

13 year old Female with Too Many Periods

Abnormal Uterine Bleeding

Materials for Learners:

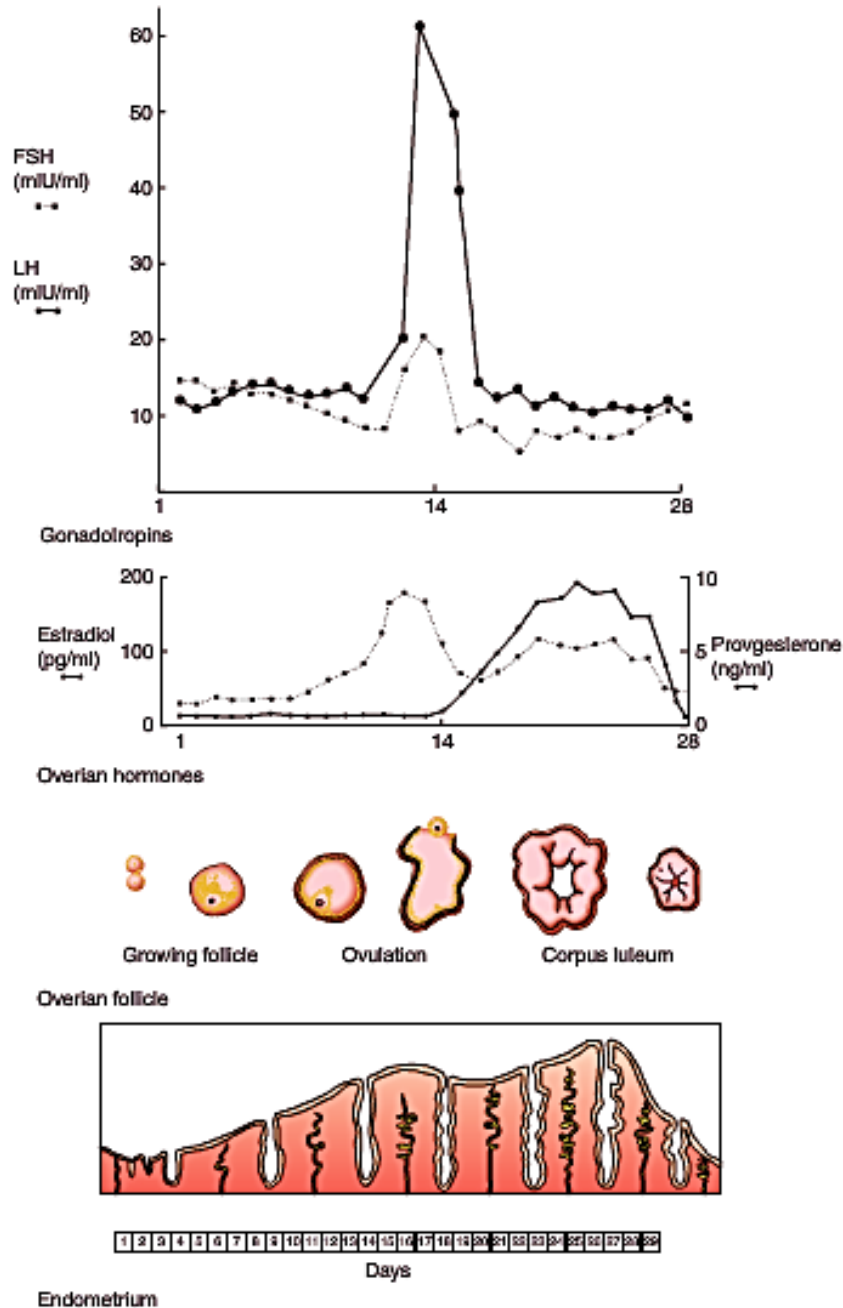
- Handout #1: Normal Ovulatory Menstrual Cycle (Figure 1)
- Handout #2: Etiologies of Amenorrhea (Figure 2) &
Categorizing AUB (Table 1)
- Handout #2: Suggested Oral Contraceptive Regimens (Table 2)
- Clinical Pearls
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Handout #1

