

ACUTE ABNORMAL UTERINE BLEEDING (AUB)

ALGORITHM

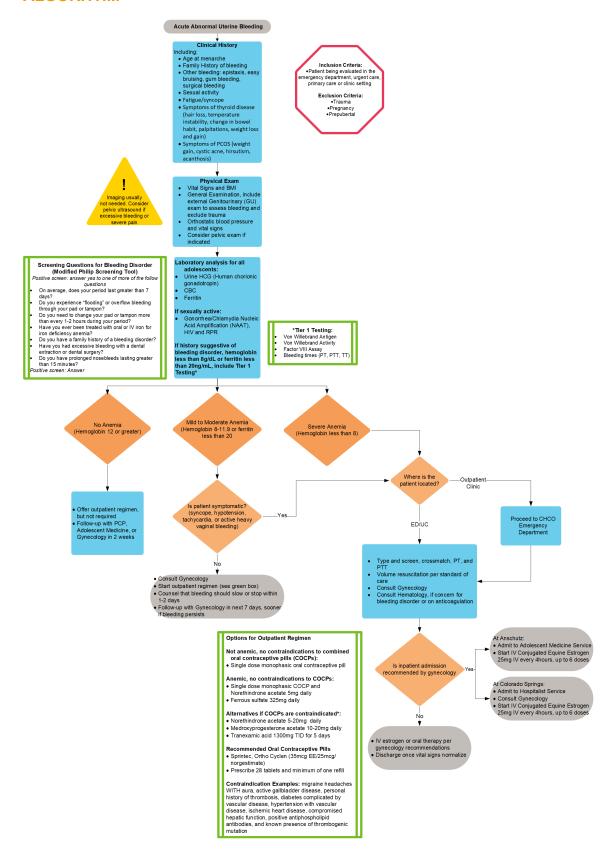




TABLE OF CONTENTS

Algorithm

Target Population

Background | Definitions

Initial Evaluation

Clinical Management

Therapeutics

Laboratory Studies | Imaging

Parent | Caregiver Education

References

Clinical Improvement Team

TARGET POPULATION

Inclusion Criteria

• Postpubertal females seen in the ED, urgent care, primary care or clinical setting with heavy uterine bleeding, not due to trauma or pregnancy

Exclusion Criteria

- Pregnancy
- Bleeding due to trauma
- <u>Pre</u>pubertal females, or girls who have started puberty within the previous year and should not yet be menarchal

BACKGROUND | DEFINITIONS

"Abnormal Uterine Bleeding" (AUB) is an umbrella term used to describe bleeding that is determined to be "abnormal" by the patient, her family, and/or her medical provider. AUB, in the absence of trauma or pregnancy, in young, reproductive aged females is most often due to anovulation and, less commonly due to a bleeding disorder. However, recent evidence suggests that upwards of 20-50% of adolescents with heavy menstrual bleeding will be diagnosed with an underlying bleeding disorder, so providers should ask screening questions to all adolescents presenting with heavy menstrual bleeding.²⁻⁴

In the normal menstrual cycle, the endometrium is stimulated to proliferate by endogenous estrogen, which is produced by the ovary at the onset of puberty. Menarche will typically occur 2 to 3 years after the onset of breast growth, which usually corresponds with Tanner IV breast development. Menstrual cycles usually occur every 21-45 days and are less than 7 days, but irregularity due to anovulatory cycles is common, especially in the first several years following menarche. Numerous studies have shown that 50-80% of menstrual cycles in the first two years after menarche are anovulatory, creating dysfunctional endometrial shedding. Anovulatory cycles create an environment of unopposed estrogen stimulation and endometrial proliferation, without



progestin-induced stabilization. The end result is disorderly shedding of the endometrial lining without prostaglandin-mediated vasoconstriction and platelet-plugging of arterioles.⁸ This may ultimately lead to episodes of heavy uterine bleeding, prompting an emergency room visit.

INITIAL EVALUATION

- Vital signs
- History and physical, including external GU exam
- CBC
- Ferritin
- HCG (usually urine HCG)
- If concerns about hemodynamic instability, type and screen, crossmatch, and obtain labs to assess for hemostasis (PT, aPTT, fibrinogen) and recommend Gynecology and Hematology service consultation
- If sexually active: Gonorrhea and Chlamydia NAAT (via urine or endocervical swab), HIV Antibody, and Rapid plasma reagin (RPR)
- If bleeding history suggests bleeding disorder, and/or patient is anemic: Von Willebrand Factor Antigen, Von Willebrand Activity, Factor VIII Assay, PT/PTT, and Thrombin Time

Initial evaluation should include assessment for hemodynamic stability, CBC, ferritin and HCG testing. 1,2 If there are concerns about hemodynamic instability (hypotension, tachycardia, shortness of breath, mental status changes) a type and screen, crossmatch, and labs to assess for hemostasis are indicated. An exam, including an external genitourinary (GU) exam, and detailed history should be obtained from the patient and her family. Menstrual history should include duration of menstrual bleeding (number of days), frequency of pad or tampon exchange, and passage of clots > quarter size. Personal bleeding history should include inquiring about patient's history of bleeding gums, nosebleeds, and bleeding with prior surgical procedures. A brief family history assessing for increasing bleeding among first-degree relatives is also important.

