

# Abnormal Uterine Bleeding

Topic- based Uworld Questions

Block 1, 2, 7, 8



A 47-year-old woman comes to the office due to abnormal uterine bleeding. The patient has had several days of heavy bleeding every 2-3 weeks for the past 4 months. Last week, she had heavy bleeding with passage of large clots, which prompted her to be evaluated. Menarche was at age 16 and the patient was on estrogen/progestin-containing oral contraceptives during most of her 20s and 30s for treatment of dysmenorrhea. She stopped taking oral contraceptives at age 33 when she underwent a tubal ligation after the delivery of her last child. She had a cervical conization at age 29 after an abnormal Pap test, but all subsequent Pap tests have been normal. The patient takes no daily medications. She smokes a pack of cigarettes daily and has a 20-pack-year history. Vital signs are normal. BMI is 39 kg/m<sup>2</sup>. An endometrial biopsy is performed and shows endometrial adenocarcinoma. Which of the following is the most significant risk factor for this patient's biopsy result?

- A. Age at menarche
- B. Body mass index
- C. Oral contraceptive use
- D. Prior abnormal Pap test
- E. Tobacco use

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- A. Age at menarche (2%)
- B. Body mass index (69%)
- C. Oral contraceptive use (4%)
- D. Prior abnormal Pap test (3%)
- E. Tobacco use (19%)

Omitted

Correct answer  
B69%  
Answered correctly01 sec  
Time Spent03/15/2020  
Last Updated

Explanation

**Endometrial hyperplasia/cancer**

Endometrial hyperplasia/cancer	
<b>Risk factors</b>	<p>Excess estrogen</p> <ul style="list-style-type: none"><li>• Obesity</li><li>• Chronic anovulation/PCOS</li><li>• Nulliparity</li><li>• Early menarche or late menopause</li><li>• Tamoxifen use</li></ul>
<b>Clinical features</b>	<ul style="list-style-type: none"><li>• Heavy, prolonged, intermenstrual &amp;/or postmenopausal bleeding</li></ul>
<b>Evaluation</b>	<ul style="list-style-type: none"><li>• Endometrial biopsy (gold standard)</li><li>• Pelvic ultrasound (postmenopausal women)</li></ul>
<b>Treatment</b>	<ul style="list-style-type: none"><li>• Hyperplasia: progestin therapy or hysterectomy</li><li>• Cancer: hysterectomy</li></ul>

PCOS = polycystic ovary syndrome.

**Endometrial adenocarcinoma** is a common gynecologic malignancy that presents with either **abnormal uterine bleeding** (as seen in this premenopausal patient) or postmenopausal bleeding. Diagnosis is via endometrial biopsy, and treatment includes hysterectomy with bilateral salpingo-oophorectomy with or without chemoradiation (depending on stage).

The underlying cause of most cases of endometrial cancer is chronic **unopposed estrogen exposure**. In the uterus, estrogen causes the proliferation of the endometrium to allow for implantation associated with pregnancy. In ovulatory patients, an increase in progesterone protects against unopposed endometrial proliferation by downregulating estrogen receptors and regulating mitosis.

However, in conditions where estrogen levels are disproportionately high, the endometrium has unregulated proliferation, leading to development of endometrial cancer. The most common risk factor is **obesity** (ie, elevated BMI) because adipose tissue increases the conversion of androgens



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However, in conditions where estrogen levels are disproportionately high, the endometrium has unregulated proliferation, leading to development of endometrial cancer. The most common risk factor is **obesity** (ie, elevated BMI) because adipose tissue increases the conversion of androgens to estrogens, which results in increased uterine estrogen exposure and **chronic anovulation**. Other risk factors for endometrial cancer are related to unopposed estrogen and include nulliparity, tamoxifen use, and early age of menarche (**Choice A**).

**(Choice C)** Oral contraceptives, which contain only progestin or a combination of estrogen/progestin, are protective against endometrial cancer because the progestin component stimulates endometrial proliferation and shedding.

**(Choice D)** A prior abnormal Pap test is a risk factor for cervical cancer; however, it does not affect the risk of endometrial cancer.

**(Choice E)** Tobacco use decreases the risk of endometrial cancer, likely by stimulating estrogen metabolism in the liver and decreasing serum estrogen levels.

#### Educational objective:

Endometrial adenocarcinoma can present with abnormal uterine bleeding and is diagnosed via endometrial biopsy. Risk factors are related to excessive uterine estrogen exposure; the most common risk factors are obesity and chronic anovulation.

