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Abnormal Vaginal Bleeding in Adolescents

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Abnormal Vaginal Bleeding in Adolescents

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Author Disclosure
Drs Hayden Gray and Emans are supported in part by the Leadership Education in Adolescent Health Project, T71 MC00009 from the Maternal and Child Health Bureau (Title 5, Social Security Act), Health Resources and Services Administration, Department of Health and Human Services. The use of combined oral contraceptive pills, as described for treatment of vaginal bleeding in adolescents, is considered to be "off label" but represents the standard of care for this condition.

Objectives After completing this article, readers should be able to:

1. Describe normal and abnormal patterns of vaginal bleeding in adolescents.
2. Discuss the differential diagnosis of abnormal vaginal bleeding in adolescents.
3. Outline a strategy for diagnosis and management of abnormal vaginal bleeding.

Introduction

Many young women experience irregular or heavy vaginal bleeding in the course of their development. In most cases, the abnormal bleeding is due to anovulation and immaturity of the hypothalamic-pituitary-ovarian feedback mechanisms. However, abnormal bleeding may be the presenting sign of multiple medical illnesses that require long-term treatment and follow-up, and pediatricians must recognize and exclude other potential causes of bleeding.

Definitions and Pathophysiology

It is essential to review normal menstrual physiology before discussing abnormalities. An ovulatory menstrual cycle is comprised of three phases: follicular, ovulatory, and luteal. The follicular phase of the menstrual cycle typically lasts about 2 weeks but may vary from 7 to 21 days or longer. In the follicular phase, the hypothalamus releases pulses of gonadotropin-releasing hormone, stimulating the pituitary to release follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH and LH stimulate the development of ovarian follicles and the synthesis of steroid hormones. FSH increases the number of granulosa cells in the ovary, promotes estrogen secretion by increasing aromatase, and increases the number of FSH receptors on the granulosa cells. LH stimulates the ovarian theca cells to enhance the secretion of both estrogen and androgens, which are converted to testosterone and estrogen in ovarian and peripheral tissue. Rising estrogen concentrations stimulate proliferation of the endometrial lining and exert a negative feedback effect on FSH. They also exert a positive feedback effect on LH, resulting in the midcycle LH surge that stimulates ovulation. Both negative and positive feedback mechanisms must be functional for ovulation to occur.

At ovulation, the ovary releases an oocyte, and the remaining ovarian follicle becomes the corpus luteum. This begins the luteal phase, which lasts approximately 14 days and varies less in duration than the follicular phase. The corpus luteum produces progesterone and smaller amounts of estrogen. Progesterone stabilizes the endometrial lining and promotes the growth of glandular tissue and blood vessels in preparation for fertilization. When no fertilization occurs, the corpus luteum deteriorates. The resultant decrease in progesterone (and estrogen) triggers menstrual sloughing of the endometrial lining. The same decrease stimulates the increase of LH and FSH via negative feedback.

The length of the normal cycle often is 26 to 30 days but may vary from 21 to 35 days, depending primarily on the length of the follicular phase. The average amount of menstrual blood loss is 30 to 40 mL. A loss of more than 80 mL is considered to be pathologic and may lead to iron deficiency anemia. (1) Normal menstrual flow lasts from 3 to 7 days; a menstrual period lasting longer than 10 days is considered to be pathologic. Menorrhagia, or hypermenorrhea, is heavy (>80 mL) or prolonged (>7 d) vaginal bleeding that occurs at regular cyclic intervals. Metrorrhagia, or acyclic bleeding, refers to irregular vaginal bleeding. Menometrorrhagia is heavy vaginal bleeding occurring at

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irregular intervals. Polymenorrhea is the term applied to frequent vaginal bleeding at intervals more often than every 21 days.

We use the term “abnormal vaginal bleeding” to refer to all cases of irregular, heavy, or frequent bleeding. The term “dysfunctional uterine bleeding” (DUB) often is substituted, although true DUB implies bleeding that is not due to underlying anatomic abnormalities or systemic conditions. DUB in young women is caused most frequently by chronic anovulation and immaturity of the hypothalamic-pituitary-ovarian axis and is a diagnosis of exclusion.

