

Amenorrhea

Topic- based Uworld Questions

Block 1, 2, 7, 8



A 19-year-old woman comes to the office due to amenorrhea for the last 5 months. The patient underwent menarche at age 14 and previously had regular menses every 28 days, typically lasting 4-5 days. She has no headaches, visual disturbances, heat intolerance, palpitations, hot flashes, or night sweats. The patient has no medical problems or previous surgeries. She takes no medications and does not use tobacco, alcohol, or illicit drugs. The patient is a national gymnastics champion and attends the local college. She has never been sexually active. Blood pressure is 110/60 mm Hg and pulse is 54/min. Height is 165 cm (5 ft 5 in) and BMI is 20 kg/m². Physical examination shows a muscular woman. She has mild facial acne but no thyromegaly or facial hair. Breast development and pubic hair are Tanner stage V. Pelvic examination reveals normal external genitalia, vagina, and cervix. On bimanual examination, there is a small, mobile uterus and no adnexal masses. Pregnancy test is negative. TSH and prolactin levels are normal. What is the most likely diagnosis in this patient?

- A. Androgenic steroid use
- B. Congenital adrenal hyperplasia
- C. Hypothalamic amenorrhea
- D. Ovarian fibrothecoma
- E. Polycystic ovarian syndrome
- F. Primary ovarian insufficiency
- G. Subclinical hyperthyroidism

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- A. Androgenic steroid use (28%)
- B. Congenital adrenal hyperplasia (0%)
- C. Hypothalamic amenorrhea (64%)
- D. Ovarian fibrothecoma (0%)
- E. Polycystic ovarian syndrome (0%)
- F. Primary ovarian insufficiency (4%)
- G. Subclinical hyperthyroidism (0%)

Omitted

Correct answer

C



64%

Answered correctly



01 sec

Time Spent



03/15/2020

Last Updated

Exercise-induced hypothalamic amenorrhea	
Clinical presentation	<ul style="list-style-type: none"> • Strenuous exercise • Relative caloric deficiency • Stress fractures • Amenorrhea • Infertility
Hormone levels	<ul style="list-style-type: none"> • ↓ GnRH • ↓ LH/FSH • ↓ Estrogen
Long-term consequences	<ul style="list-style-type: none"> • ↓ Bone mineral density • ↑ Total cholesterol • ↑ Triglycerides
Treatment	<ul style="list-style-type: none"> • Increased caloric intake • Estrogen • Calcium & vitamin D

This conditioned athlete has **secondary amenorrhea** likely due to functional **hypothalamic amenorrhea**. This type of amenorrhea often occurs in women with the athlete's triad: amenorrhea, osteoporosis, and an eating disorder. They are thought to have a **relative caloric deficiency** secondary to inadequate nutritional intake compared to the amount of energy expended. Women with this condition have been shown to have **decreased** levels of **gonadotropin-releasing hormone (GnRH)**, with a subsequent **decrease** in **LH secretion**, resulting in **estrogen deficiency**. These women are at increased risk for conditions associated with estrogen deficiency, including infertility, vaginal atrophy, breast atrophy, and decreased bone mineral density (eg, osteopenia).

(Choices A and B) Androgenic steroid use and congenital adrenal hyperplasia present with virilization (eg, male-pattern baldness, deepening

This conditioned athlete has **secondary amenorrhea** likely due to functional **hypothalamic amenorrhea**. This type of amenorrhea often occurs in women with the athlete's triad: amenorrhea, osteoporosis, and an eating disorder. They are thought to have a **relative caloric deficiency** secondary to inadequate nutritional intake compared to the amount of energy expended. Women with this condition have been shown to have **decreased** levels of **gonadotropin-releasing hormone (GnRH)**, with a subsequent **decrease in LH secretion**, resulting in **estrogen deficiency**. These women are at increased risk for conditions associated with estrogen deficiency, including infertility, vaginal atrophy, breast atrophy, and decreased bone mineral density (eg, osteopenia).

(Choices A and B) Androgenic steroid use and congenital adrenal hyperplasia present with virilization (eg, male-pattern baldness, deepening voice, clitoromegaly) and hypertension. Patients using androgenic steroids also present with aggressive behavior and mood disorders, which are not seen in this patient.

(Choice D) Ovarian fibrothecoma, a type of ovarian sex cord-stromal tumor, may secrete androgens but more commonly secretes estrogen. This patient has no evidence of excess androgens (eg, hirsutism) or estrogen (eg, breast tenderness) and no adnexal mass.