#### References

- [American Association of Clinical Endocrinologists, American College of Endocrinology, and Androgen Excess and PCOS Society Disease State Clinical Review: guide to the best practices in the evaluation and treatment of polycystic ovary syndrome—part 1.](#)
- [Diagnosis and management of endometrial cancer.](#)
- [Reproductive factors and the risk of endometrial cancer.](#)

A 32-year-old woman, gravida 3 para 3, comes to the office due to abnormal uterine bleeding. Menarche was at age 13, and her menstrual cycles were monthly until a year ago. The patient then began to have irregular menses that occurred every 45-60 days with heavy bleeding and passage of clots but no cramping. She has not had a menstrual period for the last 4 months. The patient has no hot flashes, acne, or abnormal hair growth. She takes levothyroxine for hypothyroidism and her only surgery was a tubal ligation after her last delivery. Height is 160 cm (5 ft 3 in) and weight is 120.2 kg (265 lb). Speculum examination is normal and bimanual examination is limited by body habitus. Urine pregnancy test is negative. Laboratory results are as follows:

TSH      2.9  $\mu$ U/mL (normal: 0.5-5.0)

Prolactin    16 ng/mL (normal: <20)

FSH      20 mIU/mL (normal: 5-30)

Which of the following is the most likely diagnosis in this patient?

- A. Adenomyosis
- B. Anovulation
- C. Endometrial polyp
- D. Hypothyroidism
- E. Primary ovarian insufficiency
- F. Uterine leiomyoma

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Notes



Calculator



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TSH 2.9  $\mu$ U/mL (normal: 0.5-5.0)

Prolactin 16 ng/mL (normal: <20)

FSH 20 mIU/mL (normal: 5-30)

Which of the following is the most likely diagnosis in this patient?

- A. Adenomyosis (6%)
- B. Anovulation (64%)
- C. Endometrial polyp (5%)
- D. Hypothyroidism (2%)
- E. Primary ovarian insufficiency (9%)
- F. Uterine leiomyoma (12%)

Omitted

Correct answer



64%

Answered correctly



01 min, 10 secs

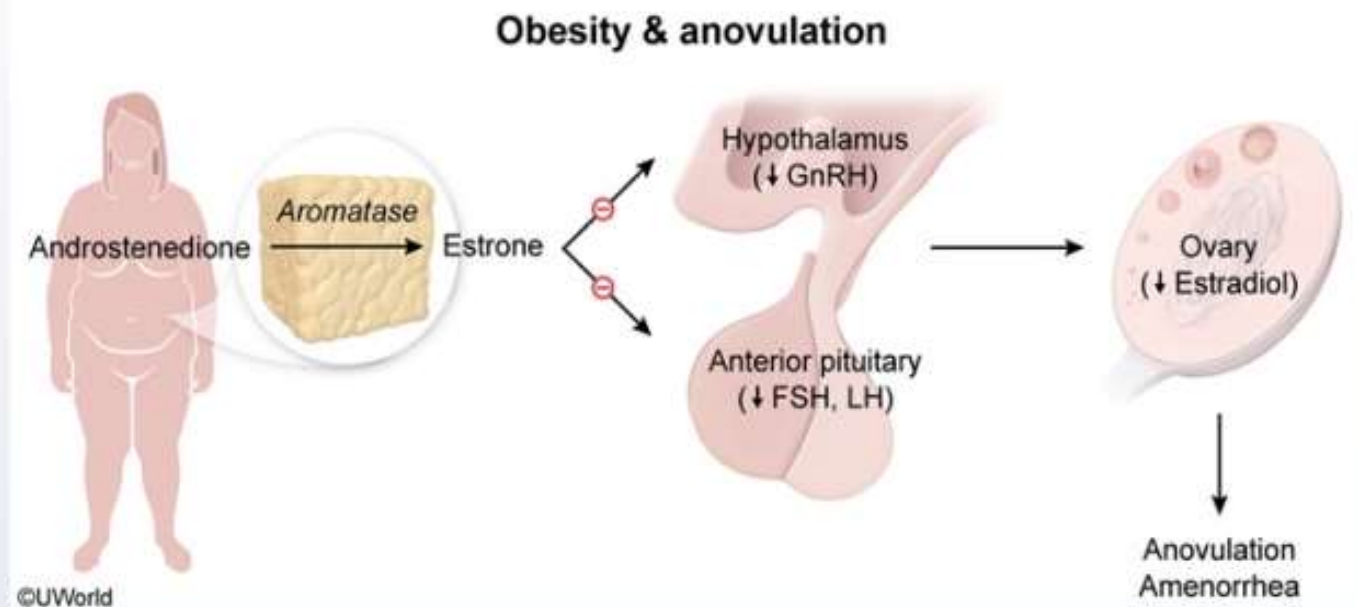
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03/07/2020

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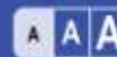


This patient's chronic ( $\geq 6$  months) abnormal uterine bleeding is likely secondary to excess adipose tissue associated with **obesity**. Excess adipose tissue affects the **hypothalamic-pituitary-ovarian axis** by 2 major mechanisms:

- Obesity causes increased insulin resistance and hyperglycemia, which decrease the production of sex hormone-binding globulin, causing elevated free androgen (eg, androstenedione) levels.
- The increased free androgens are **aromatized in the adipose tissue to estrone** (a type of estrogen), which leads to persistently elevated estrone levels.