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Epidemiology

It is estimated that about one in five women experiences abnormal bleeding during the time in her life that she is menstruating. Abnormal vaginal bleeding is an extremely common complaint in young women that frequently results in referral to specialists. Patient self-reports of bleeding may be unreliable, however. The pediatric clinician must be able to obtain a history and perform an appropriate assessment and laboratory studies to identify those who have disease. (2)

In the first 2 to 3 years after menarche, menses frequently are irregular, presumably because the positive and negative feedback systems of the hypothalamic-pituitary-ovarian axis have not yet matured. In a longitudinal cohort study of young women in Finland, 85% of menstrual cycles were anovulatory in the first year following menarche, and it was not until 3 years after menarche that most cycles were ovulatory. (3) The same study showed that girls who have earlier menarche achieve regular ovulation earlier than those who menstruate later.

Differential Diagnosis

The differential diagnosis of abnormal vaginal bleeding is extensive (Table 1). Recognition of the pattern of bleeding may be helpful in determining its cause. The most common condition is anovulatory bleeding due to an immature hypothalamic-pituitary-ovarian axis, often

termed DUB, which, as noted previously, is a diagnosis of exclusion. Anovulatory bleeding is the most common cause of acyclic bleeding and may be associated with anovulation from sports participation (such as swimming), stress, and disordered eating such as bulimia in addition to endocrinopathies such as hypothyroidism, hyperthyroidism, diabetes mellitus, and Cushing syndrome. The same disorders that result in irregular bleeding may cause amenorrhea. Patients who have polycystic ovary syndrome (PCOS) may have heavy or extended bleeding with long or very short cycles. (4) PCOS occurs in 5% to 10% of adolescents and often is associated

with overweight, insulin resistance, acanthosis nigricans, hirsutism, and acne as well as a family history of type 2 diabetes mellitus or PCOS. Turner syndrome and other causes of premature ovarian failure present most typically with amenorrhea, but may present with polymenorrhea.

In developing countries, tuberculosis is a common cause of abnormal uterine bleeding. Trauma from acute injuries such as those received while waterskiing as well as by sexual trauma may result in bleeding.

Cyclic abnormal bleeding (menorrhagia) may suggest bleeding disorders or uterine pathology. It is difficult to estimate what proportion of young women who have menorrhagia have bleeding disorders because published studies often focus on the most severe cases and do not include adolescents. One Canadian study reviewed data from adolescent patients hospitalized for menorrhagia over a 9-year period and found an underlying bleeding disorder in one in five girls who required hospitalization, one in four who had hemoglobin concentrations less than 10 g/dL (100 g/L) on presentation, one in three who required transfusion, and one in two who presented with menorrhagia from her very first menses. (5) Another Canadian study performed with similar patients over 10 years found a much lower rate of newly diagnosed bleeding disorders (2 of 61 patients). (6) In an 8-year study of both inpatients and outpatients, 13% of adolescents presenting with menorrhagia had thrombocytopenia. Of those who had no thrombocytopenia, a significant proportion of those undergoing hematologic testing had an inherited bleeding disorder. (7) In general, the most common bleeding disorders causing menorrhagia are thrombocytopenia (due to immune thrombocytopenic purpura or iatrogenic thrombocytopenia caused by che-

Table 1. Differential Diagnosis of Abnormal Vaginal Bleeding in the Adolescent Girl

Anovulatory Uterine Bleeding	Cervical Problems
Endocrine Disorders	<ul style="list-style-type: none"> • Cervicitis • Polyp • Hemangioma • Carcinoma or sarcoma
<ul style="list-style-type: none"> • Hypo- or hyperthyroidism • Adrenal disease • Hyperprolactinemia • Polycystic ovary syndrome • Ovarian failure 	Uterine Problems
Pregnancy-related Complications	<ul style="list-style-type: none"> • Submucous myoma • Congenital anomalies • Polyp • Carcinoma • Use of intrauterine device • Ovulation bleeding
<ul style="list-style-type: none"> • Threatened abortion • Spontaneous, incomplete, or missed abortion • Ectopic pregnancy • Gestational trophoblastic disease • Complications of termination procedures 	Ovarian Problems
Infection	<ul style="list-style-type: none"> • Cyst • Tumor (benign, malignant)
<ul style="list-style-type: none"> • Cervicitis • Vaginitis • Endometritis • Pelvic inflammatory disease 	Endometriosis
Bleeding Disorders	Trauma
<ul style="list-style-type: none"> • Thrombocytopenia (eg, idiopathic thrombocytopenic purpura, leukemia, aplastic anemia, hypersplenism, chemotherapy) • Clotting disorders (eg, von Willebrand disease, disorders of platelet function, liver dysfunction) 	<ul style="list-style-type: none"> • Vaginal laceration
Vaginal Abnormalities	Foreign Body (eg, retained tampon)
<ul style="list-style-type: none"> • Carcinoma or sarcoma 	Systemic Diseases
	<ul style="list-style-type: none"> • Diabetes mellitus • Renal disease • Systemic lupus erythematosus
	Medications
	<ul style="list-style-type: none"> • Hormonal contraceptives • Anticoagulants • Platelet inhibitors • Androgens • Spironolactone • Antipsychotics

