Abnormal Uterine Bleeding
Heavy Menstrual Bleeding in Adolescents

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Definition:

Abnormal uterine bleeding can generally be defined as bleeding that falls outside of the expected norms for menstrual regularity, frequency, duration, or volume. Based on the National Institute for Health and Care Excellence, heavy menstrual bleeding is excessive menstrual blood loss that interferes with physical, social, emotional or quality of life[1]. Normal menstrual cycles in adolescents typically last for 7 days or fewer and occur 21-45 days apart. The average cycle requires the use of 3-6 pads or tampons per day[2].

Incidence:

It is thought that up to 20-30% women experience abnormal uterine bleeding during their menstrual life[3].

Etiology/Differential Diagnosis:

Anovulation is the most common etiology of abnormal uterine bleeding during adolescence[3,4]. During the first 2-3 years following menarche, many cycles are anovulatory due to the immaturity of the hypothalamic-pituitary-ovarian axis, which can subsequently lead to abnormal bleeding[5]. Abnormal uterine bleeding may be due to either structural or non-structural causes. Structural causes include polyps, adenomyosis, leiomyomas, malignancy and hyperplasia. Non-Structural causes include coagulopathy, anovulation, endometrial and iatrogenic[4,5]. Non-structural causes are more common in female adolescents[3]. Bleeding disorders are found in 20-33% of women with heavy menstrual bleeding[6]. An expanded differential diagnosis is in Table 1.

Table 1: Differential Diagnosis of Causes of abnormal uterine bleeding in Adolescents[7,8]

Anovulatory Bleeding · Immature HPO axis · Nutritional deficiency/malnutrition · Chronic illness	Uterine Problems · Submucous myoma · Congenital anomalies · Polyp · Carcinoma · Use of IUD · Ovulation bleeding
Endocrine Disorders · Hypo- or hyperthyroid · Adrenal disease · Hyperprolactinemia · Polycystic ovary syndrome · Ovarian failure	Ovarian Problems · Functional cyst · Tumor
Pregnancy-related complications · Threatened ab · Spontaneous, incomplete, missed ab · Ectopic pregnancy · Gestational trophoblastic disease · Complications of termination procedures · Endometriosis	Trauma · Vaginal laceration
Infection · Cervicitis · Vaginitis · Endometritis · PID	Foreign body (retained tampon)
Bleeding Disorders · Thrombocytopenia (ITP, TTP, leukemia, apastic anemia, hypersplenism, chemotherapy) · Clotting disorders (von Willebrand disease, disorders of platelet function, liver dysfunction)	Systemic Diseases · Diabetes mellitus · Renal disease · Systemic lupus erythematosus
Cervical Problems · Cervicitis · Polyp · Hemangioma · Carcinoma or sarcoma	Medications · Hormone containing pills · Anticoagulants · Platelet inhibitors · Androgens · Spironolactone · Antipsychotics

Vaginal abnormalities · Carcinoma or sarcoma	

Diagnostic Evaluation:

History: Menstrual history should include the onset of menarche, cycle length and variability over time, frequency, amount of menstrual blood loss, number of pads or tampons used, presence of clots, and the effect on quality of life. A confidential history should establish if patient is sexually active, including consensual and coerced sex. Specific questions should be asked to determine the possibility of bleeding/coagulation disorder PCOS, hypothyroidism, hyperprolactinemia, adrenal disorder[3,7,8]. A suggested list of questions are listed in Table 2. Chronic medical conditions and current medications should be reviewed[8]. Family history should be reviewed for coagulation or thromboembolic disorder, cancer and reproductive problems, such as PCOS, ovarian cyst and etc[3,8]. An additional list of screening questions should be reviewed to determine if the patient is at risk for coagulopathy as detailed in Table 3.

Table 2: History and Review of Systems[7,8]

Menses	· Age of menarche · Menses frequency · Menses duration · Menses volume · Presence of dysmenorrhea · Presence of clots and size · Time of changing in menses pattern
Sexual and Reproductive History	· Sexual activity · Consensual or non-consensual sex · Number of partners · New partners · Condom use and adherence · Birth control use history · History of STI · Date and result of last STI lab · History of sexual abuse or assualt
Past Medical History	· Chronic illness · Medications (Hormone containing pills, anticoagulants, SSRI, antipsychotic, herbal medication)

Family History	· Bleeding disorder · Menstrual disorders (irregular or heavy menses or ovarian cysts) · Endocrine disorders (PCOS, thyroid diseases or diabetes)
Social History	· Social stressors · Substance use · Diet · Exercise pattern
Review of System	General: · Weight loss or gain · Fatigue · Fever · Chills CV: · Palpitation · Chest pain Resp: · Shortness of breath GI: · Abdominal pain · Pica · Changes in bowel · Changes in bladder function GU · Dyspareunia · Vaginal discharge or odor · Pelvic pain or pressure Neuro: · Dizziness · Headache · Vision changes Endocrinology · Cold or heat intolerance · Nipple discharge Heme: · Easy bruising · Nose bleeding Derm: · Acne · hirsutism