Figure 1: Normal Ovulatory Menstrual System



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Handout #2:

Figure 2: Etiologies of AUB

Etiologies of Abnormal Uterine Bleeding

PALM: Structural causes

- Polyp
- Adenomyosis
- Leiomyoma
- Malignancy and hyperplasia

COEIN: Nonstructural

- Coagulopathy
- Ovulatory dysfunction
- Endometrial
- Iatrogenic
- Not Yet Classified

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Table 1: Categorizing AUB

	Mild	Moderate	Severe
Cycle	Prolonged (>8 days) or shortened cycles for more than 2 mo	Moderately prolonged (menses > 7 d) or multiple shortened cycles < 21 days	Prolonged, heavy
Hgb	> 11 g/dL	9-11 g/dL	< 9 g/dL

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Handout #3: Table 2: Suggested Oral Contraceptive Regimens

Use a monophasic pill such as:

- Norgestrel 0.3 mg/ethinyl estradiol 30 µg (Lo/Ovral, Low-Ogestrel).^a
- Levonorgestrel 0.15 mg/ethinyl estradiol 30 µg (Nordette/Levlen).^a

For all patients:

- Advise the patient to keep a menstrual calendar.
- Ensure iron stores are replete.

For mild bleeding (menses slightly prolonged or cycle slightly more frequent, without anemia):

- May be observed for several cycles and provided treatment with iron and NSAIDs such as ibuprofen or naproxen sodium.
- If choose to treat with OCP: One pill daily for 21 d, followed by 1 wk of placebo pills, Or one hormone pill continuously for 84 day cycles or longer.
- Continue this regimen for 3–6 mo.^b And then consider cyclic progestin therapy.

For moderate bleeding (menses >7 d or cycle <3 wk and mild anemia);

- One pill twice a day until bleeding stops, followed by one pill a day for at least 21 d, then 1 wk of placebo pills. Alternatively, if the patient is not bleeding at the time of the visit and is not already on hormonal therapy, and anemia is mild, one pill a day for 21 d is acceptable.
- Follow closely.
- Do not start cyclic hormonal therapy until hematocrit has normalized (i.e., patient should remain on continuous hormonal therapy using 21-d pills without breaks or placebos until Hct is normal).
- If patient remains stable and bleeding is under control, continue cyclic 21 day or extended cycles for 3–6 mo.^b
- Follow serial hematocrits; if bleeding persists may need to continue twice-daily pill for a short interval.

For severe bleeding with moderate anemia (Hgb <9 g/dL):

- Admit to hospital if bleeding heavily, significant anemia, and/or orthostatic vital signs. Outpatient treatment may be considered if hemoglobin >8g/dL, vital signs stable, bleeding slowing, and patient and family are reliable, have transportation, and can be reached by phone.
Transfusion needs are individualized on the basis of hemoglobin, orthostatic symptoms, amount of ongoing bleeding, and the ability to gain control of the bleeding. Most patients can be treated with oral combined medications as below; occasionally intravenous conjugated estrogens (Premarin) 25 mg every four hours for two to three doses are used in severe acute hemorrhage. It is very important to remember that the estrogen will stop the bleeding but if a progestin is not added a re-bleed from estrogen withdrawal will occur when the IV estrogen is discontinued. Consider anti-fibrinolytic therapy.

- One pill four times a day for two to four days, with antiemetic as needed two hours before each pill; followed by one pill three times a day for three days; and then one pill twice a day for at least 21 days and until hematocrit >30%.
- Follow closely with serial hematocrits/hemoglobins; if anemia or bleeding persists may need to continue twice-daily pill and/or eliminate pill-free interval.
- Once hematocrit is recovering, cycle using 21 once-daily pills and five to seven days of placebo or extended cycles for six months. Patients will need several months of iron to replete iron stores, as well as folate supplementation.

Hct = hematocrit; Hgb = Hemoglobin; NSAIDs = nonsteroidal anti-inflammatory drugs; OCP = oral contraceptive pill.