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motherapy) and von Willebrand disease. Up to 95% of young women who have von Willebrand disease experience menorrhagia. Classically, menorrhagia may be the presenting symptom in von Willebrand disease, with a history of heavy bleeding from the very first menstrual

period. (8) Typically, there also is a family history of menorrhagia.

Cyclic bleeding with superimposed intercycle bleeding may raise suspicion of cervical disease. In sexually active teenagers, infection with *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, either as asymptomatic cervicitis or endometritis or as part of pelvic inflammatory disease, may produce intermenstrual bleeding. *Trichomonas* infection also may produce cervical inflammation. Foreign bodies, including retained tampons, may produce a similar bleeding pattern; foul-smelling discharge is suggestive. Cervical hemangiomas, cervicitis from cystic fibrosis, uterine polyps, and congenital malformations with partial obstruction of the genital outflow tract are less common. Endometriosis also may be associated with cyclic bleeding that has superimposed abnormal bleeding.

It cannot be overemphasized that conditions of pregnancy, including ectopic pregnancy, threatened or spontaneous abortion, and complications of induced abortion, can present with any bleeding pattern. It is essential to rule out pregnancy in all adolescents (regardless of stated sexual history) who present with unexplained irregular or heavy bleeding, especially in those who previously have had regular cycles.

Clinical Aspects

The presentation of abnormal bleeding varies widely, from the subtle onset of fatigue due to iron deficiency anemia to acute mental status changes or syncope caused by severe blood loss. When taking a history, the clinician should ask about the recent reported pattern of bleeding as well as the menstrual history. A young woman should be asked about the date of her first period, her usual pattern of bleeding, including frequency and duration of menses, and the presence of menstrual cramping, in addition to the date of her last menstrual period. Dysmenorrhea may suggest the presence of ovulatory cycles. Early during the taking of the history, the patient should be asked confidentially whether she has ever had sexual intercourse or sexual contact (consensual or nonconsensual) and whether she has ever had a sexually transmitted infection, keeping in mind that not all patients may disclose this information.

The review of systems should focus on signs and symptoms of some of the medical conditions that may produce irregular menses in the patient and her family members: PCOS (acne, hirsutism, acanthosis nigricans, weight gain; family history of PCOS, type 2 diabetes mellitus, or infertility), thyroid disease (weight changes, cold or heat intolerance, growth patterns), bleeding dis-

orders (gingival bleeding, epistaxis, bruising, family history of bleeding disorder), and hypothalamic amenorrhea (psychosocial stressors, eating-disordered behavior, weight loss, intensive athletics).

It is important to ask adolescents about medication use that may produce unusual patterns of menstrual bleeding. Adolescents, intentionally or otherwise, may fail to divulge that they are using contraceptive methods that would alter their cycles. A long-term progestin such as depot medroxyprogesterone acetate often produces irregular bleeding initially before inducing amenorrhea. Copper intrauterine devices (IUDs) also may produce heavy or irregular bleeding. Teenagers should be asked about whether they are using oral contraceptives or other hormonal therapies and the regularity with which they are taking them. Prescribed psychotropic medications such as risperidone elevate prolactin concentrations and typically result in amenorrhea, but also can present with irregular menses. Teens also should be asked about use of illicit drugs, herbs, and dietary supplements.