A CBC is recommended in all patients because reports of amount of bleeding and product use are a not a reliable predictor of actual blood loss. Ferritin is also indicated to assess for iron deficiency.^{9,10} Assessment of pregnancy (typically with a urine HCG) must be documented in all reproductive aged females.

In sexually active females, testing for Gonorrhea and Chlamydia (via urine or endocervical NAAT), as well as serologies for syphilis and HIV should be obtained.

For patients with a personal or family history suggestive an acquired or inherited bleeding disorder, additional "Tier I" hematologic testing is warranted to evaluate for an underlying bleeding disorder.^{8,9}

A pelvic ultrasound is typically not indicated, unless there is significant pain worrisome for ovarian cyst, torsion, partial vaginal outflow tract obstruction, appendicitis, or other cause of acute pelvic pain.⁹



CLINICAL MANAGEMENT

Consultation with Gynecology should be obtained if anemia (defined by a Hb < 12 g/dL) and/or iron deficiency (ferritin < 10ng/mL) is present to assist with medical management and follow up. Consultation *must be obtained* in all cases when there are concerns about hemodynamic instability, IV estrogen is administered, and/or when severe anemia is detected.

Hematology should be consulted if there is concern for an underlying blood disorder, if the patient is on chronic anti-coagulation or for severe iron deficiency anemia (Hb < 8 g/dL and Ferritin < 20).

Adolescent Medicine should be consulted if Gynecology is unavailable. Further, Adolescent Medicine will be the admitting service for any patients requiring inpatient admission. Hematology should be consulted if there is concern for an underlying blood disorder or if the patient is on chronic anti-coagulation.

Treatment is individualized based on the acuity of the bleeding, the presence or absence of anemia, and the desire of the patient and her family for management of the bleeding. ¹¹ In patients who are anemic (defined by a Hb < 12 g/dL) and/or iron deficient (ferritin < 10 ng/mL), hormonal therapy is recommended to prevent further blood loss. In patients who are not anemic or iron deficient, hormonal therapy should be discussed and can be offered if management is desired.

Outpatient follow-up is essential within the next 7 days with Gynecology at Anschutz Campus to review pending lab results, consider additional testing, assure that bleeding is controlled, and offer treatments based on the patient's individualized needs. Iron supplementation should be recommended to all patients with anemia and/or iron deficiency. For patients who live in Colorado Springs, follow up should also occur within 7 days, with the following options available:

- Gynecology at Anschutz Campus via Telehealth
- Gynecology at Highlands Ranch South Campus
- Adolescent Medicine in Colorado Springs

If Tier 1 testing is performed given concerns for an underlying bleeding disorder, and returns abnormal, refer to outpatient Hematology.

THERAPEUTICS

See <u>algorithm</u> for outpatient regimen options (green box)

Hormonal Therapy

For patients with acute AUB who are initially hemodynamically unstable, IV Conjugate Equine Estrogen 25mg IV should be administered. This can be repeated every 6 hours (for up to 6 doses) until oral hormonal therapy is initiated. Consultation with Gynecology or Hematology should



be actively engaged in managing the medical treatment of these patients while in the hospital and will develop a plan for close outpatient monitoring and follow-up. Adolescent Medicine service should be consulted if Gynecology is unavailable.

If the patient is hemodynamically stable and anemia is not severe (hemoglobin levels > 8.0 g/dL), outpatient treatment with iron supplementation and hormonal management should be initiated. Hormonal therapy is the mainstay of outpatient treatment for AUB. Numerous hormonal regimens have been shown to be effective and little evidence exists in the adolescent population to support the use of one regimen over the other. Progestins form the foundation of hormonal management of heavy menstrual bleeding. Progestins exert their effect by downregulating estrogen receptors, thereby reducing glandular proliferation and inducing endometrial atrophy. Progestins can be administered orally, by injection or via intrauterine device, although in the setting of acute bleeding, we primarily recommend oral therapy. Long-term, they can be administered in combination with estrogen in the form of oral contraceptive pills, which helps establish regular and predictable cycles. However, in the setting of anemia, particularly when severe, moderate to high dose progestin regimens are preferred to achieve menstrual suppression and allow the adolescent to avoid further blood loss and recover her normal hematologic status. Stand-alone progestins in the United States include the following:

- Norethindrone acetate 5 20mg daily
- Medroxyprogesterone acetate 10-20mg daily

There is no evidence to clearly recommend one hormonal method over another, so the choice will primarily depend on patient factors and provider preference. Increased side effects including nausea, vomiting, bloating and weight gain may occur with higher-dose taper regimens.^{9,11} Given the side effects that can be caused by high-dose tapers, one recommended treatment regimen that is associated with rapid amenorrhea and few side effects is the following:

