Facilitator Preparation: Facilitators should thoroughly review this module. They should also prepare or photocopy handouts to distribute during the course of the case presentation and the "Materials for Learners" packet.

Open the Discussion: Introduce the case title and the objectives of the session. Explain that this will be an interactive case discussion prompted by a series of multiple choice questions and not a lecture. Distribute Part I of the case and ask one or more of the participants to read it aloud.

13 year old Female with Too Many Periods

Abnormal Uterine Bleeding

Case Authors:

Areej Hassan MD MPH
Harvard Medical School
Boston Children's Hospital

Expert Content Reviewer:

Jean Emans MD
Harvard Medical School
Boston Children's Hospital

Objectives:

- Distinguish normal versus abnormal menstrual function.
- Describe the typical presentation of an adolescent with abnormal uterine bleeding (AUB).
- List a differential diagnosis for abnormal menstrual bleeding in an adolescent and formulate a diagnostic plan.
- Describe the basic management of AUB

Part I:

Introduction:

A 13 year old girl, Jovani, presents with heavy vaginal bleeding for three days. She is feeling lightheaded and dizzy.

Current History:
Jovani's last menstrual period prior to this bleed was two weeks ago, lasting for 9 days. She began bleeding again three days ago and describes it as "heavy." She is passing clots. She is feeling weak, and feels dizzy when she stands up too quickly. She has been changing pads every ½ to 1 hour. She is also complaining of significant cramping somewhat relieved by ibuprofen.

Her menarche occurred 1 year ago, and it lasted 10 days. She then had menstrual periods at irregular intervals, averaging every 2 to 3 months, and lasting 7 to 10 days. However, over the past 3 months, she tells you that her periods have been occurring more frequently, about every 2 to 3 weeks. She denies PMS symptoms.

Jovani states that she does not have intermenstrual spotting. She denies new stresses in her life, no significant weight changes, no history of easy bleeding or bruising. Review of

systems is also negative for visual changes, headache, hirsutism, acne, heat or cold intolerance, palpitations, and skin changes. She plays soccer about 2 hours a day.

Past Medical History:
Jovani has been seen by PCP for yearly checkups; no previous diagnoses. She does not take any medications regularly.

Family History:
Her mother's menarche was at age 13. She had irregular, but not frequent or heavy periods, for the first 2 to 3 years. No history of bleeding disorders.

Following this reading, ask all participants "*So what do you think about this case? What would you like to focus on during our discussion today*?" List agenda items on a blackboard or flipchart. Then use the questions below to start the discussion. Remember that the key to successfully leading a small group is facilitation of the discussion rather than lecture. Draw as many participants as possible into the discussion. Allow silences while group members think about questions.

Potential Discussion Questions:

What defines a normal menstrual period?

- Duration of flow: 3-7 days
- Cycle length: 21-35 days for adults; however in adolescents, cycles can range from 21-45 days in the first several years after menarche
- Blood loss: average 20-80 mL
- 10-15 soaked tampons or pads per cycle

What questions can you ask an adolescent to help quantitatively assess blood loss?
Unfortunately, estimation of blood loss by self-report is often inaccurate. Questions that may be helpful include:

- Do you bleed heavier than one pad or tampon an hour? Do you experience "flooding" or "gushing"?
- Do you use more than 6 pads/tampons per day on your heaviest days?
- Do you pass clots bigger than one half inch diameter or have soiling related to bleeding on clothing?
- Are your activities limited by the amount of menstrual flow?

What terms are used to describe excessive menstrual bleeding?

- Menorrhagia: prolonged (>seven days) or excessive (>80 ml) uterine bleeding at regular intervals
- Metrorrhagia: bleeding at irregular, frequent intervals
- Menometrorrhagia: prolonged bleeding occurring at irregular intervals
- Polymenorrhea: bleeding occurring at regular intervals of <21 days.
- Abnormal uterine bleeding (previously referred to as dysfunctional uterine bleeding; also known as heavy menstrual bleeding): in adolescents most frequently results from excessive, prolonged, unpatterned bleeding from the

endometrium *unrelated to structural or systemic disease,* and thus other diagnoses must be excluded.

- Instead of the vocabulary above, the American College of Obstetrics and Gynecology (ACOG) has supported the adoption of the International Federation of Obstetrics and Gynecology (FIGO) terminology. AUB, defined as bleeding from the uterus that is abnormal in regularity, volume frequency, or duration, is classified as either "heavy menstrual bleeding" or "intermenstrual bleeding."