Patients frequently both underreport and overreport the severity of vaginal bleeding. Adolescents tend to report very light periods and extraordinarily heavy periods (with changing of pads every 30 min) accurately, but determining the extent of bleeding in patients reporting “heavy” periods is more problematic. Thus, it is wise to obtain objective data during the physical examination, including vital signs and laboratory studies. Vital signs should include orthostatic measurements, with pulse and blood pressure obtained in the lying and standing positions, if tolerated. The physical examination should focus on detecting signs of the conditions in the differential diagnosis of abnormal bleeding: obesity, hirsutism, acne, acanthosis nigricans, or clitoromegaly (Fig. 1) (normal clitoral glans width is 2 to 4 mm) suggestive of PCOS or other androgen excess; thyroid enlargement or nodules (thyroid disorders); and bruising or petechiae (bleeding disorders).

Patients who experience unexplained, persistent, or severe bleeding also should undergo a bimanual and speculum pelvic examination. For patients who do not tolerate even a one-finger bimanual or rectoabdominal examination, pelvic ultrasonography can provide important information and may be all that is possible in the young teen. Examination under anesthesia rarely is necessary because most patients respond promptly to medical therapies.

Laboratory studies should include a complete blood count, including measurement of hemoglobin, hematocrit, and platelet count, and a urine pregnancy test. If available, the CHr (hemoglobin content of the reticulo-



Figure 1. Clitoromegaly. Reprinted with permission from Emans SJ, Luafer MR, Goldstein DP, eds. *Pediatric and Adolescent Gynecology*. 5th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2005:270–286.

cyte) is a good measure of iron deficiency, even in patients who have normal hemoglobin values. Similarly, an elevated reticulocyte count can help confirm a history of excessive bleeding in a patient who has a normal hemoglobin concentration.

Prothrombin time, partial thromboplastin time, von Willebrand panel, and possibly a platelet function assay, a rapid screening test for platelet function, should be considered for those who present with severe bleeding, a history of severe bleeding dating from the very first menstrual period, or other bleeding elsewhere. Of note, specimens for the von Willebrand test should be drawn before hormonal therapies are started because estrogen increases concentrations of von Willebrand factor.

Other tests to include are a screen for gonorrhea and *Chlamydia* infection (urine-based or preferably cervical) in sexually active patients; measurement of thyroid-stimulating hormone to screen for thyroid disease; and testosterone, free testosterone, and dehydroepiandrosterone sulfate in those suspected of having PCOS. Patients who have amenorrhea need to be evaluated with a pregnancy test, with additional endocrinologic studies typically obtained after 6 months of absent cycles or persistent oligomenorrhea if an initial diagnosis is not evident.

Management

The management of abnormal vaginal bleeding depends on its severity and cause. Confirmation of the duration and severity of bleeding by using a menstrual calendar (Fig. 2) often is helpful. Many adolescents experiencing perimenarchal DUB require only reas-

YEAR { _____ }		MENSTRUAL CYCLE RECORD																														
DAY →	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	
JAN																																
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Enter appropriate letter in proper calendar day square →

- S = Spotting
- B = Bleeding
- T = Pill Taken

Figure 2. Menstrual calendar.

insurance and supplemental iron therapy. Nonsteroidal anti-inflammatory drugs such as ibuprofen and naproxen sodium can help reduce blood loss. Even in severe cases of bleeding, the primary treatments are medical, and bleeding usually decreases significantly with 24 to 36 hours of hormonal therapy; surgical intervention rarely is necessary in adolescents. The goal of medical therapies is to stop bleeding, usually by giving a combination oral contraceptive (COC) containing estrogen, which promotes clotting and causes endometrial proliferation, and progestin, which stabilizes the endometrial lining. Some studies have shown that COCs decrease menstrual blood loss, both during regular menstrual cycles and during menorrhagia. Because no large randomized, controlled trials support any particular hormone regimen, choice is based on clinical experience (Table 2). (9)(10)

We typically use a monophasic pill containing a potent progestin, such as norgestrel 0.3 mg/ethinyl estradiol 30 mcg or levonorgestrel 0.15 mg/ethinyl estradiol 30 mcg. Patients who have von Willebrand disease generally benefit from long-term hormonal therapies to control bleeding. Such patients should be referred to a hematologist for a desmopressin challenge to see if they respond so this form of therapy can be considered. All patients experiencing abnormal vaginal bleeding should receive iron supplementation; those who have severe bleeding also may benefit from folic acid. Written patient information is extremely helpful as an adjunct to office counseling. (11)