(Choice E) Patients with polycystic ovarian syndrome have signs of androgen excess (eg, severe nodulocystic acne on the chest and back), obesity, and enlarged ovaries on examination. This patient has mild acne, but her normal BMI and pelvic examination make this diagnosis less likely.

(Choice F) Patients with primary ovarian insufficiency (POI) typically have vasomotor symptoms (eg, hot flashes, night sweats) associated with amenorrhea. POI is typically associated with a concomitant autoimmune disorder or Turner syndrome.

(Choice G) A patient with subclinical hyperthyroidism is typically asymptomatic, with a decreased TSH level.

Educational objective:

Secondary amenorrhea is relatively common in female athletes and results from hypothalamic amenorrhea (eg, GnRH deficiency). The subsequent decreased LH secretion and estrogen deficiency result in decreased bone mineral density.

References

- [Neuroendocrine control of ovulation.](#)

A 32-year-old woman comes to the office for evaluation of absent menses. The patient had a vaginal delivery 4 months ago, and she has not had a menstrual period since delivery. Her postpartum course was complicated by a postpartum hemorrhage, requiring blood transfusion and emergency suction and sharp curettage. At her postpartum visit 2 months ago, the patient was started on combination oral contraceptives and has had no vaginal bleeding or spotting during her week of placebo pills. Prior to this pregnancy, she had regular, monthly menstrual cycles with 3-4 days of moderate bleeding. The patient has had increased fatigue since returning to work and is bottle-feeding. She has no headaches, galactorrhea, or hot flashes. Vital signs are normal. BMI is 31 kg/m². Pelvic examination shows clear vaginal discharge throughout the vault and a well-rugated vagina. The uterus is small and anteverted, and there are bilateral small, nontender ovaries. Urine pregnancy test is negative. FSH and TSH levels are normal. Which of the following is the most likely diagnosis in this patient?

- A. Asherman syndrome
- B. Gestational trophoblastic disease
- C. Polycystic ovary syndrome
- D. Postpartum thyroiditis
- E. Primary ovarian insufficiency
- F. Sheehan syndrome

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- A. Asherman syndrome (58%)
- B. Gestational trophoblastic disease (0%)
- C. Polycystic ovary syndrome (0%)
- D. Postpartum thyroiditis (3%)
- E. Primary ovarian insufficiency (5%)
- F. Sheehan syndrome (30%)

Omitted

Correct answer

A



58%

Answered correctly



02 secs

Time Spent



01/14/2020

Last Updated

Explanation

Intrauterine adhesions	
Risk factors	<ul style="list-style-type: none"> • Infection (eg, septic abortion, endometritis) • Intrauterine surgery (eg, curettage, myomectomy)
Clinical features	<ul style="list-style-type: none"> • Abnormal uterine bleeding • Amenorrhea • Infertility • Cyclic pelvic pain • Recurrent pregnancy loss
Evaluation	<ul style="list-style-type: none"> • Hysteroscopy

This patient has **Asherman syndrome**, the formation of **intrauterine adhesions** that can follow intrauterine surgery, such as an emergency suction and sharp curettage. Asherman syndrome occurs commonly after **suction and sharp curettage** for delivery complications, such as postpartum hemorrhage and endometritis, because the postpartum uterus is soft, enlarged, and more prone to aggressive curettage. During this procedure, the basalis layer of the endometrium can inadvertently be injured, creating a denuded, adherent intrauterine surface prone to synechiae and endometrial cavity obliteration.

Because of complete or partial **obliteration of the endometrium**, patients typically develop very light menses or **secondary amenorrhea** that does not respond to a progesterone challenge, as evidenced by **no withdrawal bleeding** during the placebo week of oral contraceptives. Asherman syndrome is a structural cause of amenorrhea; therefore, patients have normal FSH and TSH levels. Diagnosis and treatment are via hysteroscopy, which can lyse adhesions.

(Choice B) Gestational trophoblastic disease (eg, choriocarcinoma) can cause abnormal uterine bleeding after pregnancy. The persistent trophoblastic tissue secretes hCG; this patient has a negative pregnancy test, making this diagnosis unlikely.

(Choice C) Polycystic ovary syndrome causes abnormal uterine bleeding, particularly in obese patients (BMI ≥ 30 kg/m²). However, patients have a thickened endometrium due to chronic anovulation and continued endometrial proliferation; therefore, they would have bleeding during the placebo week of oral contraceptives.

