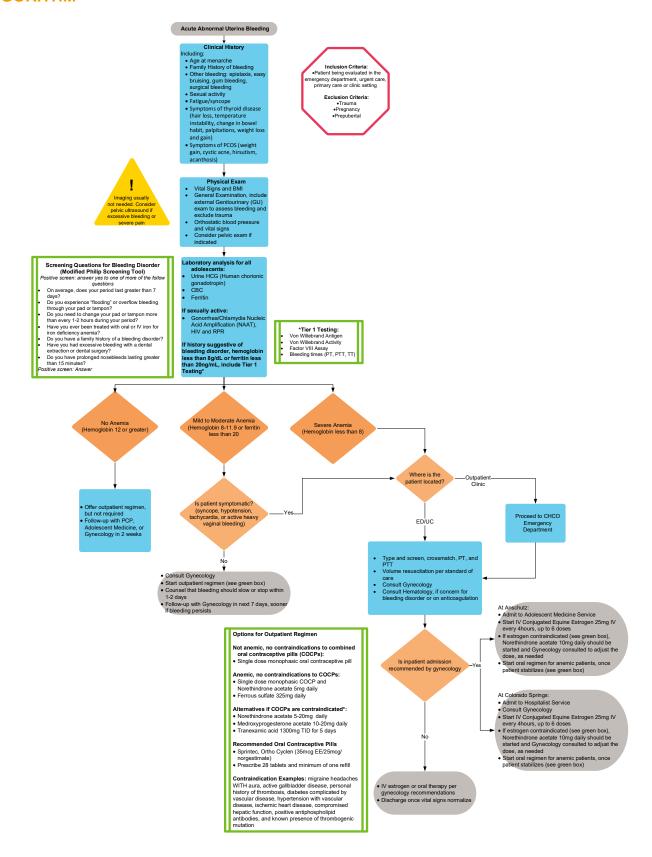


ACUTE ABNORMAL UTERINE BLEEDING (AUB)

ALGORITHM



CLINICAL PATHWAY



TABLE OF CONTENTS

Algorithm

Target Population

Background | Definitions

Initial Evaluation

Clinical Management

Therapeutics

<u>Laboratory Studies | Imaging</u>

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
- Prepubertal 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.¹

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.⁵ Numerous studies have shown that 50-80% of menstrual cycles in the first two years after menarche are anovulatory, creating dysfunctional endometrial shedding.^{6.7} 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

In CHCO ED please use the <u>Smart text</u> for ED provider note: EDUC VAGINAL BLEEDING [28994] And, <u>Order Set</u> "ED VAGINAL BLEEDING"

- 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 anticoagulation 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.

CLINICAL PATHWAY



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 < 10ng/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 algorithm 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 4 hours (for up to 6 doses) until oral hormonal therapy is initiated. If the patient has a contraindication to IV Estrogen, High dose oral progestin therapy should be initiated, with Norethindrone acetate 10mg oral daily (and may be increased at the discretion of Gynecology). 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:

CLINICAL PATHWAY



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)

It is also important to note that once the patient treated with IV estrogen begins to stabilize, they should be transitioned to an oral outpatient regimen that is designated specifically for anemic patients (see Green Box in algorithm).

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. However, if the patient is hemodynamically unstable and cannot tolerate oral intake or progestin therapy is unavailable, then IV estrogen should be initiated until oral progestin therapy can be started.

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. 16,17 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 English and Spanish
- Getting Started: Birth Control Pills- English and Spanish
- Hormonal therapy for period problems- English and Spanish
- Dysmenorrhea Painful Periods & Cramps- English and Spanish