For patients who have a medical contraindication or

parental or patient preference to avoid COC therapy, oral progestins (such as medroxyprogesterone acetate 10 mg daily for 12 to 14 d or norethindrone acetate 5 mg daily for 12 to 14 d) may be used each month to induce withdrawal bleeding and prevent buildup of the endometrium under the influence of unopposed estrogen. Although long-acting progestins such as depot medroxyprogesterone ultimately may induce amenorrhea, the first 6 months of use typically are accompanied by irregular bleeding. In extreme cases (eg, bone marrow transplantation or long-term anticoagulant therapy with high INR and bleeding), long-acting gonadotropin-releasing hormone agonists (such as depot leuprolide) may be useful

in arresting menstrual cycles entirely; hormonal replacement (“add back”) therapy with low-dose estrogen/progestin or norethindrone acetate is important for long-term therapy to prevent bone loss. For bone marrow transplant recipients, the 3-month formulation should be administered at least 1 month prior to the expected transplant because the agonist phase will result in menstrual bleeding 3 weeks after the injection. The levonorgestrel-releasing IUD is another option for women who have heavy bleeding, but it should be reserved for older adolescents and young adults who are in a monogamous relationship and have a very low risk of contracting a sexually transmitted disease.

Prognosis and Follow-up

Most teenage girls who have abnormal bleeding due to immaturity of their hypothalamic-pituitary-ovarian axis establish regular menstrual cycles within the first 2 years after menarche. Iron therapy, serial hematocrit measurements, and the use of a menstrual calendar (Fig. 2) may be all that is required for such patients. Long-term follow-up is important, however, to ensure that patients ultimately achieve regular cycles. Some of the conditions that produce irregular and abnormal bleeding have significant clinical sequelae. Chronic anovulation in PCOS predisposes patients to endometrial carcinoma in their adult years. It is essential for such patients to receive long-term therapy with oral contraceptives or cyclic progestins to ensure regular shedding of the endometrium.

Table 2. Suggested Oral Contraceptive Regimens

Use a monophasic pill such as:

- Norgestrel 0.3 mg/Ethinyl estradiol 30 mcg
- Levonorgestrel 0.15 mg/Ethinyl estradiol 30 mcg

For all patients:

- Advise the patient to keep a menstrual calendar
- Ensure that 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 nonsteroidal anti-inflammatory drugs such as ibuprofen or naproxen sodium
- If choose to treat: One pill daily for 21 d, followed by 1 wk of placebo pills; continue regimen for 3 to 6 mo.*

For moderate bleeding (menses >7 d or cycle <3 wk; hemoglobin 10 to 11 g/dL [100 to 110 g/L]):

- One pill twice a day until bleeding stops, followed by one pill a day for 21 d, then 1 week of placebo pills. Alternatively, if the patient is not bleeding at the time of the visit and anemia is mild, one pill a day for 21 d.
- Follow closely.
- If patient remains stable and bleeding is under control, continue once-daily regimen for 3 to 6 mo.
- Follow serial hematocrits; if bleeding persists, may need to continue twice-daily pill for a short interval.

For severe bleeding with moderate anemia (hemoglobin 8 to 10 g/dL [80 to 100 g/L]):

- Consider inpatient admission unless patient and family are reliable, have transportation, and can be reached by phone.
- One pill four times a day for 2 to 4 d, with antiemetic as needed 2 h before each pill.
- One pill three times a day for 3 d, with antiemetic, as needed.
- One pill twice a day for 2 wk, with or without antiemetic.
- Follow closely with serial hematocrits; if anemia or bleeding persists, may need to continue twice-daily pill or eliminate pill-free interval.
- Cycle using 21 once-daily pills and 5 to 7 d of placebo for 6 mo.*

For severe bleeding with severe anemia (hemoglobin <7 g/dL [70 g/L], orthostatic vital signs, or heavy bleeding with hemoglobin <10 g/dL [100 g/L]):

- Admit for inpatient management. 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 25 mg every 4 h for 2 to 3 doses is used in severe acute hemorrhage.
- One pill (containing either 30 mcg ethinyl estradiol/0.3 mg norgestrel or 50 mcg ethinyl estradiol/0.5 mg norgestrel or 30 mcg ethinyl estradiol/0.15 mg levonorgestrel) every 4 h until bleeding slows (usually 24 to 36 h), with antiemetics.
- One pill four times a day for 2 to 4 d, with antiemetic as needed.
- One pill three times a day for 3 d, with antiemetic, as needed.
- One pill twice a day for a total of 21 d or until hematocrit is >30% (0.30).