^a Mention of brand name does not imply endorsement of a particular product.

^b It is important to reconsider a patient's need for birth control before discontinuing oral contraceptive therapy.

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Of note, medroxyprogesterone can be used if the patient or parent does not want to use oral contraceptives, or there is a medical contraindication to estrogens, but would not be first line with anemia.

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Clinical Pearls:

- Abnormal menses include those that last for longer than 7 days, occur more frequently than every 21 days or less frequently than every 45 days, and those that result in iron deficiency anemia.
- Anovulation is the most common cause of abnormal uterine bleeding including frequent or prolonged menses in young adolescents, but this is a diagnosis of exclusion; the clinician must perform a history, physical examination, and laboratory tests to exclude other medical causes.
- Because complications of pregnancy may present with any bleeding pattern, pregnancy should be excluded in all those who have unexplained bleeding even those who deny sexual activity.
- Most abnormal bleeding can be managed medically. Evidence is insufficient to support any particular hormone regimen over another for treatment. Non-hormonal treatments, such as tranexamic acid, can reduce menstrual blood loss but has not been found to reduce the duration of menses nor regulate menstrual cycle. Tranexamic acid is not yet approved in under 18 year olds. Progestin IUDs (Mirena) also appear to be another promising therapy for some adolescents with persistent AUB.
- After completing a course of hormonal therapy, adolescents with history of AUB should not have prolonged amenorrhea because of risk of again developing heavy bleeding. Patients should be instructed to contact their provider (or take progestin) if they go more than 6-8 weeks **without a menstrual bleed**.

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Knowledge questions:

1. *Which of the following statements is most correct?*
 - a. Adolescents have ovulatory cycles from time of menarche.
 - b. Adolescents with bleeding disorders have had other signs of bleeding prior to menarche.
 - c. Adolescents with AUB present with persistent daily bleeding for multiple weeks.
 - d. Patients with polycystic ovary syndrome (PCOS) may present with abnormal bleeding.

2. *Which of the following questions should be asked to help narrow the differential diagnosis?*
 - a. How do you feel about your weight? Are you trying to lose weight? How?
 - b. Are you sexually active? Have you ever had intercourse?
 - c. Are you using birth control pills? Any other medications?
 - d. All of the above.

3. *You are seeing a 15 year old patient for heavy menstrual bleeding that has been ongoing for several weeks; menarche was one year ago. This is her third menstrual bleed. She has no significant past medical, family, or psychosocial history and takes no medications. Review of systems is positive for persistent bleeding for three weeks and fatigue. She is noted to be orthostatic on exam, and have active vaginal bleeding. No other significant exam findings. Which of the following is the most appropriate next step?*
 - a. Administer IV fluids. When her dizziness improves, discharge home to follow-up with PCP.
 - b. Start an oral contraceptive pill.
 - c. Order an abdominal CT.
 - d. Order initial laboratory tests including CBC, reticulocyte count, urine HCG, type and cross.

4. *You are seeing a patient with moderate AUB. Her history, examination, and laboratory tests thus far are consistent with anovulatory bleeding. Which of the following is the most appropriate next step?*
 - a. Observation, ibuprofen, reassurance.
 - b. Hormonal treatment, iron supplementation
 - c. Blood transfusion.
 - d. Dilation and curettage (D&C)

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Answers to Knowledge Questions

1. *Which of the following statements is most correct?*

Preferred response: D “Patients with polycystic ovary syndrome (PCOS) may present with abnormal bleeding.”

The spectrum of irregular menses present in adolescents with PCOS includes primary or secondary amenorrhea, oligomenorrhea, anovulatory regular menses, and frequent cycles with abnormal uterine bleeding. These adolescents typically also have signs of androgen excess (acne, hirsutism) or insulin resistance such as acanthosis nigricans; over half are obese.