In these patients, the high estrone levels affect GnRH pulses at the level of the hypothalamus, resulting in high-frequency, short-interval GnRH pulses. These pulses preferentially produce LH, resulting in an imbalance in LH and FSH release from the anterior pituitary (although the overall change in concentration is minimal). The LH/FSH imbalance results in a lack of LH surge, causing **anovulation** and subsequent **abnormal uterine bleeding**. Treatment options include weight loss and combination oral contraceptives, which regulate menstrual cycles and protect the endometrium.





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**(Choice A)** Patients with [adenomyosis](#) typically have heavy monthly menstrual bleeding with dysmenorrhea, which is not seen in this patient.

**(Choice C)** [Endometrial polyps](#) are common in obese patients because the estrogen receptor on the endometrium responds to estrogen excess. However, patients with endometrial polyps typically have bleeding between regular, monthly menstrual cycles. Endometrial polyps do not cause amenorrhea, making this diagnosis unlikely.

**(Choice D)** Patients with hypothyroidism can have abnormal uterine bleeding because the increased release of thyrotropin-releasing hormone from the hypothalamus causes increased prolactin levels. The elevated prolactin level inhibits FSH and LH release from the pituitary, leading to anovulation and abnormal uterine bleeding. However, this patient's TSH is normal, making this diagnosis unlikely.

**(Choice E)** Primary ovarian insufficiency is a type of hypergonadotropic hypogonadism (eg, menopause) in women age <40 that causes anovulation and subsequent abnormal uterine bleeding. In contrast to this patient, those with primary ovarian insufficiency have vasomotor symptoms (eg, hot flashes) and an elevated FSH level (>40 mIU/mL).

**(Choice F)** [Uterine leiomyomas](#) (fibroids) cause heavy, regular menstrual bleeding rather than irregular menses or amenorrhea, making this diagnosis unlikely.

#### Educational objective:

The increased adipose tissue associated with obesity increases the peripheral conversion of androgens to estrone, a type of estrogen.

Chronically elevated estrone levels disrupt the hypothalamic-pituitary-ovarian axis and result in anovulation and abnormal uterine bleeding.

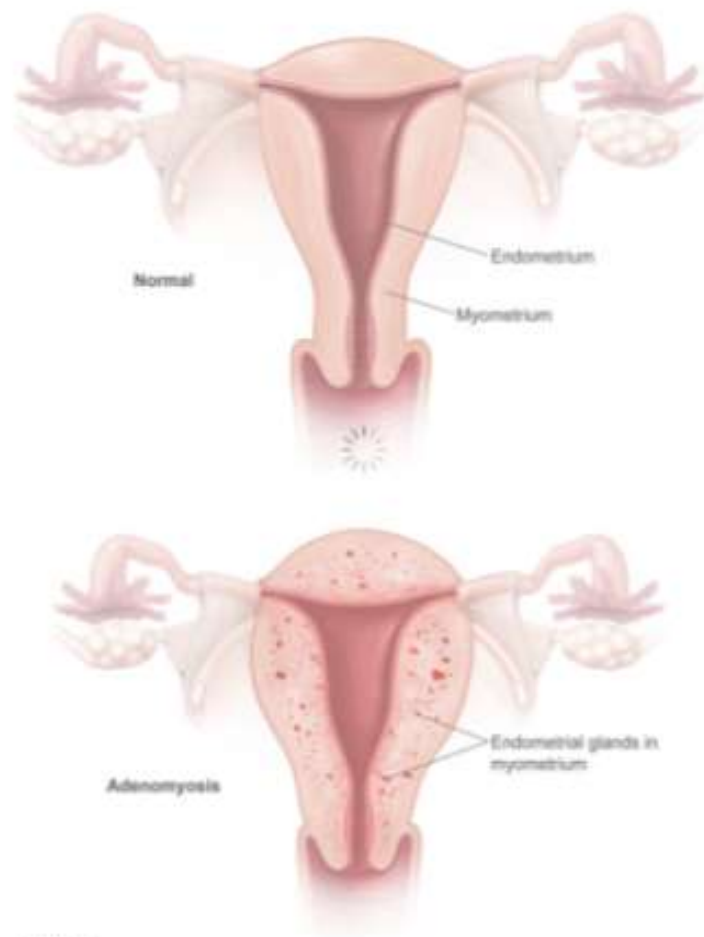
#### References

- [Bariatric surgery in obese women of reproductive age improves conditions that underlie fertility and pregnancy outcomes: retrospective cohort study of UK National Bariatric Surgery Registry \(NBSR\).](#)