Table 3: Bleeding Disorder Screening[7]

Positive screen is one or more of the following:	
· Heavy bleeding since menarche	**Kouides Questionnaire**
· One of the following ○ Post-partum hemorrhage ○ Surgery-related bleeding ○ Bleeding associated with dental work	
· Two or more of the following ○ Bruising 1 or 2 times per month ○ Epistaxis 1 or 2 times per month ○ Frequent gum bleeding ○ Family history of bleeding symptoms	
· Clots >10 mm	**Adolescent Screen**
· Description of "gushing"	

Physical Examination: Focus on detecting signs of conditions known to cause abnormal bleeding such as obesity, hirsutism, acne, acanthosis that might suggest androgen excess/PCOS; thyroid enlargement or nodules that may suggest thyroid derangement; and bruising or petechiae that might suggest bleeding disorders (Table 4). An external genitourinary and abdominal exam should be performed in all patients presenting with abnormal bleeding[3,7,8]. If the patient is sexually active a speculum exam and bimanual exam should also be included. If the patient is experiencing pain and an internal GU exam cannot be performed (i.e. if the patient is not sexually active) a transabdominal pelvic ultrasound should be considered[7].

Table 4: Physical Exam[7,8]

Vital Sign	· Temperature · Weight · Heart rate · Blood pressure
Eyes	· Visual field
Neck	· Thyroid exam
Chest	· Nipple discharge · Breast tanner stage

GI	· Abdominal tenderness · Abdominal mass · Hepatomegaly · Splenomegaly
GU	· Tanner staging · External genitalia exam · Pelvic exam if indicated
Derm	· Acanthosis nigricans · Acne · Hirsutism · Petechiae or bruising

Guideline Inclusion Criteria:

Post-menarchal adolescent female (up to age 18)
Patient/parent report of heavy menstrual bleeding

Guideline Exclusion Criteria:

Pregnancy
Contraindication to estrogen
Active malignancy
Inability to tolerate po medication

Practice Recommendations and Clinical Management

(for full recommendations see attached pathway)

Principles of Clinical Management

The initial management of heavy menstrual bleeding should be based on vital signs, symptoms, hemoglobin level and bleeding status. Patient's ability to take estrogen based on CDC medical eligibility[9] should be assessed prior to any management decisions. The most relevant absolute contraindications to estrogen in adolescent patients are listed in Table 5.

Table 5. Sample of absolute contraindications to estrogen[9]

History of migraine headache with aura
Personal history of DVT/PE/CVA or known clotting disorder
Malignant HTN

All patients should have a prompt hemodynamic assessment upon presentation. Significant hemodynamic compromise should be treated per normal protocol with fluid resuscitation and stabilization. Treatment of bleeding should be done simultaneously and per treatment protocol. If a patient is not able to take po medication, should be excluded from the treatment algorithm. Once hemoglobin level is available, use level and amount of current bleeding to determine appropriate therapy.

Labs:

First tier labs should be collected from all patients with abnormal uterine bleeding. Second tire labs should be considered based on history and physical exam as stated in Table 6 [3,7,8]. It is important to obtain labs prior to blood transfusion.

Table 6. Laboratory Testing[3,7,8]

First Tier Labs (All Patient)	
Urine HCG CBC with diff PT/PTT/INR TSH/FT4	
Second Tier Labs	
Von Willebrand panel – Von Willebrand factor antigen, activity and factor VIII level	If at least 1 criteria were met in table 3
FSH, LH, free and total testosterone, DHEA-S	If patient has irregular menses
Urine NAAT for chlamydia and gonorrhea	If patient is sexually active or has pelvic pain

Imaging:

In the majority of adolescents presenting with abnormal uterine bleeding with heavy and prolonged cycles, routine imaging is not needed as the etiology is typically related to anovulation and not structural causes[10]. However, if the patient is complaining of abdominal or pelvic pain imaging may be warranted[7]. Sexually active patients with abdominal/pelvic pain and bleeding can be considered for a transvaginal pelvic ultrasound to augment the speculum and bimanual exam. Non-sexually active patients with abdominal/pelvic pain and bleeding can be considered for a transabdominal ultrasound. For patients whose bleeding is not responding to appropriate hormonal management at 24 hours, consider an ultrasound.

Admission Criteria:

A patient with a hemoglobin level of less than 8 and active bleeding should be considered for hospital admission. Patients with hemoglobin of greater than 8 but less than 10 should be considered for admission if there are concerns about their adherence to therapy and they have continued heavy bleeding, unstable vital signs, or persistently symptomatic.

Inpatient Management:

Once a decision is made to admit, pad count should be started. Blood transfusion should be considered based on a patient's hemoglobin level and symptoms. Administration of estrogen-containing or progesterone-only containing pills should begin immediately in the emergency room. Dosing and duration of the treatment with these medications depend on the severity of anemia[7,8].