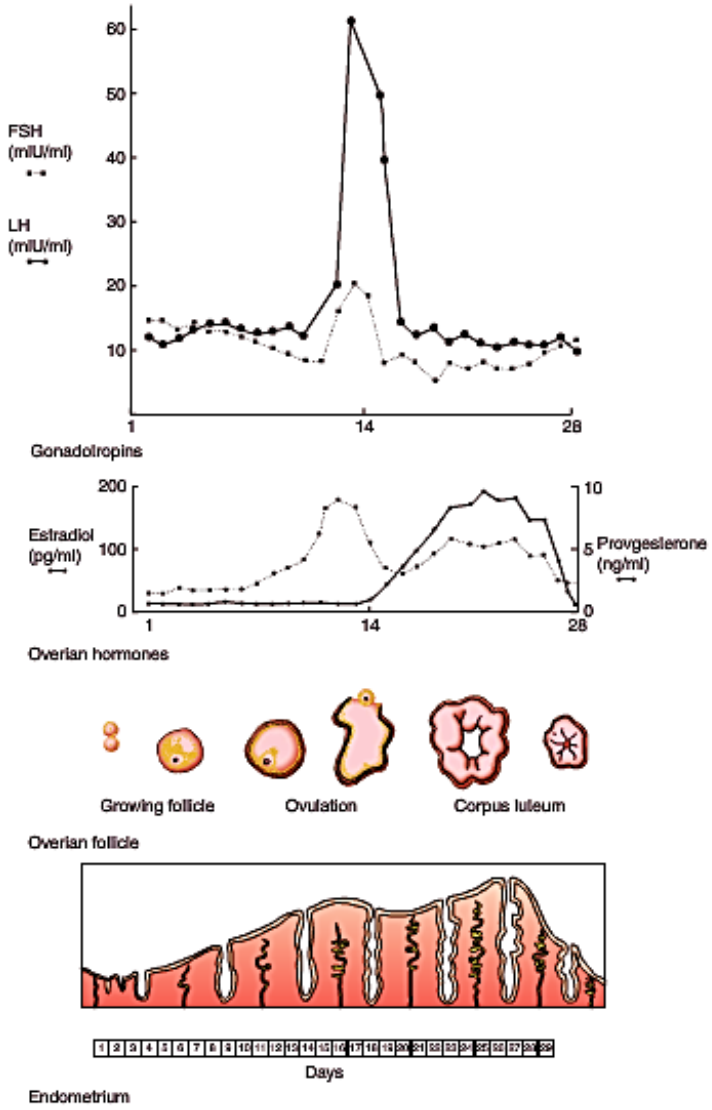
What is involved in the normal ovulatory feedback system?
Ask learners to refer to Figure 1 in their packet.

The menstrual cycle is divided into a follicular phase, an ovulatory phase, and a luteal phase.

- In the follicular phase, pulsatile GnRH secreted from the hypothalamus stimulates the secretion of FSH and LH from the pituitary. FSH then increases the number of granulosa cells in the ovarian follicle, increases the number of receptors for FSH on the granulosa cells, and induces the granulosa cells to acquire an aromatizing enzyme that allows the conversion of androgen precursors to estradiol. Estradiol also amplifies the effect of FSH. The theca cells, under LH stimulation, secrete androstenedione, testosterone, and estradiol.
- A dominant follicle emerges by day 5 to 7 of the cycle, and the rising estradiol level causes proliferation of the number of glandular cells and stroma in the endometrium of the uterus. After the LH surge midcycle, ovarian follicular rupture occurs and the oocyte is released.
- The corpus luteum develops from the ruptured follicle and secretes progesterone. Under the influence of rising estrogen and progesterone levels, the endometrium enters the secretory phase, characterized by coiling of the endometrial glands and increased vascularity of the stroma.
- Within 8 or 9 days after ovulation, if fertilization does not occur, regression begins. Progesterone and estrogen levels begin to decline, and the endometrium undergoes necrotic changes that result in menstrual bleeding. As estrogen levels decline in the late luteal phase, the negative feedback of estrogen on FSH secretion decreases and FSH begins to rise to initiate new follicular development

.