In these patients, the high estrone levels affect GnRH pulses at the level of the hypothalamus, resulting in high-frequency, short-interval GnRH

## Exhibit Display

Normal uterus vs adenomyosis



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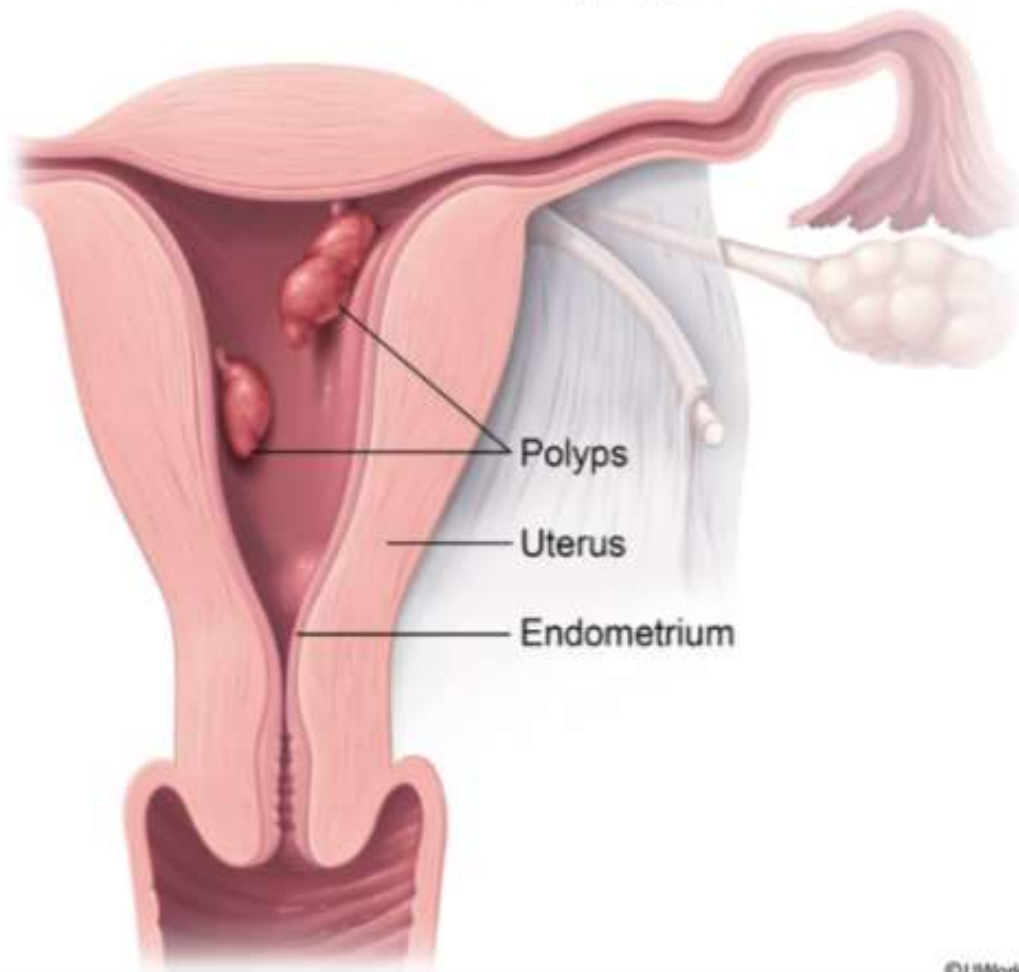
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In these patients, the high estrone levels affect GnRH pulses at the level of the hypothalamus, resulting in high-frequency, short-interval GnRH

