# Clinical practice guidelines for treatment of Dysfunctional Uterine Bleeding

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**Developed by:**

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*This clinical guideline is intended as an evidence-based guide for clinical care and not as a replacement for clinical decision making. These guidelines will be reviewed and updated as necessary every three years.*

**Purpose:** *To develop standardization of care of patients diagnosed with dysfunctional uterine bleeding at JDCH*

## Background:

Abnormal uterine bleeding (AUB) refers to bleeding that is excessive or occurs outside of normal cyclic menstruation. Anovulatory cycles are the most common cause of AUB in adolescents, and are related to immaturity of the hypothalamic-pituitary-ovarian axis. They usually occur during the first 12 to 18 months after menarche and generally resolve with maturation of the hypothalamic-pituitary-ovarian axis (7).

Other common causes include: pregnancy, infection, the use of hormonal contraceptives, stress (psychogenic or exercise induced), bleeding disorders, and endocrine disorders such as hypothyroidism, or polycystic ovarian syndrome (2). Depending on the severity, treatment ranges from observation to pharmacological therapy or in extreme cases surgery. Initial evaluation of the patient with acute AUB should include a prompt assessment for signs of hypovolemia and potential hemodynamic instability (1).

### Definition:

**Severe uterine bleeding** is defined as heavy bleeding that causes a decrease in the hemoglobin to <10 g/dL and may or may not cause hemodynamic instability. Criteria for hospitalization include, but are not limited to (12, 13, 14):

- Hemoglobin concentration <7 g/dL or <10 g/dL with active heavy bleeding
- Hemodynamic instability (e.g. tachycardia, hypotension, orthostatic vital signs)
- Symptomatic anemia (e.g. fatigue, lethargy)
- Need for intravenous conjugated estrogen (e.g. cannot take oral medications, continued heavy bleeding after 24 hours of estrogen-progestin combination therapy)
- Need for surgical intervention; patients who may require surgery should be treated with intravenous therapy and maintained NPO

**History and physical examination:**

History should focus on the menstrual history of the patient including gynecologic age (months since menarche), frequency, severity, and duration of menstrual bleeding. Other considerations include: past or present hormonal contraceptive use, sexual contact history, diet and exercise history, evidence of past non-gynecologic bleeding, and risk factors for thrombus formation if high dose estrogen is being considered in the treatment plan. The patient should be asked about duration, pattern, and volume of bleeding.

It is sometimes difficult for patients and clinicians to accurately estimate the volume of blood loss. Excessive menstrual bleeding is often defined clinically, ex: soaks a pad or tampon more than every two hours, interferes with activities [ex, wakes from sleep]; and/or interferes with physical, emotional, social, and/or material quality of life (8, 9, 10, 11).

Physical examination should take into consideration evidence of hemodynamic instability, signs of androgen excess, growth metrics, and include an external genital examination in all patients. Pelvic examination may be traumatic for adolescent girls, especially those who are not sexually active. Unless the bleeding is severe, the pelvic and rectal examination may be postponed pending a trial of medical therapy, if such therapy is warranted (2).

**Laboratory evaluation:**

Initial laboratory testing should include:

1. CBC, retic
2. Type and screen
3. Hemoglobin electrophoresis
4. Pregnancy test , serum quantitative is preferred
5. PT/INR/ aPTT, and fibrinogen

Adolescents with heavy menses since menarche who present with acute abnormal uterine bleeding should undergo testing for bleeding diatheses, including von Willebrand disease. Peripheral blood should be obtained from the patient for evaluation of bleeding disorders prior to giving blood transfusions AND before giving any sort of hormone therapy, especially if von Willebrand disease is suspected. If a bleeding disorder is considered, consultation with a hematologist is suggested. Initial testing for bleeding diatheses should include:

1. Von Willebrand panel (Factor VIII activity is included in panel). Do not send von Willebrand panel if they have already been taking OCP's. If factor VIII level is elevated please consult hematology as continued estrogen may be contraindicated.