*It is important to consider a patient's need for birth control before deciding to discontinue oral contraceptive therapy.

Reprinted with permission from Emans S. Dysfunctional uterine bleeding. In: Emans SJ, Laufer MR, Goldstein DP, ed. *Pediatric and Adolescent Gynecology*. 5th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2005:270–286.

Summary

Abnormal menses include those that last for longer than 7 days, occur more frequently than every 21 days (from the first day of one period to the first day of the next period) or less frequently than every 35 days, and those that result in iron deficiency anemia. DUB is the most common cause of 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. Patient reports of menstrual blood loss can be unreliable; objective data such as hemoglobin concentrations and reticulocyte count should be obtained to monitor symptoms. 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, although randomized, controlled trials have shown that COCs decrease the amount of blood loss during menses.

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PIR Quiz

Quiz also available online at www.pedsinreview.org.

5. You are evaluating a 16-year-old girl who has had heavy, irregular menstrual bleeding for the past 2 months. She denies abdominal pain and vaginal discharge. Menarche occurred at 12 years, and she reports previously regular cycles with a normal amount of bleeding. Her weight and height are at the 25th percentile, and results of her physical examination, including an external genitalia and bimanual examination, are normal. Of the following, the *most* important first test to order is:
 - A. Abdominal and pelvic ultrasonography.
 - B. Cervical culture for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.
 - C. Thyroid-stimulating hormone measurement.
 - D. Urine pregnancy test.
 - E. von Willebrand panel.

6. A 17-year-old girl presents to your office with irregular menstrual bleeding. Menarche occurred at 13 years of age. She reports regular 5-day cycles since age 15 years, but over the past 2 months, she has experienced bleeding between cycles. She reports occasional whitish vaginal discharge but denies abdominal pain. She is sexually active but usually uses condoms. Her weight and height are at the 50th percentile. Her general physical examination findings are normal, but her pelvic examination reveals mild irritation of the cervix. Of the following, the *most* likely cause of her metrorrhagia is:
 - A. *Chlamydia trachomatis* infection.
 - B. Ectopic pregnancy.
 - C. Endometriosis.
 - D. Hypothyroidism.
 - E. Polycystic ovary syndrome.

7. A 13-year-old girl comes to your office with a complaint of extremely heavy, painless bleeding since menarche 18 months ago. Cycles are regular, occurring approximately every 30 days, and she finds it necessary to change her pad every hour throughout menses. She is very active in sports at her school, and she denies sexual activity. Her mother reports that she, herself, had heavy periods when she was an adolescent. The girl's physical examination findings are normal, and her height and weight are at the 50th percentile. An external genitalia examination reveals no abnormalities. Of the following, the *most* likely cause is:
 - A. Anovulation from sports participation.
 - B. Diabetes mellitus.
 - C. Endometriosis.
 - D. Hypothyroidism.
 - E. von Willebrand disease.

8. A 15-year-old girl who has dysfunctional uterine bleeding presents with lightheadedness and fatigue for the past 3 days. You performed an evaluation for her heavy bleeding last month and found no underlying pathologic cause. She and her mother have been reliable and compliant with therapy in the past. She is alert and cooperative, has mild pallor, and appears tired. Her vital signs, including orthostatic blood pressures, are normal. Except for persistent painless heavy vaginal bleeding, results of her physical examination are normal. Her hemoglobin is 8 g/dL (80 g/L). Her urine pregnancy test is negative. Of the following, the *most* appropriate management is to:
 - A. Admit the girl to the hospital for immediate packed red blood cell transfusion.
 - B. Advise the girl to keep a menstrual calendar and return at her next cycle.
 - C. Prescribe monophasic progestin/estradiol therapy and see her again in 2 days.
 - D. Prescribe nonsteroidal anti-inflammatory medication.
 - E. Prescribe oral folic acid and recheck her hemoglobin in 1 week.

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