Figure 1: Normal Ovulatory Menstrual Cycle



(Reprinted with permission from S.J. Emans and M.R. Laufer, *Emans, Laufer, Goldstein's Pediatric and Adolescent Gynecology*, 6th ed. Lippincott, Williams & Wilkins; Wolters Kluwer, 2012)

What is the differential diagnosis of abnormal menstrual bleeding?

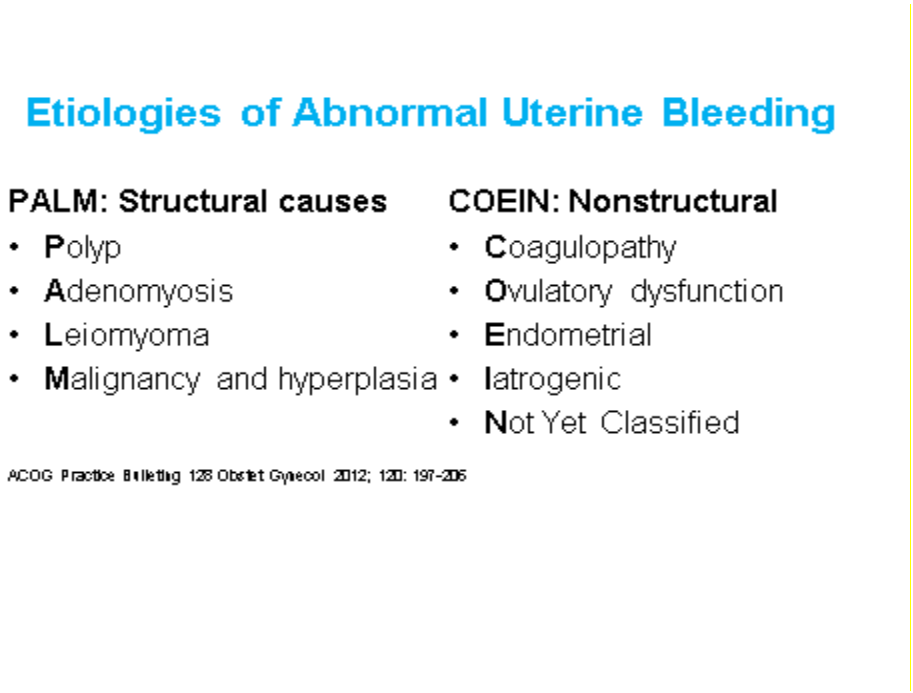
The most common disorders in adolescents are listed below:

- Anovulatory uterine bleeding
- Disorders of pregnancy: threatened abortion, miscarriage, ectopic pregnancy, trophoblastic disease
- Infection, Pelvic inflammatory disease
- Hematologic disorders: Thrombocytopenia, leukemia, aplastic anemia, clotting disorders, von Willebrand's disease, platelet disorders
- Endocrine disorders: Hypo- or hyperthyroidism, adrenal disease, diabetes mellitus, hyperprolactinemia, polycystic ovary syndrome, ovarian failure
- Other gynecological disorders:

    - Vaginal abnormalities: carcinoma or sarcoma, laceration
    - Cervical disorders: cervicitis, polyp, hemangioma
    - Uterine disorders: congenital anomalies (obstructed uterus; fistula development), breakthrough bleeding associated with oral contraceptive use, ovulation bleeding, submucous myoma (fibroid)
    - Ovarian cysts, tumors
    - Endometriosis
    - Foreign body (e.g., retained tampon)
    - Systemic diseases (cystic fibrosis, tuberculosis, renal failure)
    - Hemangiomas or other vascular anomalies in the vagina or on the cervix
- Systemic diseases
- Trauma
- Medications: anticoagulants, platelet inhibitors, androgens, spironolactone, tricyclic antidepressants, anti-psychotics, IUD

Ask learners to refer to Figure 2 in their packet.
As noted earlier, the American College of Obstetrics and Gynecology (ACOG) has supported the adoption of the International Federation of Obstetrics and Gynecology (FIGO) terminology and classification system for assessing AUB in women using the mnemonic PALM-COEIN as a reminder of etiologies. While a useful framework, the major focus of this mnemonic is adults, not adolescents where additional diagnoses such as sexually transmitted infections and pregnancy and listed diagnoses such as anovulatory cycles and von Willebrand's disease figure more prominently in the differential diagnosis.

Figure 2:



.
Should you talk to this teenager alone?