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## Endometrial polyps



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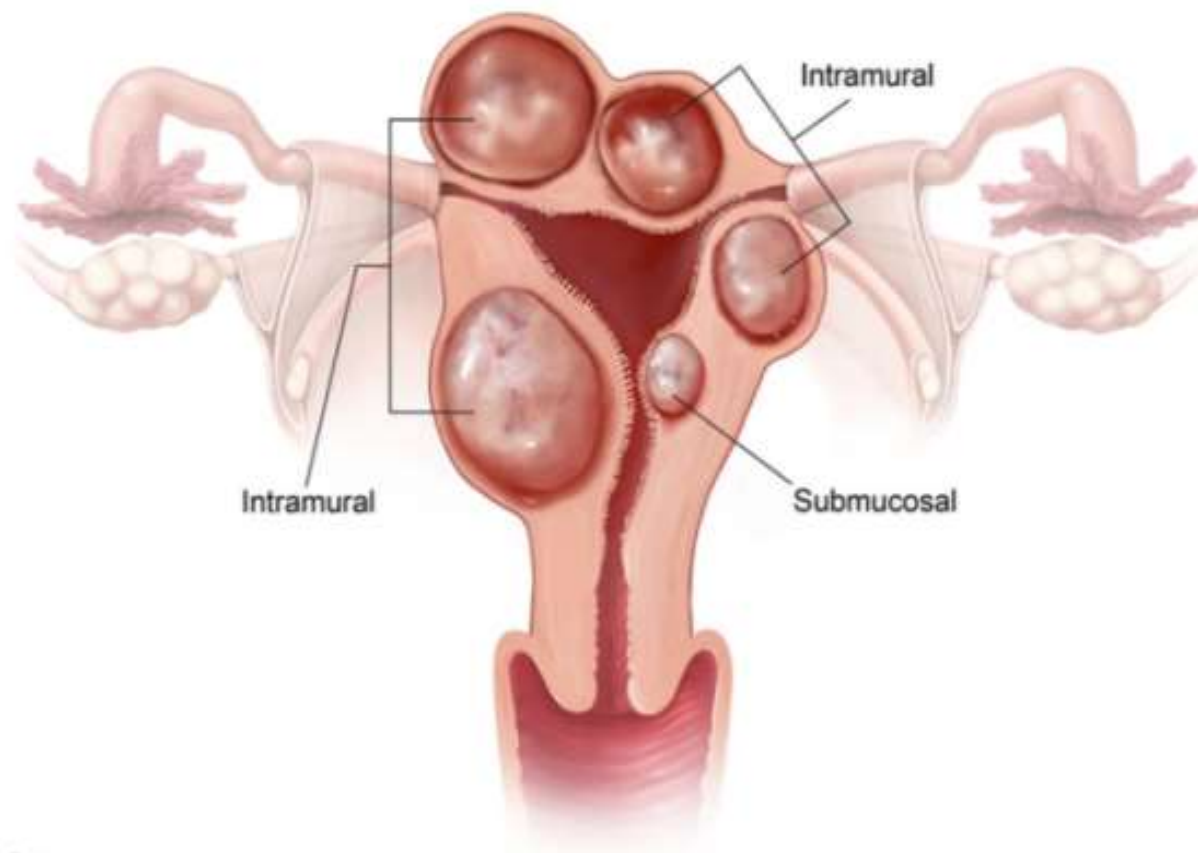
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In these patients, the high estrone levels affect GnRH pulses at the level of the hypothalamus, resulting in high-frequency, short-interval GnRH

### Exhibit Display

#### Uterine fibroids



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A 15-year-old girl is brought to the office due to prolonged, irregular menstrual periods. Menses occur at 2- to 4-month intervals and last for 7-10 days with heavy bleeding and passage of large clots. The patient's menstrual cycles are nonpainful and she has no associated dizziness, fatigue, palpitations, or abnormal vaginal discharge. Menarche was at age 14 and her last menstrual period was a month ago. She has no other chronic medical conditions or previous surgeries. The patient has never been sexually active. Blood pressure is 110/70 mm Hg and pulse is 72/min. Height and weight are at the 40th and 56th percentiles, respectively. The thyroid is without nodules. The skin has no discoloration or ecchymosis. Breast and pubic hair development are Tanner stage V. External pelvic examination shows no lacerations, lesions, discharge, or bleeding. The hymenal membrane is intact. Hemoglobin is 10.4 g/dL. PT and aPTT are normal. Which of the following is the best next step in management of this patient?

- A. Order pelvic MRI
- B. Perform cervical nucleic acid amplification testing
- C. Perform endometrial biopsy
- D. Perform hysteroscopy
- E. Place copper-containing intrauterine device
- F. Start oral progesterone therapy

Submit



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- A. Order pelvic MRI (5%)
- B. Perform cervical nucleic acid amplification testing (1%)
- C. Perform endometrial biopsy (2%)
- D. Perform hysteroscopy (5%)
- E. Place copper-containing intrauterine device (1%)
- F. Start oral progesterone therapy (84%)

