ACUTE ABNORMAL UTERINE BLEEDING (AUB)

ALGORITHM

Inclusion Criteria:
• Patient being evaluated in the emergency department, urgent care, primary care or clinic setting

Exclusion Criteria:
• Trauma
• Pregnancy
• Prepubertal female

Clinical History
Including:
• Age at menarche
• Family History of bleeding
• Easy Bruising, epistaxis, frequent gum bleeding, surgery-related bleeding
• Sexual activity

Physical Exam
• Vital Signs and BMI
• General Examination, include external Genitourinary (GU) exam to assess bleeding and exclude trauma
• Consider pelvic exam if indicated

Laboratory analysis for all adolescents:
• HCG (Human chorionic gonadotropin)
• CBC
• Ferritin

If sexually active:
• Gonorrhea/Chlamydia Nucleic Acid Amplification (NAAT)

If history suggestive of bleeding disorder, include Tier 1 Testing*

Patient Hemodynamically stable?

Yes

Laboratory analysis for all adolescents:
• HCG (Human chorionic gonadotropin)
• CBC
• Ferritin

If sexually active:
• Gonorrhea/Chlamydia Nucleic Acid Amplification (NAAT)

If history suggestive of bleeding disorder, include Tier 1 Testing*

Anemia?

Yes

Start outpatient regimen; counsel that bleeding should slow or stop within 1-2 days of treatment.
Follow-up with outpatient provider in next 7 days, sooner if bleeding persists.

No

Offer outpatient regimen
Follow-up with outpatient provider in next 7 days.

No

Concern for hypovolemia based on hypotension, tachycardia, Shortness of breath, mental status changes
• Complete lab assessment, type and screen, crossmatch if unstable, Tier 1 testing*
• Call gynecology, adolescent medicine, or hematology

Yes

Start IV conjugated Equine Estrogen 25mg IV every 4 hours, up to 6 doses
Once stable, start oral option listed in outpatient regimen

No

Options for Outpatient Regimen

Not anemic, no contraindications to combined oral contraceptive pills (COCPs):
• Single dose monophasic combined oral contraceptive pill (COCP)

Anemic, no contraindications to combined oral contraceptive pills (COCPs). Also consider if bleeding prolonged or otherwise difficult to manage:
• Single dose monophasic COCP combined with norethindrone acetate 5mg daily
• Multi-dose taper monophasic COCP, three times a day (TID) for 7 days, followed by 1 active tab daily
• Start Iron supplementation

Alternatives if combined oral contraceptive pills (COCPs) are contraindicated or non-hormonal treatment indicated:
• Norethindrone Acetate 5-15mg daily
• Medroxyprogesterone acetate 10-20mg daily
• Norethindrone acetate 0.35mg daily (Progestin-only Pill- POP); can use twice a day (BID) or TID if needed to stop bleeding
• Tranexamic acid 1300mg TID for 5 days

*Tier 1 Testing: Von Willebrand Factor (VWF) Antigen, Von Willebrand Factor (VWF) Activity, Factor VIII Assay, Prothrombin Time (PT)/Partial Thromboplastin (PTT)
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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.

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. 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. This may ultimately lead to episodes of heavy uterine bleeding, prompting an emergency room visit.
INITIAL EVALUATION

In CHCO ED please use the Smart text for ED provider note: EDUC VAGINAL BLEEDING [28994]
And, Order Set “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 (for example: PT, aPTT, fibrinogen) and consider hematology service consultation
- If sexually active: Gonorrhea and Chlamydia NAAT (via urine or endocervical swab)
- If bleeding history suggests bleeding disorder, and/or patient is anemic: Von Willebrand Factor Antigen, Von Willebrand Activity, Factor VIII Assay, PT/PTT

Initial evaluation should include assessment for hemodynamic stability, CBC, ferritin and HCG testing. 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, including 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 indicated to assess for iron deficiency. 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) should be obtained.

For patients with possible hemodynamic instability, anemia, or those 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. Consider hematology service consultation.

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.

CLINICAL MANAGEMENT

Consultation with Gynecology, Hematology, and/or Adolescent Medicine can be obtained at any time to assist with management, as well as assessment, of AUB. Consultation should be obtained in all cases when there are concerns about hemodynamic instability, IV estrogen is administered, and/or when severe anemia is detected.

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. In patients who are anemic, hormonal therapy is recommended to prevent further blood loss. In patients who are not anemic, hormonal therapy should be discussed and can be offered if management is desired. Outpatient follow-up is essential within the next 7 days (with PCP or with the specialist, based on individual factors) 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.
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. Gynecology, Hematology, and/or Adolescent Medicine 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.

Hormonal therapy is the mainstay of outpatient treatment for AUB. The hormone progesterone stabilizes the endometrial lining and, with continued therapy, induces atrophy of the endometrium. Progesterone can be administered in several different forms. This clinical pathway highlights the options of:

1. A combined oral contraceptive pill (COCP), single dose, or multi-dose taper if patient is anemic
2. Combined oral contraceptive pill (COCP) along with norethindrone acetate
3. Progesterone alone in the form of norethindrone acetate or medroxyprogesterone acetate.

There is no evidence to clearly recommend one treatment option over another, so the choice will primarily depend on patient factors and provider preference. Gynecology, Hematology, and/or Adolescent Medicine consultation can be obtained at anytime when mild or no anemia is detected, or when there are questions about which therapy to offer. It is strongly recommend 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.

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.

Iron Supplementation

For patient who are anemic, or who have iron deficiency, iron supplementation should be initiated. One option is elemental iron 3-6 mg/kg divided into twice each day dosing. This should be used for a minimum of 3 months.

Anti-fibrinolytic Therapy

If anemic give a minimum of a 3-month trial. 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. Further extended therapy should only be done in direct consultation with Hematology or Adolescent Gynecology to determine if the patient requires extended therapy given concern for or management of an underlying bleeding disorder.
LABORATORY STUDIES | IMAGING

Hemodynamically stable patients:
Laboratory analysis for all adolescents:
- HCG - human chorionic gonadotropin
- CBC
- Ferritin

If sexually active:
- Gonorrhea/Chlamydia NAAT

If history suggestive of bleeding, include Tier 1 Testing:
- Von Willebrand Factor (VWF) Ag, VWF Activity, Factor VIII Assay, PT/PTT

Hemodynamically unstable patients, also obtain:
- Type and Screen, Crossmatch
- Other labs to assess for hemostasis (for example: 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
- Hormonal therapy for period problems - English
- Dysmenorrhea Painful Periods & Cramps - English and Spanish
REFERENCES


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