- Teens need to be seen alone, even if only briefly to ask sensitive questions. Explaining this to the parent is important.
- Confidentiality should be protected for teens unless a clinician identifies a serious risk.
- An adolescent girl should be offered the choice of having her mother (or female guardian) in or out of the room during the examination.

Distribute Part II of the case and have participant(s) read it aloud.

Part II:

Next Steps:

Psychosocial History:
Jovani denies sexual activity, alcohol and tobacco use, weight control methods, and family and school stresses. She is vegetarian.

Physical Exam:
Her height and weight are 25th percentile for age, and her heart rate is 72 supine and 110 standing. Blood pressure is 105/68 supine and 92/50 standing.
In general, she is alert, comfortable, in no acute distress. She appears to be slightly pale. Thyroid exam is normal, Lungs clear bilaterally. Heart RRR s1 s2, she has a soft systolic ejection murmur heard best at LUSB. Breasts are Tanner IV without galactorrhea. Her abdomen is soft, NT, ND, no masses on palpation. Her pubic hair is Tanner IV and external genitalia are normal with no evidence of trauma or laceration. No clitoromegaly. Tissues are well estrogenized, slow active ooze coming from vaginal canal. She has no hirsutism, acne, petechiae or ecchymoses. A one-finger bimanual vaginal/abdominal exam reveals a firm, small uterus and normal ovaries bilaterally. No hirsutism, acne, petechiae, or ecchymoses; capillary refill < 2 sec.

Pause and begin next set of discussion questions.
Potential discussion questions:

What further workup would you consider?

- 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.
- Another important test is a serum or urine HCG test to exclude pregnancy. Type and screen is helpful in the case that patient may require a blood transfusion.
- Adolescents who have ever been sexually active should be evaluated with tests for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* (nucleic acid amplification tests using vaginal, cervical, or urine samples).
- Other tests which may be helpful include an erythrocyte sedimentation rate to assess for infection, coagulation studies including PT, PTT, fibrinogen, and von

Willebrand's panel (von Willebrand factor antigen, ristocetin co-factor activity, and factor VIII activity) if a bleeding disorder is a strong possibility (heavy bleeding since menarche, a personal or family history of excessive bleeding, liver dysfunction, or if there is a significantly low hemoglobin level).

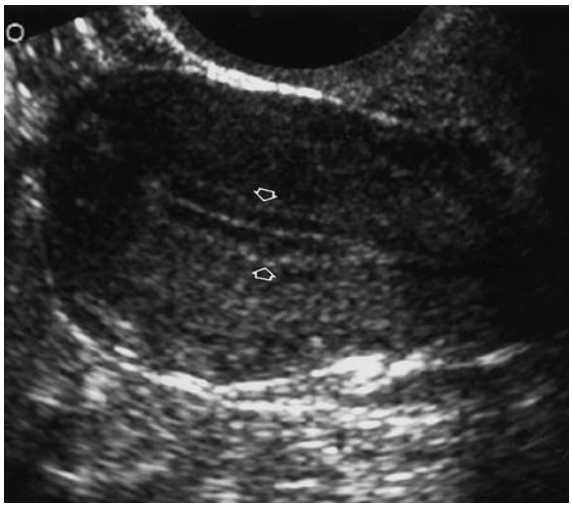
- Endocrinologic studies should also be considered if suspicion of polycystic ovary syndrome or a thyroid disorder (e.g. TSH, LH, FSH, prolactin, testosterone, DHEAS). The initial results will help guide management treatment.

Distribute Lab results and US image. Ask participants to evaluate for abnormalities.

Initial Laboratory results:
urine pregnancy test negative
white blood cell count 9,500/mm3
hemoglobin 9.1 gm/dl
hematocrit 29.6%
MCV 71 fl
platelets 321,000/mm3
TSH pending
Von Willebrands panel pending
Coags (PT/PTT/INR): 10.3 sec / 28 sec / 0.96 (wnl)

Transabdominal US

- Bilateral ovaries: normal, no cysts. No sign of free fluid in pelvis; greatest possible thickness of uterine stripe: 7mm



Reprinted with permission from MR Laufer

What is your diagnosis?

- History, exam, and laboratory results are consistent with abnormal uterine bleeding (previously known as dysfunctional uterine bleeding)
- Most adolescents are anovulatory in the first year following menarche. Yet many do not have abnormal bleeding because normal negative feedback of rising

estrogen levels suppresses FSH production and results in anovulatory but limited menstrual flow.