Omitted  
Correct answer  
F

84%  
Answered correctly

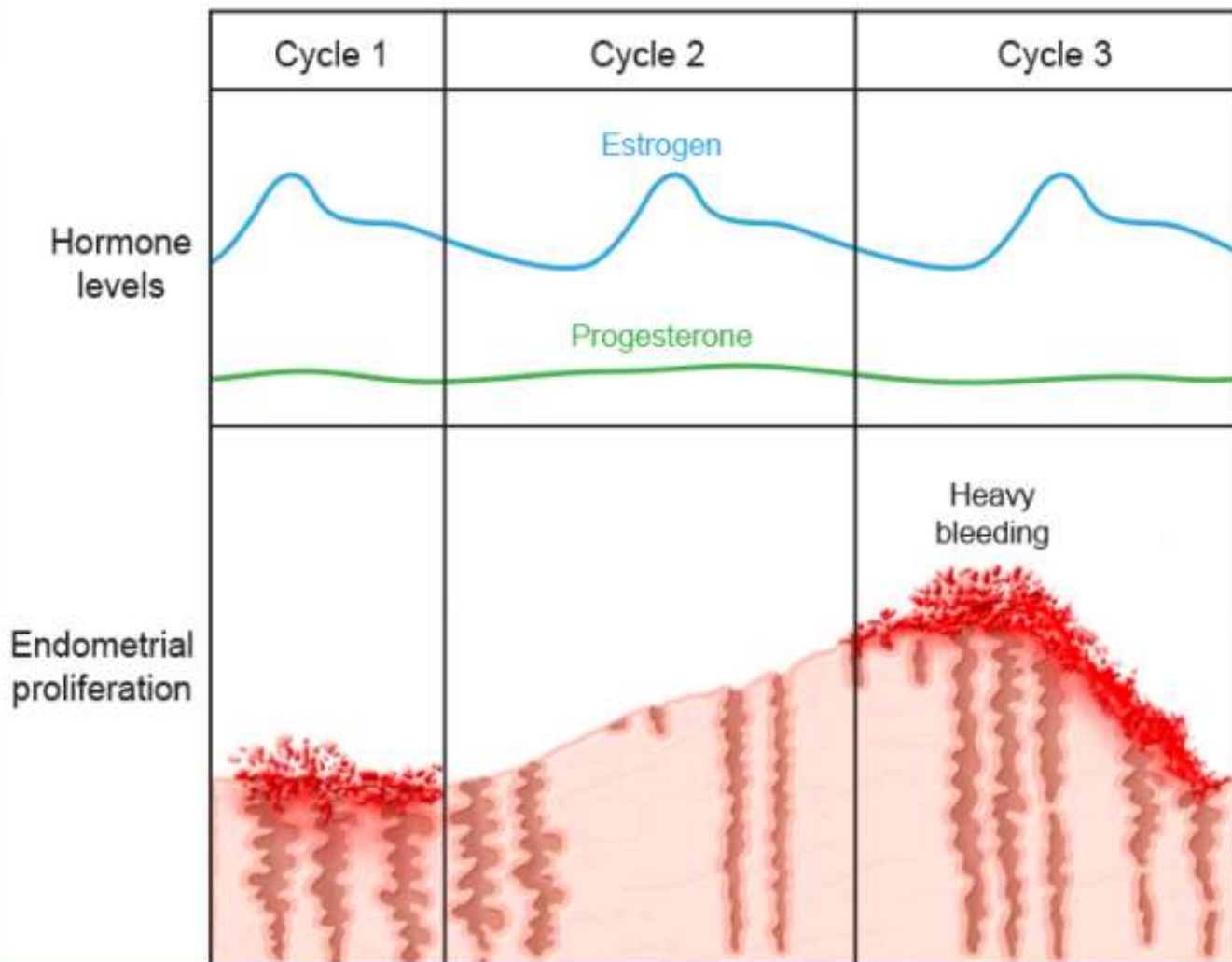
02 secs  
Time Spent

03/18/2020  
Last Updated

Explanation



### Effect of anovulatory cycles on the endometrium



During the first year after menarche, adolescents often have **anovulatory cycles** with **heavy, irregular menstrual bleeding** due to an immature hypothalamic-pituitary axis. In ovulatory cycles, the corpus luteum produces progesterone after ovulation; progesterone differentiates the proliferative endometrium into secretory endometrium. As the corpus luteum degenerates, the decrease in progesterone leads to normal menses through a decrease in endometrial blood supply and shedding of the lining.

In contrast, anovulatory cycles do not produce progesterone (eg, no corpus luteum development) and there is no differentiation into secretory endometrium. Therefore, these patients have continued **unopposed estrogen stimulation** resulting in uncontrolled **proliferation of the endometrium**. Bleeding occurs when the endometrial lining becomes too thickened and unstable (eg, breakthrough bleeding). **Progesterone** treatment helps stabilize this uncontrolled proliferation due to estrogen by causing differentiation into secretory endometrium. Cyclic progesterone withdrawal then causes menstruation.

**(Choice A)** Congenital anomalies of the reproductive tract (eg, Müllerian agenesis) typically present with primary amenorrhea rather than abnormal uterine bleeding. In patients with suspected anomalies, a pelvic MRI can be used to evaluate the structure of the reproductive tract.

**(Choice B)** Nucleic acid amplification testing is used in the evaluation of **acute cervicitis**, which presents with postcoital or intermenstrual spotting rather than heavy menses. Acute cervicitis is typically caused by a sexually transmitted infection (eg, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*) and is unlikely in a patient who is not sexually active.