Single dose oral contraceptive pill AND norethindrone acetate 5mg daily

If the patient requires inpatient admission or demonstrates evidence of continued heavy vaginal bleeding, consultation with Gynecology, Hematology or Adolescent Medicine should be obtained and additional medications may be added to the initial regimen. These medications include:

- Conjugated equine estrogen 25mg IV q 4 hours (up to 6 doses)
- Norethindrone acetate 10-20mg daily
- Medroxyprogesterone acetate 10-20mg daily
- Tranexamic acid 3900mg daily (administered 1300mg in three divided doses daily)

Consultation Services

Gynecology consultation can be obtained at any time when mild or no anemia is detected, when there are questions about which therapy to offer, or when severe anemia and inpatient admission is required. Adolescent Medicine should be consulted if Adolescent Gynecology is unavailable.



Further, all inpatient admissions will be to Adolescent Medicine, with Gynecology serving as an inpatient consulting service. Hematology should be consulted if there is concern for an underlying blood disorder or if the patient is on chronic anti-coagulation.

It is strongly recommended to consult with a specialist in all cases of significant anemia to review differential diagnosis and outpatient treatment, and to develop a concrete plan for outpatient monitoring and follow-up.

Contraindications to Estrogen

There are several medical contraindications to estrogen-containing combined oral contraceptive pills. Examples include: migraine headaches WITH aura, active gallbladder disease, personal history of thrombosis, diabetes complicated by vascular disease, hypertension with vascular disease, ischemic heart disease, compromised hepatic function, positive antiphospholipid antibodies, and known presence of thrombogenic mutation. The U.S. Medical Eligibility Criteria for Contraceptive Use is an evidence-based tool published by the CDC which lists over 60 medical conditions and can help guide treatment choice. Click Here to access the Summary Chart of U.S. Medical Eligibility Criteria for Contraceptive Use.

When a contraindication to estrogen is present, we recommend progestin therapy alone for outpatient therapy. For patients who require inpatient admission, a high dose progestin taper is recommended rather than IV estrogen.

Iron Supplementation

For patient who are anemic, or who have iron deficiency, iron supplementation should be initiated. We recommend Ferrous sulfate 325mg (65mg elemental iron) one tablet daily or every other day; more frequent dosing should be avoided given evidence of decreasing iron absorption with twice daily dosing regimens. This should be used for a minimum of 3 months.

Anti-fibrinolytic Therapy

Tranexamic acid (TXA) is an anti-fibrinolytic that can be used in the treatment of heavy menstrual bleeding. TXA should only be used for a maximum of 5 consecutive days per month. Consultation with Gynecology or Hematology should occur if a provider elects to start a patient on TXA, given theoretical risks of thrombosis in the setting of estrogen-containing oral contraceptive pills.

LABORATORY STUDIES | IMAGING

Hemodynamically stable patients:

Laboratory analysis for all adolescents:



- HCG- human chorionic gonadotropin
- CBC
- Ferritin

If sexually active:

Gonorrhea/Chlamydia NAAT, HIV, RPR

If history suggestive of bleeding, include Tier 1 Testing:

Von Willebrand Factor (VWF) Ag, VWF Activity, Factor VIII Assay, PT/PTT, Thrombin Time

Hemodynamically unstable patients, also obtain:

- Type and Screen, Crossmatch
- Other labs to assess for hemostasis (PT, aPTT, fibrinogen)

PARENT | CAREGIVER EDUCATION

In Care of Kids Handouts:

- Abnormal Uterine Bleeding in the Emergency Room <u>English</u> and <u>Spanish</u>
- Getting Started: Birth Control Pills- English and Spanish
- Hormonal therapy for period problems- English and Spanish
- Dysmenorrhea Painful Periods & Cramps- English and Spanish

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CLINICAL IMPROVEMENT TEAM MEMBERS

Jennifer Woods, MD | Adolescent Medicine
Molly Richards, MD | Adolescent Medicine
Diane Straub, MD | Adolescent Medicine
Bernadette Johnson, MD | Emergency Medicine
David Listman, MD | Emergency Medicine COS
Alexandria Dulchavsky, MD | Emergency Medicine NOC
Veronica Combs, MD | Emergency Medicine NOC
Genevieve Moyer, MD | Hematology
Karol Kerr, MD | CCBD
Bridget Pace, PharmD | Pharmacy North
Ashley Crane, RN | Gynecology

APPROVED BY

Clinical Care Guideline and Measures Review Committee – August 23, 2021 Pharmacy & Therapeutics Committee – September 2, 2021

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COLORADO SPRINGS REVIEWED BY	Michael DiStefano, MD Chief Medical Officer Children's Hospital Colorado-Colorado Springs
APPROVED BY	Lalit Bajaj, MD, MPH Chief Quality and Outcomes Officer Children's Hospital Colorado

REVIEW | REVISION SCHEDULE

Scheduled for full review on date here September 2, 2025



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