- The group of adolescents with DUB have delayed positive feedback and delayed establishment of ovulatory menses, and 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.

How would you categorize this patient's AUB?
A useful categorization of AUB is as follows:

- Mild AUB:

1. Menses are longer than normal or cycle is shortened to less than 21 days (1st day of one menstrual period to 1st day of next menstrual period) for 2 or more months. Flow is slightly to moderately increased.
2. Normal hemoglobin.

- Moderate AUB:

1. Menses are moderately prolonged (>7 days) or cycle is shortened with frequent menses (every
1-3 weeks). Flow is moderate to heavy.
2. Mild anemia.

- Severe AUB:

1. Prolonged bleeding with disruption of normal cycles, and very heavy flow.
2. Hemoglobin reduced, often to less than 9 gm. Clinical signs of blood loss may be present.

Table 1: Categorizing Abnormal Uterine Bleeding (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

Given the above laboratory findings, this patient has moderate AUB.

How would you manage this patient's AUB?

Ask learners to turn to Table #2 in their packet for hormonal and non-hormonal options and allow a few minutes for learners to review its contents before discussing management options.

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.

(Reprinted with permission from S.J. Emans and M.R. Laufer, *Emans, Laufer, Goldstein's Pediatric and Adolescent Gynecology*, 6th ed. Lippincott, Williams & Wilkins; Wolters Kluwer, 2012)

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.

NON-HORMONAL TREATMENT

- Non-steroidal anti-inflammatory drugs may lessen heavy bleeding but do not reduce the overall duration of menses
- Tranexaminic acid (antifibrinolytic agent recently approved for use in the US) has been shown to significantly reduce menstrual blood loss (up to 40%) in women with menorrhagia; it can be used only for five days (1300 mg PO TID).
    - It is considered more potent than aminocaprioic acid with fewer side effects. Most common side effects include nausea and diarrhea. Serious side effects include retinal clots and ligneous conjunctivitis with prolonged exposure but is reversible.
    - No data on use in patients under 18 or on COCs but may be of use in those with refractory AUB or patients with bleeding disorders

Distribute Part III: Ask someone to read follow-up aloud.

Part III
Epilogue:

- You prescribe an iron supplement as well as a 0.3 mg norgestrel/30 μg ethinyl estradiol oral contraceptive pill, and describe the side effects of this medication. Jovani will take them twice a day until the bleeding slows or stops, then daily and will skip the placebo week until her hematocrit and indices (MCV) returns to normal.
- Jovani returns for a follow-up visit one week later and says that the bleeding stopped after 3 days on the oral contraceptives. She is not having any side effects. She continues with one pill a day dosing and at return appointment eight weeks later, her hemoglobin is 11.4 gm and hematocrit is 33.2%.
- You instruct her to start using the placebo week of the pill to resume cyclic bleeding. She will continue on iron therapy to complete three month course. She will continue to take OCPs for six months in total and will address at that time discontinuing with close monitoring.

- Her remaining workup including von Willebrand's panel returns normal.

Refer back to group's learning agenda and summarize the key teaching points that were made. This will give the group a sense of accomplishment, and emphasize the important messages. Suggest further sources of reading or other information if there are agenda items that were not covered in the discussion.

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 tranexaminic 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.**

Knowledge questions:

Ask learners to complete the knowledge questions in their packet. If time allows, questions and answers can be discussed as a group, or learners can complete and review answers on their own.

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)

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 cyclicity 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 cyclicity 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 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.

References:

1. Gray S, Emans SJ. Abnormal Vaginal Bleeding in Adolescents. Emans SJ and Laufer MR (eds.) *Emans, Laufer and Goldstein's Pediatric and Adolescent Gynecology*, sixth edition in press Philadelphia: Lippincott, Williams and Wilkins; 2012
2. Ansel S, Jones GS. Etiology and treatment of dysfunctional uterine bleeding. *Obstet Gynecol* 1974;44(1).
3. Treloar AE, et al. Variation of the human menstrual cycle through reproductive life. *Int J Fertil* 1967;12(1 Pt 2):77–126
4. Ahuja SP et al. Overview of bleeding disorders in adolescent females with menorrhagia. *J Pediatr Adolesc Gynecol*. 2010 Dec;23(6 Suppl):S15-21
5. James AH et al. Von Willebrand disease and other bleeding disorders in women: consensus on diagnosis and management from an international expert panel. *Am J Obstet Gynecol* 2009:201:12.e1
6. Lethaby A, et al. Nonsteroidal anti-inflammatory drugs for heavy menstrual bleeding.