Adolescents have mostly anovulatory cycles in the first one to two years following menarche, thought to be related to an immature hypothalamic-pituitary-ovarian axis. A study of hormone patterns in young adolescents with anovulatory bleeding shows higher-than-normal levels of FSH in relation to LH supporting a maturation defect. The higher levels of FSH may cause rapid follicular maturation, increase estrogen synthesis, and impair midcycle LH surge. However, many adolescents do not have abnormal bleeding, because normal negative feedback of rising estrogen levels suppresses FSH production and results in limited menstrual flow. Although the etiology of AUB is not entirely understood, it appears that adolescents with AUB not only have delayed positive feedback and delayed establishment of ovulatory menses, but also lack normal negative feedback. Rising levels of estrogen do not cause a fall in FSH and subsequent suppression of estrogen secretion. The endometrium becomes excessively thickened, and heavy irregular menstrual flow results.

While adolescents with bleeding disorders may have a history of epistaxis, petechiae, gingival bleeding, prolonged bleeding from minor wounds, and ecchymoses, many teenagers with von Willebrand disease (vWD) may not have a prior history of injuries and may be diagnosed only because of profuse menstruation starting with menarche. vWD is the most common inherited bleeding disorder, with an estimated incidence of 1-2% of the general population. About 35% of women with vWD PRESENT with menorrhagia. Classically females with vWD have heavy bleeding from their first period and have a family history of menorrhagia. Rarely, girls can acquire vWD later in life (i.e. young women with SLE can produce anti-von Willebrand factor antibody).

Although some adolescents with AUB may present with weeks of persistent bleeding, there are other presentations as well. Some adolescents have normal cyclic intervals but very heavy bleeding at the time of each cycle; others may present with superimposed bleeding at any time through their cycle. Categorizing bleeding as cyclic or acyclic may be useful. An adolescent with heavy cyclic bleeding may have a bleeding disorder such as Von Willebrand’s disease. An adolescent with superimposed or intermenstrual bleeding may have a sexually transmitted infection, foreign body, uterine polyp,

congenital malformation of the uterus, or endometriosis. Adolescents with no cyclicality or cycles of less than 21 days or more than 45 days usually have anovulatory AUB.

2. *Which of the following questions should be asked to help narrow the differential diagnosis?*

Preferred response: D “All of the above.”

All of the above questions should be asked confidentially to help narrow the differential diagnosis. There are a multitude of medical problems associated with disordered eating including irregular periods. Disordered eating behaviors and weight loss can interfere with normal cyclicality by impacting ovulation or rarely interfering with normal coagulation.

All patients with irregular bleeding should be asked whether they are sexually active, whether bleeding was noted post-coital, and whether contraception was used. In addition, sexually active patients should be asked about history of sexually transmitted infections, recent screening, or potential exposure to a new partner with possible infection. Pregnancy related complications, trauma from intercourse, and gonococcal and Chlamydia infections can all cause irregular bleeding. Clinicians should have a low threshold for pregnancy and STI testing regardless of reported sexual history.

The possibility of breakthrough bleeding in the adolescent taking hormonal contraceptives also needs to be explored. Often times, adolescents may have obtained the method confidentially and family may not be aware. Adolescents may experience irregular bleeding when they initially start on a method, or if they have forgotten or not using birth control as instructed.

3. *You are seeing a 15 year old patient for heavy menstrual bleeding that has been ongoing for several weeks; menarche was one year ago. This is her third menstrual bleed. She has no significant past medical, family, or psychosocial history and takes no medications. Review of systems is positive for persistent bleeding for three weeks and fatigue. She is noted to orthostatic on exam, and have active vaginal bleeding. No other significant exam findings. Which of the following is the most appropriate next step?*

Preferred response: D “Order initial laboratory tests including CBC, reticulocyte count, urine HCG, type and cross.”