Optional tests include:

1. TSH, Free T4

2. Iron, TIBC and ferritin
3. LFT's
4. Urine gonococcal and Chlamydia trachomatis antigens (1).
5. If PCOS is suspected, check thyroid function test (TSH), serum prolactin levels, and androgen level prior to starting hormone therapy.

**Imaging:**

Pelvic ultrasound should be performed in all patients with a complaint of pelvic pain and may be performed in the hospitalized patient with severe bleeding to exclude structural causes such as fibroids, polyps, and/or ovarian tumors. It is not necessary in patients with suspected anovulatory bleeding with no complaints of pain (2).

**Treatment for severe cases, actively bleeding with hgb < 10 g/dL :**

**A. When estrogen is not contraindicated:**

1. IV estrogen (Premarin) 25 mg IV every 4-6 hours for up to 6 doses.
2. Antiemetic medication should be prescribed one hour before every dose to alleviate side effects of nausea and vomiting (3).
3. RBC transfusion should be considered in patients who (3):
    a. Are hemodynamically unstable
    b. Have very low hemoglobin concentrations (< 7 g/dL)
    c. Who have symptomatic anemia
4. Oral hormonal contraceptives (3)
    a. After the bleeding subsides, the patient should be switched to a taper of combination monophasic oral contraceptive that contains at least 35 mcg of estradiol, with the following schedule:
        - One pill every six hours until the bleeding stops (usually within 24 hours, up to 3 days), then
        - One pill every eight hours for three days, then
        - One pill every twelve hours for three days, then
        - One pill daily, skipping the placebo pills until hgb is > 10 g/dL

        Of note, there are some studies that recommend starting combined oral contraceptive taper (as described above) simultaneously with IV Premarin for refractory/severe cases (18).

    b. JDCH pharmacy now has Kelnor on formulary, ethynodiol diacetate-ethinyl estradiol 1 mg-35 mcg (both for inpatient and outpatient use).

c. In patients with significant anemia (hemoglobin <10 g/dL), OCP's should be taken continuously (discarding the placebo) to avoid withdrawal menses for at least 3 months or until the hemoglobin is > 10 g/dL (13, 15).
d. In patients whose acute bleeding was controlled with an estrogen-containing regimen and whose hemoglobin remains is ≥10 g/dL, we suggest monophasic combination oral contraceptive pills with at least 30 mcg ethinyl estradiol be continued cyclically (ie, 21 days of hormone-containing pills, followed by three to seven days of placebo [non hormone-containing] pills or no pills to induce withdrawal bleeding) for three to six months.

5. Iron deficiency
    a. For girls with severe anovulatory uterine bleeding, initiate iron supplementation as soon as the patient is stable and able to take pills by mouth. Depending upon the severity of iron deficiency, give 65 to 130 mg elemental iron (typically, one to two tablets) once daily for at least three months (19).
    b. Consider concurrent preventative medication for constipation.

**B. When estrogen is contraindicated:**

1. Risks of estrogen therapy include venous VTE and coronary or cerebral thrombosis.
2. Estrogen therapy is contraindicated in women at high risk for such complications (4):
    **a.** Venous thromboembolism (VTE), acute or history
    **b.** Inherited thrombophilia (eg. factor V Leiden mutation, prothrombin gene mutation)
    **c.** Stroke
    **d.** Malignancy
3. Some women with contraindications to estrogen therapy (e.g. HTN, migraine with aura, Diabetes, SLE, smoking) can be treated with estrogen therapy for a short period of four weeks or less (4).
4. It is recommended for those who cannot take estrogen to give a progestin only pill (use one of the following) (3):
    a. Norethindrone 5-10 mg, tapering from Q 8 hr until bleeding stops, then Q 12 hrs., then once daily (17).
    b. Micronized progesterone 200 mg orally nightly for the first 12 days of each calendar month.
    c. Medroxyprogesterone 10 mg orally nightly for the first 10 days of each calendar month.
5. Patients should continue oral progestin-only regimen for at least six months after bleeding is controlled, after which hormonal therapy can be discontinued to determine whether a normal menstrual pattern has been established, (16).