**(Choice C)** An **endometrial biopsy** is an invasive procedure that can be used to diagnose endometrial hyperplasia, a condition that is rare in adolescents. An endometrial biopsy may be indicated in an adolescent with risk factors for hyperplasia (eg, obesity) or if symptoms do not improve with medical management.

**(Choice D)** A hysteroscopy is a procedure that can be used to evaluate the endometrium for structural causes of abnormal bleeding (eg, **endometrial polyp**, submucosal leiomyoma) and may be indicated if pharmacotherapy fails.

**(Choice E)** A copper-containing intrauterine device is a long-acting, reversible form of contraception that causes heavier, longer menses. Therefore, it is not recommended in patients with heavy menstrual bleeding and anemia.

**Educational objective:**

Adolescents often have anovulatory cycles with irregular, heavy menstrual bleeding due to an immature hypothalamic-pituitary axis. Progesterone



In contrast, anovulatory cycles do not produce progesterone (eg, no corpus luteum development) and there is no differentiation into secretory endometrium. Therefore, these patients have continued **unopposed estrogen stimulation** resulting in uncontrolled **proliferation of the endometrium**. Bleeding occurs when the endometrial lining becomes too thickened and unstable (eg, breakthrough bleeding). **Progesterone** treatment helps stabilize this uncontrolled proliferation due to estrogen by causing differentiation into secretory endometrium. Cyclic progesterone withdrawal then causes menstruation.

**(Choice A)** Congenital anomalies of the reproductive tract (eg, Müllerian agenesis) typically present with primary amenorrhea rather than abnormal uterine bleeding. In patients with suspected anomalies, a pelvic MRI can be used to evaluate the structure of the reproductive tract.

**(Choice B)** Nucleic acid amplification testing is used in the evaluation of [acute cervicitis](#), which presents with postcoital or intermenstrual spotting rather than heavy menses. Acute cervicitis is typically caused by a sexually transmitted infection (eg, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*) and is unlikely in a patient who is not sexually active.

**(Choice C)** An [endometrial biopsy](#) is an invasive procedure that can be used to diagnose endometrial hyperplasia, a condition that is rare in adolescents. An endometrial biopsy may be indicated in an adolescent with risk factors for hyperplasia (eg, obesity) or if symptoms do not improve with medical management.

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**(Choice E)** A copper-containing intrauterine device is a long-acting, reversible form of contraception that causes heavier, longer menses. Therefore, it is not recommended in patients with heavy menstrual bleeding and anemia.

#### Educational objective:

Adolescents often have anovulatory cycles with irregular, heavy menstrual bleeding due to an immature hypothalamic-pituitary axis. Progesterone normalizes menstruation by stabilizing unregulated endometrial proliferation.

#### References

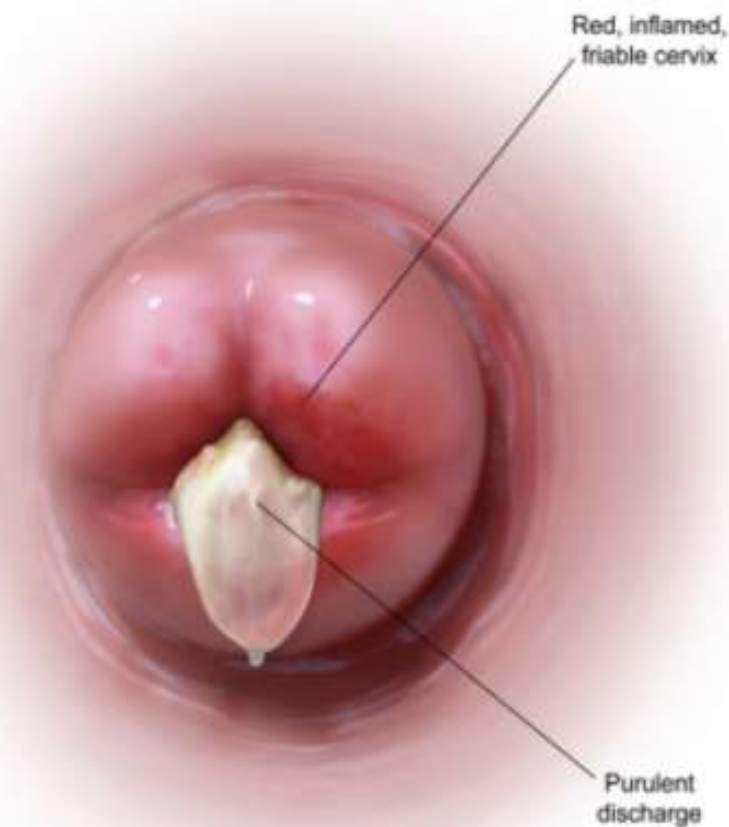
- [Abnormal uterine bleeding and dysfunctional uterine bleeding in pediatric and adolescent gynecology](#)
- [Evaluation and management of adolescents with abnormal uterine bleeding](#)