Patient’s history and physical exam raise concerns for significant blood loss. She is dizzy, orthostatic by pulse, and noted to have active bleeding on exam. However, her blood pressure is stable, she is mentating well, and exam is significant for easily palpated peripheral pulses and normal capillary refill. She should have further evaluation to assess degree of anemia and possible etiology of bleeding, as well as to determine a management plan to control bleeding. The most important test is a complete blood count (with differential and platelet count) to assess if the adolescent is anemic. In the face of a normal hemoglobin/hematocrit and an impressive history of bleeding, a reticulocyte count can indicate the magnitude of actual blood loss, while the concentration of hemoglobin in the reticulocyte (CHr) can provide a sensitive indicator of iron sufficiency

or deficiency. If CHr is not available, the ferritin level is an alternative measure of iron status. Another important test is a serum or urine HCG test to exclude pregnancy. Type and screen is helpful in the case of a patient with significant ongoing blood loss or anemia such that patient may require a blood transfusion.

Discharging home after IV fluids is not indicated at this time. She should have further evaluation to assess degree of anemia and possible etiology of bleeding, as well as to determine management plan to control bleeding. Starting an oral contraceptive pill is definitely an option, but patient should first have laboratory workup completed to determine if and what type of medical treatment is required. Of note, hormonal workup and von Willebrand panel should be drawn before starting on the pill since levels will be altered.

An abdominal CT is not indicated. An ultrasound is helpful as the first line of imaging if a pelvic mass is felt, a uterine anomaly is suspected, or bimanual examination cannot be accomplished in a girl with significant bleeding. Additionally, it allows for assessment of endometrial lining. For inconclusive ultrasound evaluations, and high level of suspicion for concern for structural lesions, MRI would be next step in assessment of pelvic organs.

4. You are seeing a patient with moderate AUB. Her history, examination, and laboratory tests thus far are consistent with anovulatory bleeding. Which of the following is the most appropriate next step?

Preferred response: B “Hormonal treatment, iron supplementation”

Oral contraceptive pills are the simplest treatment for moderate AUB. The estrogen component heals the endometrial bleeding sites by causing tissue proliferation and the progestins induce endometrial stability. Medroxyprogesterone can be used if the patient or parent does not want to use oral contraceptives, or there is a medical contraindication to estrogens but would not be first line with anemia. The levonorgestrel releasing intrauterine system (Mirena IUD) is another option for reducing heavy menstrual bleeding but not in a young adolescent with her first episode of AUB.

For most patients, estrogen/progestin therapy such as 0.3 mg norgestrel/30 ug ethinyl estradiol (LoOvral) or 0.15 mg levonorgestrel/30 µg ethinyl estradiol (Levlen, Nordette, Levora) are good choices. For mild bleeding and minimal anemia, the patient can be told to take one tablet once a day for 21 days. If the bleeding is more significant or there is anemia, the hormone tablets are taken twice a day (b.i.d.) for 3 to 4 days until bleeding stops, then daily (q.d.) to finish at least a 21-day cycle.

If oral medroxyprogesterone acetate is used, it is given as 10 mg q.d. for 10 to 14 days, starting on the 14th day of the menstrual cycle (e.g., day 14-28) or starting on the first day of each month (eg. October 1-14, November 1-14, December 1-14). Oral norethindrone acetate (aygestin) can also be used (5 to 10 mg daily for 10-14 days) especially when cycles have not been successfully regulated by medroxyprogesterone; norethindrone partially converts to ethinyl estradiol which may do a better job of stabilizing endometrium. Combination hormone pills are preferable to above when hematocrit below 33% and no contraindications to estrogen.

Although nonsteroidal anti-inflammatory drugs (e.g. naproxen sodium, ibuprofen) can be prescribed to lessen flow, in this case the patient is anemic and actively bleeding requiring further intervention. Transfusion should be considered by each individual case and can usually be avoided if hematocrit is not significantly low, vital signs are stable, and medical team is able to rapidly gain control of bleeding. Transfusion alone will not address the underlying problem of excessive bleeding nor prevent recurrence. D&C should be avoided as first line therapy for dysfunctional uterine bleeding given that the overwhelming majority of adolescents can be treated successfully with hormones alone. If various regimens of hormones fail to control bleeding within 24-36 hours in an ill patient, D&C may be needed to diagnose and treat intrauterine pathology.

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