**Refractory cases:**

A. In cases of severe menorrhagia unresponsive to 24 hours of hormonal therapy, or in those with platelet dysfunction, non-hormonal hemostatic drugs may be used. You may consider a GYN consult at this point.
    1. Hemostatic therapies include tranexamic acid, aminocaproic acid and desmopressin, which is classically used for the treatment of von Willebrand disease. Among these agents, tranexamic acid is preferred, unless the patient has increased risks for thromboembolism. Aminocaproic acid should be avoided in patients with renal impairment.
        a) Tranexamic acid is administered orally: 1300 mg PO three times per day for up to five days
        b) Aminocaproic acid may be administered orally or IV as follows:
        Aminocaproic acid 5 g orally during the first hour, followed by a continuous dose of 1 to 1.25 g per hour; treatment is continued for approximately eight hours or until the bleeding has been controlled, **or**
        Aminocaproic acid 4 to 5 g IV during the first hour of treatment, followed by a continuous infusion at a rate of 1 g per hour; treatment is continued for approximately eight hours or until the bleeding has been controlled
        c) Desmopressin is administered IV as follows:
        Desmopressin 0.3 mcg/kg IV over 15 to 30 minutes; the dose may be repeated in 48 hours if there is no response
B. Patients with a known or suspected bleeding disorder may respond to hormonal therapy, however consultation with a hematologist is recommended for these patients. Especially if bleeding is difficult to control or the physician is unfamiliar with the other options for medical management (1).
C. Surgical management is based on the clinical stability of the patient, the severity of bleeding, contraindications to medical management, or lack of response to medical management and the underlying medical condition of the patient. Surgical options include dilation and curettage (D&C), endometrial ablation, uterine artery embolization, and hysterectomy (1).

**Discharge criteria:**

The patient may be discharged to home when the bleeding has stopped or subsided and she is hemodynamically stable. Close follow-up must be maintained after discharge. Advise patients that if at any point in the tapering of OPCP's if bleeding returns/worsens, they need to call their doctor.

**Prognosis:**

Anovulatory bleeding should resolve with maturation of the hypothalmic-pituitary-ovarian axis. The long-term prognosis depends on the underlying cause. Patients with a long history of anovulatory cycles and anovulatory uterine bleeding, especially those with PCOS, have an increased risk of infertility and endometrial carcinoma (3).

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Memorial Physician Group

# New Pediatric Clinical Guideline Setup Checklist

**Guideline Name:** Dysfunctional Uterine Bleeding practice guidelines
**Goal of Clinical Guideline:** To standardize the care of patients diagnosed ō DUB.

***Does the proposed guideline meet the below four criteria?***

- ☑ The intervention is a structured **multidisciplinary** plan of care
- ☑ The intervention is used to translate guidelines or evidence into local structures
- ☑ The intervention details the steps in a course of treatment or care in a plan, pathway, algorithm, guideline, protocol or other 'inventory of actions' (i.e. the intervention had time-frames or criteria-based progression)
- ☑ The intervention aims to standardize care for a specific population

*(Lawal et al. What is a clinical pathway? Refinement of an operational definition to identify clinical pathway studies for a Cochrane systematic Review. BMC Medicine (2016) 14:35)*

**CHECKLIST**

- ☑ Physician (or an alternate author) submitting the clinical guideline must be able (directly or through virtual meeting) to attend Clinical Guidelines Meeting
- ☑ All participants in the clinical guideline development should be listed and primary author identified
- ☑ Participants who are submitting clinical guideline should sign off and include the division chief(s) from all involved specialties (for purposes of disseminating to entire division)
- ☑ All clinical guidelines should include a disclaimer ...*"this clinical guideline is intended as an evidence-based guide for clinical care and not as a replacement for clinical decision making"*
- ☑ Clinical guideline authors should submit an estimated revision schedule, i.e. every 3 years.
- ☑ References must be included in the submission.
- ☑ Authors of the guideline must identify 1-2 quality metrics that can be measured to gauge impact on care

Signature of Contributing Pathway Developers:

| Dept. Name | MD Developer Name | Signature |
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Date 6/16/2020

## Clinical Improvement Team Members

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## REVIEW/REVISION SCHEDULE