(Choice C) Polycystic ovary syndrome causes abnormal uterine bleeding, particularly in obese patients (BMI ≥ 30 kg/m²). However, patients have a thickened endometrium due to chronic anovulation and continued endometrial proliferation; therefore, they would have bleeding during the placebo week of oral contraceptives.

(Choice D) Postpartum thyroiditis is autoimmune transient thyroid disorder that can occur within a year after delivery. Symptoms can include abnormal uterine bleeding and fatigue; however, patients have abnormal TSH levels, making this diagnosis unlikely.

(Choice E) Because of low estrogen levels, primary ovarian insufficiency can cause secondary amenorrhea and no withdrawal bleeding during the placebo week of oral contraceptives. However, these patients have an elevated FSH level, making this diagnosis unlikely.

(Choice F) Sheehan syndrome can occur as a complication of postpartum hemorrhage, particularly if associated with massive hemorrhage requiring blood transfusion and emergency suction curettage. Patients can have amenorrhea, fatigue, and inability to breastfeed; however, they have low FSH and TSH levels due to panhypopituitarism, which is not seen in this patient. In addition, fatigue is a nonspecific symptom common in patients with infants at home.

Educational objective:

Asherman syndrome, the formation of intrauterine adhesions, often occurs following intrauterine surgery (eg, suction curettage). Patients with Asherman syndrome typically have amenorrhea that does not respond to a progesterone challenge due to obliteration of the endometrium.

References

- [A comprehensive review of Asherman's syndrome: causes, symptoms and treatment options.](#)
- [Hysteroscopic management of Asherman's syndrome.](#)
- [Asherman's syndrome.](#)

A 15-year-old girl is brought to the office by her mother due to concerns that her daughter has not had a menstrual period. The patient was born at 36 weeks gestation but has had no developmental delay. She is doing well in school and plays on the tennis team. The patient is healthy and takes no medications. She is not sexually active and does not use tobacco, alcohol, or illicit drugs. Family history is significant for a maternal aunt with primary infertility and a maternal grandmother with ovarian cancer. Height is 174 cm (5 ft 7 in), and weight is 63 kg (138.9 lb). Vital signs are normal. There is no acne or excessive hair growth. Breast development is sexual maturity rating (Tanner) stage 5. There is scant axillary and pubic hair. On pelvic examination, the external genitalia appear normal and speculum examination shows a blind vaginal pouch. The uterus, cervix, and ovaries are absent on bimanual examination. Karyotype analysis of this patient is most likely to show which of the following?

- A. 45,X
- B. 46,XX
- C. 46,XY
- D. 47,XXY
- E. 47,XYY

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A 15-year-old girl is brought to the office by her mother due to concerns that her daughter has not had a menstrual period. The patient was born at 36 weeks gestation but has had no developmental delay. She is doing well in school and plays on the tennis team. The patient is healthy and takes no medications. She is not sexually active and does not use tobacco, alcohol, or illicit drugs. Family history is significant for a maternal aunt with primary infertility and a maternal grandmother with ovarian cancer. Height is 174 cm (5 ft 7 in), and weight is 63 kg (138.9 lb). Vital signs are normal. There is no acne or excessive hair growth. Breast development is sexual maturity rating (Tanner) stage 5. There is scant axillary and pubic hair. On pelvic examination, the external genitalia appear normal and speculum examination shows a blind vaginal pouch. The uterus, cervix, and ovaries are absent on bimanual examination. Karyotype analysis of this patient is most likely to show which of the following?

- A. 45,X (4%)
- B. 46,XX (18%)
- C. 46,XY (71%)
- D. 47,XXY (4%)
- E. 47,XYY (0%)

OmittedCorrect answer
C71%
Answered correctly02 secs
Time Spent01/28/2020
Last Updated

Explanation

Androgen insensitivity syndrome

Androgen insensitivity syndrome	
Pathophysiology	<ul style="list-style-type: none"> • X-linked mutation in androgen receptor
Clinical features	<ul style="list-style-type: none"> • Genotypically male (46,XY karyotype) • Phenotypically female • Breast development • Absent or minimal axillary & pubic hair • Female external genitalia • Absent uterus, cervix, & upper one-third of vagina • Cryptorchid testes
Management	<ul style="list-style-type: none"> • Gender identity/assignment counseling • Gonadectomy (malignancy prevention)

This patient has **androgen insensitivity syndrome (AIS)**, an X-linked recessive condition in which **genotypically male (46,XY karyotype)** patients have nonfunctioning androgen receptors that cause peripheral androgen resistance. These patients have functioning testes, resulting in the characteristic fetal and pubertal development associated with AIS.