(Choice A) Cervical anomalies of the reproductive tract (eg, Müllerian agenesis) typically present with primary amenorrhea rather than

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#### Cervicitis



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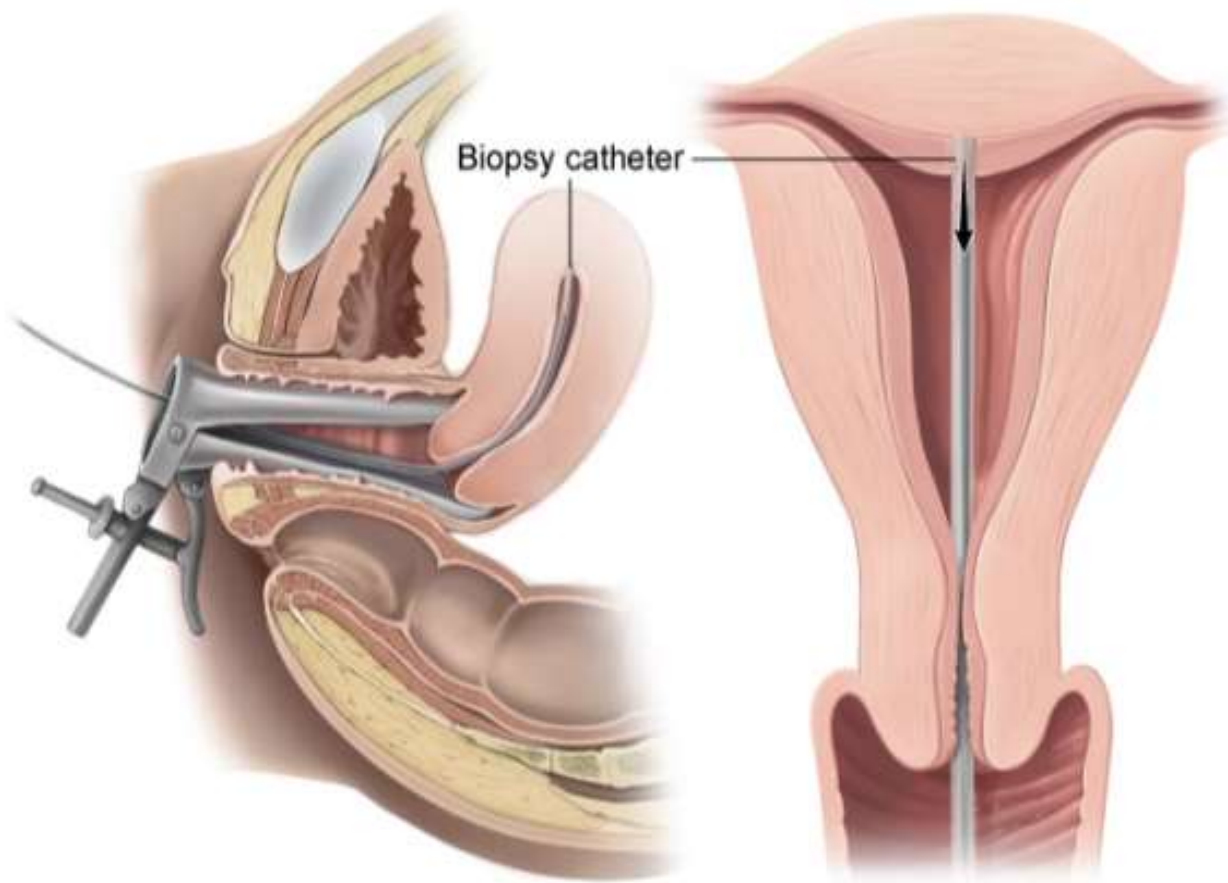
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(Choice A) Gonococcal proctitis of the reproductive tract (for Molluscum contagiosum) typically present with primary chancre rather than

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## Endometrial biopsy



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(Choice A) Congenital anomalies of the reproductive tract (eg, Müllerian agenesis) typically present with primary amenorrhea rather than

Exhibit Display

### Endometrial polyps

The diagram illustrates the internal structure of the female reproductive system, specifically the uterus and endometrium. Several red, fleshy, polypoid growths are shown protruding from the inner lining of the uterus. Labels with leader lines identify these as 'Polyps', the main organ as the 'Uterus', and the inner lining as the 'Endometrium'. A magnified view of a single polyp is shown on the right side of the diagram, revealing its lobulated, cauliflower-like surface. The diagram is presented within a window titled 'Exhibit Display' with standard window controls in the top right corner.

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