic medications for indicated reasons. Nearly 20% of these individuals developed heavy menses over time, with 43% ultimately being diagnosed with anemia and 78% requiring a blood transfusion, resulting in hospitalization.²¹ Reversal or halting of anticoagulants briefly in the acute setting to manage heavy bleeding may be necessary and should be discussed with a hematologist.

Nonhormonal Options

Antifibrinolytics are an option as stand-alone therapy or to augment hormonal therapy. These medications can be delivered intravenously or orally to help reduce menstrual blood loss. One study examined the efficacy of tranexamic acid in adolescents with heavy menstrual bleeding. The researchers conducted an open-label prospective multicenter study involving

Table 1. Medical and Hormonal Therapies for Acute HMB

Therapy	Dose	Route	Initial Frequency
Conjugated estrogen	25 mg	IV	Every 4–6 hours
50 µg ethinyl estradiol combined pill	1 tablet	Oral	Every 6 hours
30–35 µg ethinyl estradiol combined pill	1 tablet	Oral	Every 6 hours
Medroxyprogesterone	10–20 mg (maximum 80 mg/d)	Oral	Every 6–12 hours
Norethindrone acetate	5–10 mg	Oral	Every 6 hours
Tranexamic acid	10 mg/kg	IV	Every 6–8 hours
Aminocaproic acid	100–200 mg/kg (maximum 30 g/d)	IV or oral	Every 4–6 hours

HMB, heavy menstrual bleeding; IV, intravenous.

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32 girls and young women aged 10–19 years. The participants were treated with 1,300 mg of tranexamic acid orally three times daily during the first 5 days of the menstrual cycle and monitored over the course of 4 months from baseline. Throughout the study time-frame, mean blood loss was reduced and quality of life scores improved.²²

CHRONIC ABNORMAL UTERINE BLEEDING AND MAINTENANCE THERAPY

Hormonal Options

Fortunately, a number of different hormones are good options for the control of chronic AUB (Table 2). When anemia is present, iron therapy should be administered concurrently. The choice of therapy is dependent on several factors, such as patient preference, compliance, cost, previous hormones tried, ease of access to a particular therapy, and medical history.⁶ For patients desiring regulation of a cycle with predictable menses each month, a combined hormonal method is the best option. For patients desiring fewer cycles overall, progesterone-only methods and continuous combined hormonal methods with less frequent cycles are other options (Table 2). A Cochrane Review examining combined methods for managing

heavy menstrual bleeding using combined pills or combined rings compared with no treatment or placebo determined that, among eight randomized controlled trials (RCTs), combined pills decreased subjective mean menstrual blood loss through patient satisfaction in having a reduced bleeding profile. The combined ring was shown to have similar benefits, although evidence was limited.²³ A review performed in 2015 examined the benefits of continuous pill compared with other continuous combined hormonal methods such as the patch and ring. Over time, bleeding profiles were found to be favorable overall for extended cycling compared with monthly cycling. In addition, extended cycling also offered a decrease in estrogen withdrawal symptoms, reliable ovulation suppression, and a decrease in unscheduled bleeding episodes.²⁴ Another Cochrane Review examined the differences between extended cycling compared with monthly cycling for combined hormonal contraceptives. Twelve RCTs met criteria for the Review, and 11 of these found that bleeding patterns were either equivalent to or improved with extended cycling over time and that compliance was similar.²⁵

Progesterone-only methods for use in heavy menstrual bleeding are also well established. A retrospective

Table 2. Hormonal Management for Chronic Abnormal Uterine Bleeding

Therapy	Route	Dose	Frequency	Counseling
Combined OC	Oral	10–50-microgram ethinyl E2 tablets	Daily	Requires compliance. Lowest dose options at 10 micrograms have a higher amenorrhea rate. Breakthrough bleeding rates may be higher with lower dose options. May be administered cyclicly or continuously.
POP	Oral	35 micrograms norethindrone 5–15 mg norethindrone acetate	Daily	Requires compliance. No placebo week.
Combined patch	Transdermal	150 micrograms norelgestromin/35 micrograms ethinyl E2/d	Weekly	May be administered cyclicly or continuously.
Combined ring	Vaginal	0.12 mg etonogestrel/15 micrograms ethinyl E2/d	Monthly	At lower dose, breakthrough bleeding rates may be higher. May be administered cyclicly or continuously.
Injectable	IM or SC	150 mg or 104 mg DMPA	Every 3 mo	High rates of amenorrhea. Can be administered more frequently (monthly) for a few doses to achieve amenorrhea earlier.
Implant	SC	68 mg etonogestrel	Every 3 y	Gradual cessation of bleeding. High rates of breakthrough bleeding. Studies beginning to demonstrate use may be effective for up to 5 y.
IUD	Intrauterine	Levonorgestrel IUD (13.5–52 mg-formulations)	3–5 y	Gradual cessation of bleeding. Heavy bleeding episodes may predispose to expulsion of IUD. Lowest dose formulations have higher rates of breakthrough bleeding. Studies beginning to demonstrate that, for highest dose formulations, use may be effective for up to 7 y.