- Estrogen-containing pills

  Estrogen-containing pills should be monophasic (dose of estrogen and progesterone should be equal in every pill) and should contain 30-35 mcg of ethinyl estradiol[7,8]. Examples include: Nortrel 1/35 (on formulary at DCMC), Lo/Ovral, Necon 1/35, Sprintec, or Mononessa. Reassessment of bleeding should occur in 12-24 hours and if bleeding has not slowed or stopped, therapy may need to be altered which can include one of the following:

  - Increased the Estrogen-containing pills dosing frequency to every 4 hours[11]
  - Starting IV estrogen (Premarin) for 2-3 doses (must be done concurrently with an estrogen-containing pills to prevent bleeding recurrence when stopped)
  - Starting tranexamic acid with hematology consultation

- Progesterone-only Containing pills

  Progesterone-only containing pills should be started if there are any absolute contraindications to start estrogen-containing pills based on CDC recommendations (Table 5), prior side effects to estrogen or family's preference to not to use estrogen-containing pills. Medroxyprogesterone and Norethisterone Acetate are examples of progesterone- only containing pills. Reassessment of bleeding should occur in 12-24 hours and if bleeding has not slowed or stopped, therapy may need to be altered which can include one of the following:

  - Increased the medroxyprogesterone dosing to 20 mg every 6 hours[11]
  - Consult adolescent medicine

- Intravenous (IV) Conjugated Equine Estrogen

  If a patient cannot tolerate pills, IV conjugated equine estrogen should be started with consultation of adolescent medicine team. The dose for IV estrogen is 25 mg every 4-6 hours with a maximum 6 doses[11].

Consult OB/GYN if the bleeding has not stopped despite starting on Premarin. Consider other etiologies of current symptoms

- Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

  NSAIDs are effective in decreasing abnormal uterine bleeding by reducing prostaglandin levels. However, It is shown to be less effective compared to danazol, tranexamic acid and levonorgestrel-releasing intrauterine system (LNG IUS). Naproxen 10-15mg/kg/day bid (max 500mg/dose) should be started on admission[12].

- Iron supplementation:

  Iron supplementation should begin with estrogen-containing or progesterone-only containing pills. Recommended iron supplementation dosing for iron deficiency anemia is 65 to 130 mg of elemental iron daily based on severity of anemia. Ferrous sulfate 325 mg has 65 mg of elemental iron. It is recommended to start Ferrous sulfate 325 mg twice a day in adolescents with severe abnormal uterine bleeding and anemia.

- Anti-emetic:

  A well-known side effect of estrogen-containing therapy is nausea, thus patients starting on estrogen-containing or progesterone-only containing pills may benefit from an anti-emetic 2 hours prior to dosing of pills[7].

- In over 90% of cases of heavy menstrual bleeding in adolescents, bleeding stops with oral estrogen-containing or progesterone-only containing pills without need for escalation of care or surgical intervention[7,8].

Consult/Referrals

Adolescent medicine and hematology consults can be considered based on individual patient and clinician comfort.

Adolescent Medicine Clinic direct line: 512-324-6534

Indicate whether the patient was seen in the Emergency Department only or admitted to the hospital.

Patient Disposition

Discharge Criteria:

Patients who are discharged from the hospital should have normal vital signs for age and no orthostatic hypotension, tolerating PO intake, and have a good follow-up plan in place and be able to obtain

medication prior to or immediately after discharge. They should have a good understanding of the dosing of the medication, given that it is often complex.

Discharge Instructions:

Discharge Instructions for estrogen containing pills:

1. Review risks of thrombosis with estrogen-containing medication. Signs and symptoms of DVT/PE should be explained and instructions given on what to do should patient experience.
2. Provide clear dosing instructions for estrogen containing estrogen-containing pills with taper instructions written with times and dates of pills until follow-up.
3. Prescription should be sent to pharmacy with instructions to dispense 3 packages of Nortrel for ICD10: N92.0 + prescription to outpatient pharmacy. Uninsured patients should have a prescription for Ortho-Cyclen or Sprintec.
4. Discuss with the patient the possibility of re-bleeding. If it happens, a follow up with Adolescent Medicine or Primary Physician will be needed.

Discharge Instructions for progesterone-only containing pills:

1. Review the side effect of progesterone-only containing medications, including headache, nausea, bloating and abdominal pain.
2. Provide clear dosing instructions for progesterone-only containing pills with taper instructions written with times and dates of pills until follow-up.
3. Prescription should be sent to pharmacy with instructions to dispense 3 packages of Medroxyprogesterone For ICD10: N92.0 + prescription to outpatient pharmacy.
4. Discuss with the patient the possibility of re-bleeding. If it happens, a follow up with Adolescent Medicine or Primary Physician will be needed.

Outcome Measures

Discharge Prescription for
Hospital Length of Stay
Emergency Department Length of Stay
Average Cost
15 & 30 Day Readmission Rate

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