Cochrane Database Syst Rev 2007(4):CD000400.
7. Claessens EA, Cowell CA. Acute adolescent menorrhagia. *American Journal of Obstetrics and Gynecology* 1981;139:277-280.
8. Falcone T, Desjardins C, Bourque J et al. Dysfunctional uterine bleeding in adolescent. *Journal of Reproductive Medicine* 1994;39:761-764.
9. Wathen PI, Henderson MC, Witz CA. Abnormal uterine bleeding. *Medical Clinics of North America* 1995;79:329-343.
10. Cowan BD, Morrison JC. Management of abnormal genital bleeding in girls and women. *New England Journal of Medicine* 1991;324:1710-1715.
11. El-Hemaidi I, Gharaibeh A, et al. Menorrhagia and bleeding disorders. *Current Opinion in Obstetrics & Gynecology*. 2007; 19(6):513-520.
12. Mannucci, P. Treatment of von Willebrand's Disease. *NEJM* 2004; 351: 683-694.
13. Mikhail S, Kouides P. Von Willebrand Disease in the Pediatric and Adolescent Population. *J Pediatr Adolesc Gynecol*. 2010: 23:S3-10
14. American College of Obstetricians and Gynecologists and the American Academy of Pediatrics. Menstruation in girls and adolescents: Using the menstrual cycle as a vital sign. *Pediatrics* 118 (5) Nov 2006: 2245-2250
15. ACOG Practice Bulletin 128 Diagnosis of Abnormal Uterine Bleeding in Reproductive Aged Women. *Obstet Gynecol* 2012;120:197-206
16. Committee Opinion, ACOG, Management of Acute Abnormal Uterine Bleeding in Nonpregnant Reproductive-Aged Women. *Obstet Gynecol* 2013;121(4):891-896

Materials for Learners:

Packet should include the following:

- Handout #1: Normal Ovulatory Feedback Cycle (Figure 1)
- Handout #2: Etiologies of AUB (Figure 2) and Categorizing AUB (Table 1)
- Handout #3: Suggested Oral Contraceptive Regimens (Table 2)
- Clinical pearls
- Knowledge questions and answers
- References

13 year old Female with Too Many Periods

Abnormal Uterine Bleeding

Part I:

Introduction:

A 13 year old girl, Jovani, presents with heavy vaginal bleeding for three days. She is feeling lightheaded and dizzy.

Current History:
Jovani's last menstrual period prior to this bleed was two weeks ago, lasting for 9 days. She began bleeding again three days ago and describes it as "heavy." She is passing clots. She is feeling weak, and feels dizzy when she stands up too quickly. She has been changing pads every ½ to 1 hour. She is also complaining of significant cramping somewhat relieved by ibuprofen.

Her menarche occurred 1 year ago, and it lasted 10 days. She then had menstrual periods at irregular intervals, averaging every 2 to 3 months, and lasting 7 to 10 days. However, over the past 3 months, she tells you that her periods have been occurring more frequently, about every 2 to 3 weeks. She denies PMS symptoms.

Jovani states that she does not have intermenstrual spotting. She denies new stresses in her life, no significant weight changes, no history of easy bleeding or bruising. Review of systems is also negative for visual changes, headache, hirsutism, acne, heat or cold intolerance, palpitations, and skin changes. She plays soccer about 2 hours a day.

Past Medical History:
Jovani has been seen by PCP for yearly checkups; no previous diagnoses. She does not take any medications regularly.

Family History:
Her mother's menarche was at age 13. She had irregular, but not frequent or heavy periods, for the first 2 to 3 years. No history of bleeding disorders.

13 year old Female with Too Many Periods

Abnormal Uterine Bleeding

Part II:

Next Steps:

Psychosocial History:
Patient denies sexual activity, alcohol and tobacco use, weight control methods, and family and school stresses. She is vegetarian.