OC, oral contraceptive; E2, estradiol; POP, progesterone-only pill; IM, intramuscular; SC, subcutaneous; DMPA, depot medroxyprogesterone acetate; IUD, intrauterine device.

Data from Haamid F, Sass AE, Dietrich JE. Heavy menstrual bleeding in adolescents. *J Pediatr Adolesc Gynecol* 2017;30:335–40.



study involving 176 adolescent females taking norethindrone assessed bleeding profiles and discontinuations rates. The mean age of the group was 14.8 ± 2.3 years. The most common indication for use was heavy menstrual bleeding in 32% of cases. Although 40 participants were lost to follow-up, 52% continued the method and 43% eventually discontinued secondary to breakthrough bleeding. Only 20 patients in the cohort required a progesterone-only pill taper owing to ongoing heavy menstrual bleeding, of whom 79% had complete bleeding cessation within 7 days.²⁶ A Cochrane Review from 2015 focused on all progesterone-only methods to determine the effectiveness and acceptability of these methods to control heavy menstrual bleeding. Twenty-one RCTs met criteria, involving 2,082 women. The levonorgestrel intrauterine device (IUD) was found to reduce mean menstrual blood loss in 81% of 170 women in two studies that were reviewed and in 79% among three other studies reviewed, involving 335 women. The levonorgestrel IUD was ultimately not more effective in reducing menstrual blood loss compared with hysterectomy, as pointed out by this particular study; however, it was significantly more cost effective and far less invasive.²⁷

In 2019, an RCT was performed comparing combined contraceptive pills with norethindrone acetate to control breakthrough bleeding or delay menses when started late-cycle. No patients on norethindrone acetate had spotting; 10 of 25 patients randomized to the combined oral contraceptive group (control group) had spotting or irregular bleeding. Patient satisfaction was higher in the norethindrone acetate group (80%).²⁸ A prospective study involving 73 adolescents noted common treatment modalities among those presenting with heavy menses. They were subcategorized on the basis of whether they had a bleeding disorder that explained the heavy menses. Forty-six percent were diagnosed with an underlying bleeding disorder. Among those with a bleeding disorder, the levonorgestrel IUD had the highest rate of success, followed by norethindrone acetate (89% and 83%, respectively). Among those without a bleeding disorder, the transdermal patch and the levonorgestrel IUD had the highest rates of success (100% and 80%, respectively).²⁹

Nonhormonal Options

Some patients are not eager to be on hormonal therapy. For patients desiring more local control of heavy bleeding episodes each month, episodic use of aminocaproic acid or tranexamic acid orally are other alternatives. In a prospective cohort of adolescents

with heavy menstrual bleeding, all participants diagnosed with bleeding disorders who chose a nonhormonal method (tranexamic acid) had a decrease in their bleeding.²⁹

SURGICAL MANAGEMENT FOR ABNORMAL UTERINE BLEEDING

Medical therapy is, no question, the first line in the adolescent population, because maintaining fertility is paramount. When medical therapy fails, however, more invasive measures must be considered. Reversible options are applied first. Several studies have pointed to the benefits of the Bakri balloon for use in ceasing heavy postpartum bleeding. Such a balloon is too big for the purposes of controlling bleeding in an adolescent. However, case reports have shown that a 30-mL Foley balloon, after calculating the volume of the uterus by ultrasound measurements, can be used for the same tamponade effect.³⁰ In the event that tamponade therapy fails and life-saving measures become necessary, dilation and curettage, ablation, and hysterectomy become the absolute last resort in this patient population.⁶

CONCLUSIONS

The most common reasons for AUB in the adolescent include anovulatory cycles and bleeding disorders. First-line medical management may include either hormonal or nonhormonal medications for acute or chronic heavy menstrual bleeding. Uterine tamponade is a reversible option for use in this population when medical therapy needs to be augmented. Invasive and irreversible procedures are not recommend in this population unless absolutely necessary for life-saving measures, because maintenance of fertility is the primary goal.

Box 1. Normal Menstrual Cycles in Adolescent Girls

Menarche (median age): 12.43 years
Mean cycle interval: 32.2 days in first gynecologic year
Menstrual cycle interval: Typically 21–45 days
Menstrual flow length: 7 days or less
Menstrual product use: Three to six pads or tampons per day

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Box 2. Recommended Screening Tool for Adolescent Patients Who Report Heavy Menstrual Bleeding

If patient meets one or more of the following criteria, it indicates a positive screen result and warrants further evaluation:

1. Menses greater than 7 days and “flooding” or “gushing” sensation or bleeding through a pad or tampon in 2 hours
2. History of anemia
3. Family history of bleeding disorder
4. History of bleeding disorder after hemostatic challenge (ie, tooth extraction, surgery, delivery)

If patient meets one or more of the screening criteria, she warrants further evaluation.

Reprinted with permission from von Willebrand disease in women. Committee Opinion No. 580. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2013;122:1368–73.

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After completing this learning experience, the involved learner should be able to:

- List the most common causes for abnormal uterine bleeding in adolescents
- Discuss the physiologic basis for normal and abnormal menstrual function
- Outline the role of history and physical examination in the diagnostic process
- Implement treatment strategies appropriate for this age population

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