During fetal AIS development, the testes produce anti-Müllerian hormone (AMH) and testosterone. AMH acts on Müllerian structures (ie, uterus, upper one-third of vagina) and causes their regression. In contrast, testosterone has no activity on peripheral tissues, and male external genitalia (eg, penis, prostate) do not develop, defaulting to female external genitalia (eg, lower two-thirds of vagina). Therefore, these patients appear **phenotypically female** at birth.

Pubertal **patients with AIS** typically have **primary amenorrhea** (ie, no uterus and a blind vaginal pouch) and some secondary sexual characteristic development. Although the testes produce normal male pubertal-range testosterone levels, patients have no acne and **minimal to no axillary and pubic hair** due to peripheral androgen resistance. However, the increased testosterone is aromatized to estrogen and results in **breast development** and **tall stature**.

(Choice A) Patients with Turner syndrome (45 X) often have primary amenorrhea due to small, nonfunctional ovaries (ie, streak ovaries). They

phenotypically female at birth.

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(Choice A) Patients with Turner syndrome (45,X) often have primary amenorrhea due to small, nonfunctional ovaries (ie, streak ovaries). They also typically have short stature and minimal breast development (ie, "shield chest"), making this diagnosis unlikely in this patient.

(Choice B) Müllerian agenesis (Mayer-Rokitansky-Küster-Hauser syndrome [46,XX]) is the absence of the uterus, cervix, and upper one-third of the vagina. Patients with this disorder have primary amenorrhea and breast development. In contrast to this patient, those with Müllerian agenesis have ovaries as well as normal axillary and pubic hair development.

(Choice D) Patients with [Klinefelter syndrome](#) (47,XXY) can have breast development (ie, gynecomastia), tall stature, and minimal body hair. However, they have a penis and small, descended testes (ie, hypogonadism), making this diagnosis unlikely in this patient.

(Choice E) Patients with a 47,XYY karyotype appear phenotypically male and develop nodulocystic acne at puberty. They require neurodevelopmental evaluation due to the increased incidence of learning disabilities, behavioral problems, and developmental delay.

Educational objective:

Androgen insensitivity syndrome is the result of nonfunctioning androgen receptors that lead to peripheral androgen resistance. These patients are genotypically male (46,XY) but appear phenotypically female with breast development and female external genitalia; however, they have no female internal genitalia (eg, uterus, ovaries) and minimal to no axillary or pubic hair.

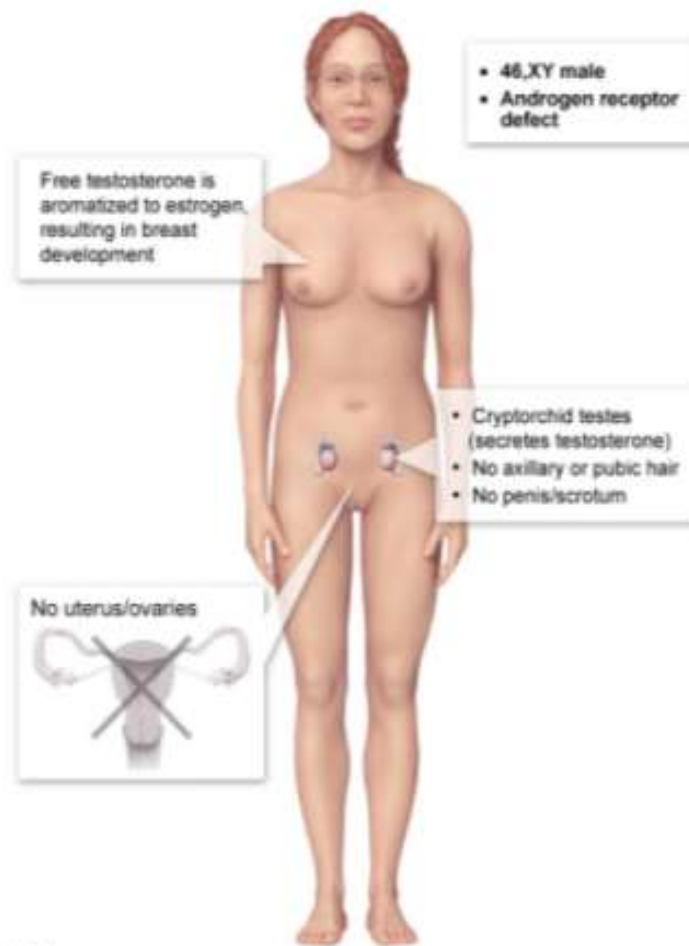
References

- [Androgen insensitivity syndrome.](#)
- [Androgen insensitivity syndrome: a review.](#)
- [Molecular biology of androgen insensitivity.](#)

phenotypically female at birth.