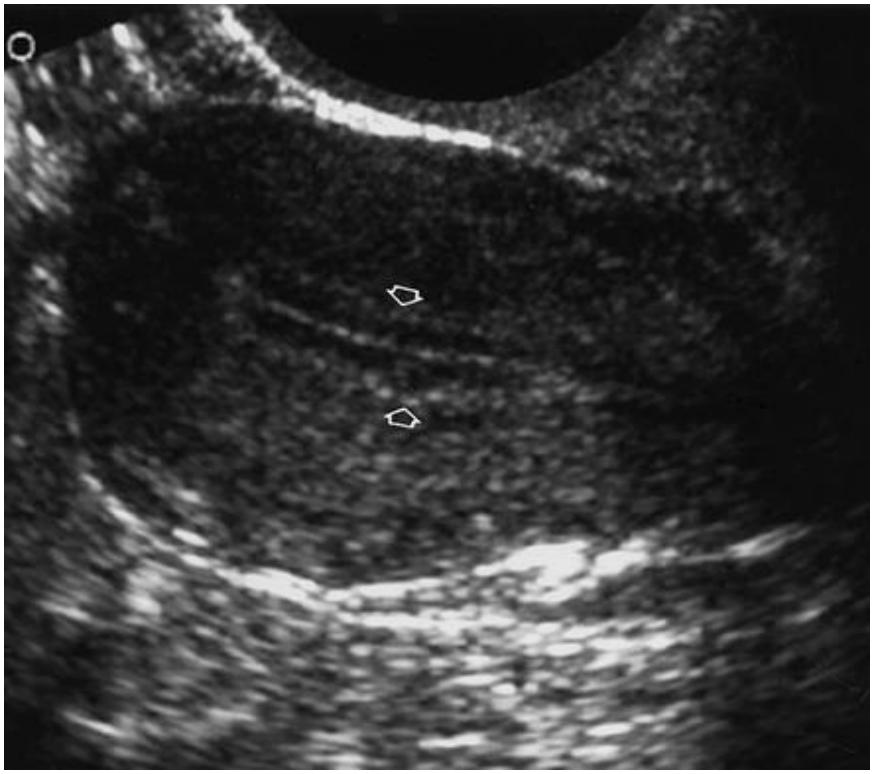
Physical Exam:
Her height and weight are 25th percentile for age, and her heart rate is 72 supine and 110 standing. Blood pressure is 105/68 supine and 92/50 standing.
In general, she is alert, comfortable, in no acute distress. She appears to be slightly pale. Thyroid exam is normal, Lungs clear bilaterally. Heart RRR s1 s2, she has a soft systolic ejection murmur heard best at LUSB. Breasts are Tanner IV without galactorrhea. Her abdomen is soft, NT, ND, no masses on palpation. Her pubic hair is Tanner IV and external genitalia are normal with no evidence of trauma or laceration. No clitoromegaly. Tissues are well estrogenized, slow active ooze coming from vaginal canal. She has no hirsutism, acne, petechiae or ecchymoses. A one-finger bimanual vaginal/abdominal exam reveals a firm, small uterus and normal ovaries bilaterally. No hirsutism, acne, petechiae, or ecchymoses; capillary refill < 2 sec.

13 year old Female with Too Many Periods

Abnormal Uterine Bleeding

Initial Laboratory results:
urine pregnancy test negative
white blood cell count 9,500/mm3
hemoglobin 9.1 gm/dl
hematocrit 29.6%
MCV 71 fl
platelets 321,000/mm3
TSH pending
Von Willebrands panel pending
Coags (PT/PTT/INR): 10.3 sec / 28 sec / 0.96 (wnl)

Transabdominal US



Reprinted with permission from MR Laufer

13 year old Female with Too Many Periods

Abnormal Uterine Bleeding

Part III

Epilogue:

- You prescribe an iron supplement as well as a 0.3 mg norgestrel/30 μg ethinyl estradiol oral contraceptive pill, and describe the side effects of this medication. Jovani will take them twice a day until the bleeding slows or stops, then daily and will skip the placebo week until her hematocrit and indices (MCV) returns to normal.
- Jovani returns for a follow-up visit one week later and says that the bleeding stopped after 3 days on the oral contraceptives. She is not having any side effects. She continues with one pill a day dosing and at return appointment eight weeks later, her hemoglobin is 11.4 gm and hematocrit is 33.2%.
- You instruct her to start using the placebo week of the pill to resume cyclic bleeding. She will continue on iron therapy to complete three month course. She will continue to take OCPs for six months in total and will address at that time discontinuing with close monitoring.
- Her remaining workup including von Willebrand's panel returns normal.