REFERENCES

- Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Committee Opinion No. 557. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2013;121:891-6.
- 2. Chi C, Pollard D. Tuddenham EG, Kadir RA. Menorrhagia in adolescents with inherited bleeding disorders. J Pediatr Adolesc Gynecol 2010; 23:215-22.
- 3. Vo KT, Grooms L, Klima J, Holland-Hall C, O'Brien SH. Menstrual bleeding patterns and prevalence of bleeding disorders in a multidisciplinary adolescent haematology clinic. Haemophilia 2013;19:71-5.
- 4. Mikhail S, Varadarajan R, Kouides P. The prevalence of disorders of haemostasis in adolescents with menorrhagia refers to a haemophilia treatment centre. Haemophilia 2007;13:627-32.
- 5. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinoin No. 651. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2015;126:e163-6.
- 6. Apter D, Viinkka V. Hormonal pattern of adolescent cycles. *J Clin endocrinol Metab* 1978;47:944-9.
- 7. Vaughn TC. Dysfunctional uterine bleeding in the adolescent. *Semin Reprod Endocrinol* 1984;2:359-64.
- 8. Munro MG, et al. The FIGO classification system ("PALM-COEIN") for causes of abnormal uterine bleeding in non-gravid women in the reproductive years, including guidelines for clinical investigation. *Int J Gynaecol Obstet* 2011;113:3-13.
- 9. Borzutzky C, Jaffray J. Diagnosis and management of heavy menstrual bleeding and bleeding disorders in adolescents. *JAMA Pediatrics* 2020; 174: 186-94.
- 10. Kouides PA, et al. Hemostasis and menstruation: appropriate investigation for underlying disorders of hemostasis in women with excessive menstrual bleeding. *Fertil Steril* 2005:84:1345-51.
- 11. Haamid F, Sass AE, Dietrich JE. Heavy menstrual bleeding in adolescents. *J Pediatr Adolesc Gynecol* 2017;30:335-40.
- 12. DeVore GR, Owens O, Kase N. Use of intravenous premarin in the treatment of dysfunctional uterine bleeding a double-blind randomized control study. *Obstet Gynecol* 1982;59:285-91.
- 13. Feridum Asku M, et al. High-dose medroxyprogesterone acetate for the treatment of dysfunctional uterine bleeding in 24 adolescents. Aust NZ J Obstet Gynaecol 1997;37:228-31.
- 14. Munro M, et al. Oral medroxyprogesterone acetate and combination oral contraceptives for acute uterine bleeding, a randomized controlled trial. *Obstet Gynecol* 2006;108:924-9.
- 15. Santos M, et al. Retrospective review of norethindrone use in adolescents. *J Pediatr Adolesc Gynecol*2014;27:41-4.
- 16. Powers JM, Buchanan GR, Adix L, et al. Effect of low-dose ferrous sulfate vs iron polysaccharide complex on hemoglobin concentration in young children with nutritional iron-deficiency anemia: a randomized clinical trial. JAMA 2017;317:2297-2304.
- 17. Stoffel NU, Cercamondi CI, Britenham G, et al. Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice-daily split dosing in iron-depleted women: two open-label randomized controlled trials. Lancet Haematol 2017;4:e524-e533.



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

MANUAL/DEPARTMENT	Clinical Care Guidelines/Quality
ORIGINATION DATE	October 16, 2017
LAST DATE OF REVIEW OR REVISION	September 2, 2021
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

Clinical pathways are intended for informational purposes only. They are current at the date of publication and are reviewed on a regular basis to align with the best available evidence. Some information and links may not be available to external viewers. External viewers are encouraged to consult other available sources if needed to confirm and supplement the content presented in the clinical pathways. Clinical pathways are not intended to take the place of a physician's or other health care provider's advice, and is not intended to diagnose, treat, cure or prevent any disease or other medical condition. The information should not be used in place of a visit, call, consultation or advice of a physician or other health care provider. Furthermore, the information is provided for use solely at your own risk. CHCO accepts no liability for the content, or for the consequences of any actions taken on the basis of the information provided. The information provided to you and the actions taken thereof are provided on an "as is" basis without any warranty of any kind, express or implied, from CHCO. CHCO declares no affiliation, sponsorship, nor any partnerships with any listed organization, or its respective directors, officers, employees, agents, contractors, affiliates, and representatives.



Discrimination is Against the Law. Children's Hospital Colorado complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Children's Hospital Colorado does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

Children's Hospital Colorado provides free aids and services to people with disabilities to communicate effectively with us, such as: Qualified sign language interpreters, written information in other formats (large print, audio, accessible electronic formats, other formats). Children's Hospital Colorado provides free language services to people whose primary language is not English, such as: Qualified interpreters, information written in other languages.

If you need these services, contact the Medical Interpreters Department at 720.777.9800.

If you believe that Children's Hospital Colorado has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with: Corporate Compliance Officer, 13123 E 16th Avenue, B450, Aurora, Colorado 80045, Phone: 720.777.1234, Fax: 720.777.7257, corporate. compliance@childrenscolorado.org. You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Corporate Compliance Officer is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services 200 Independence Avenue, SW Room 509F, HHH Building Washington, D.C. 20201 1-800-368-1019, 800-537-7697 (TDD) Complaint forms are available at www.hhs.gov/ocr/office/file/index.html.

Children's Hospital Colorado complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex.

ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1-720-777-9800.

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-720-777-9800.

주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1-720-777-9800 번으로 전화해 주십시오

注意: 如果您使用繁體中文, 您可以免費獲得語言援助服務。請致電1-720-777-9800。

ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-720-777-9800.

ማስታወሻ: የሚና7ሩት ቋንቋ ኣማርኛ ከሆነ የትርንም እርዳታ ድርጅቶች፣ በነጻ ሊያግዝዎት ተዘጋጀተዋል፡ ወደ ሚከተለው ቁጥር ይደውሉ 1-720-777-9800 (መስማት ስተሳናቸው.

ملحوظة: إذا كنت تتحدث انكر اللغة، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم 1-9800-777-720 (رقم

ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1-720-777-9800.

ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-720-777-9800

ध्यान बनु होस:्तपाइले नेपाल बोल्नहन्छ भन तपाइको निम्त भाषा सहायता सवाहरू नःशल्क रूपमा उपलब्ध छ । फोन गनु होसर् 1-720-777-9800 ।

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1-720-777-9800.

注意事項: 日本語を話される場合、無料の言語支援をご利用いただけます。1-720-777-9800まで、お電話にてご連絡ください。

Ntį: Q burų na asų Ibo, asųsų aka oasų n'efu, defu, aka. Call 1-720-777-9800.