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Androgen insensitivity syndrome



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A 16-year-old girl comes to the office for a routine health maintenance examination. The patient is in high school, is performing well academically, and plays on the tennis team. She has no concerns today. On review of systems, the patient has not reached menarche, but she says that her mother did not start menstruating until this age. She recently started wearing contact lenses for myopia and uses an over-the-counter cream for acne. Height is at the 70th percentile and weight is at the 25th percentile for age. Blood pressure is 120/70 mm Hg and pulse is 60/min. Breast development is sexual maturity rating (Tanner stage) III. Pelvic examination shows sexual maturity rating (Tanner stage) III pubic hair development and normal external genitalia. Speculum examination reveals a well-rugated vagina but no cervix. FSH levels are within the normal pubertal range. Karyotype is 46, XX. Pelvic ultrasound reveals an absent uterus. Which of the following is the best next step in management of this patient?

- A. Dihydrotestosterone and testosterone level
- B. Echocardiogram
- C. Hymenal incision
- D. MRI of the brain
- E. Renal ultrasound
- F. TSH and prolactin level

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Lab Values



Notes



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A 16-year-old girl comes to the office for a routine health maintenance examination. The patient is in high school, is performing well academically, and plays on the tennis team. She has no concerns today. On review of systems, the patient has not reached menarche, but she says that her mother did not start menstruating until this age. She recently started wearing contact lenses for myopia and uses an over-the-counter cream for acne. Height is at the 70th percentile and weight is at the 25th percentile for age. Blood pressure is 120/70 mm Hg and pulse is 60/min. Breast development is sexual maturity rating (Tanner stage) III. Pelvic examination shows sexual maturity rating (Tanner stage) III pubic hair development and normal external genitalia. Speculum examination reveals a well-rugated vagina but no cervix. FSH levels are within the normal pubertal range. Karyotype is 46, XX. Pelvic ultrasound reveals an absent uterus. Which of the following is the best next step in management of this patient?

- A. Dihydrotestosterone and testosterone level (30%)
- B. Echocardiogram (5%)
- C. Hymenal incision (1%)
- D. MRI of the brain (3%)
- E. Renal ultrasound (53%)
- F. TSH and prolactin level (5%)

Omitted

Correct answer

E



53%

Answered correctly



06 secs

Time Spent

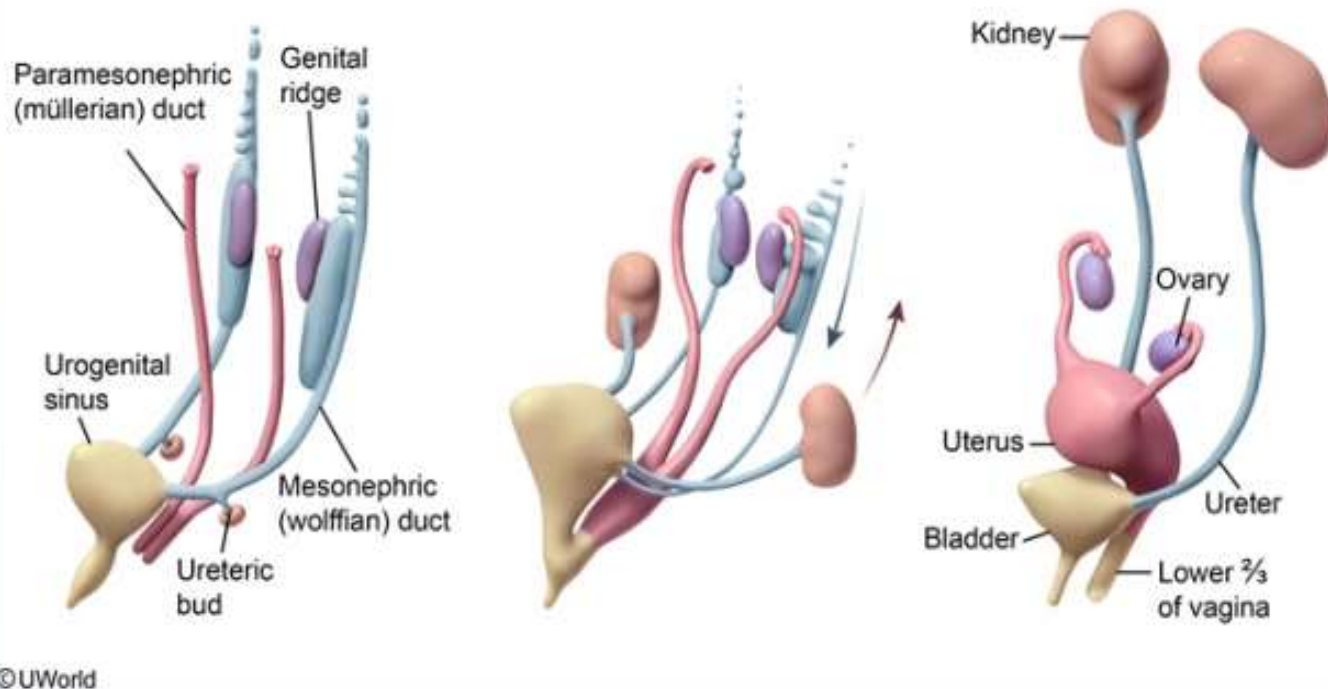


03/15/2020

Last Updated

Explanation

Urogenital development



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This patient has an **absent uterus and cervix** with otherwise normal secondary sexual characteristics (eg, breasts, external genitalia) consistent with **müllerian agenesis** (ie, Mayer-Rokitansky-Küster-Hauser syndrome), abnormal müllerian duct development. The ovaries and external genitalia develop independently of the müllerian duct system; therefore, patients have normal FSH levels (ie, normal ovarian function), normal external genitalia, and the lower 2/3 of the vagina (ie, blind vaginal pouch).

The internal genitalia derive from structures of the intermediate mesoderm, which develops into the paramesonephric (ie, müllerian) and mesonephric (ie, wolffian) ducts. The paramesonephric duct forms the uterus, fallopian tubes, cervix, and upper 1/3 of the vagina, and the mesonephric duct forms the primitive kidney. Because of their **common embryologic source** and **synchronous development** in the first trimester, internal genital anomalies are often concurrent with **renal abnormalities**. Therefore, women with müllerian agenesis should undergo

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The internal genitalia derive from structures of the intermediate mesoderm, which develops into the paramesonephric (ie, müllerian) and mesonephric (ie, wolffian) ducts. The paramesonephric duct forms the uterus, fallopian tubes, cervix, and upper 1/3 of the vagina, and the mesonephric duct forms the primitive kidney. Because of their **common embryologic source** and **synchronous development** in the first trimester, internal genital anomalies are often concurrent with **renal abnormalities**. Therefore, women with müllerian agenesis should undergo evaluation of the renal tract (ie, ureters, kidney) with a **renal ultrasound**. Common abnormalities include unilateral renal agenesis, pelvic kidneys, and duplications of the collecting system.

(Choice A) Testosterone and dihydrotestosterone levels are used to diagnose 5-alpha-reductase deficiency and androgen insensitivity syndrome (AIS). In 5-alpha-reductase deficiency, genotypic males (46,XY) appear phenotypically female until puberty; elevated testosterone levels at puberty then cause virilization (eg, clitoromegaly) and lack of breast development, which are not seen in this patient. In AIS, genotypic males appear phenotypically female through puberty and have breast development. In contrast to this patient, those with AIS have no/minimal acne or pubic hair development due to an abnormal androgen receptor.

(Choice B) Echocardiogram is performed in patients with Turner syndrome to evaluate for cardiac malformations (eg, bicuspid aortic valve, aortic coarctation). This patient has a normal karyotype and FSH level (ie, normal ovarian function), making Turner syndrome unlikely.

(Choice C) Hymenal incision is performed in patients with imperforate hymen, which causes primary amenorrhea. Patients have a uterus and a blue-tinged vaginal mass due to accumulated menstrual blood (ie, [hematocolpos](#)).

(Choices D and F) TSH and prolactin levels are ordered in women with primary amenorrhea who have a uterus and low/normal FSH. MRI of the brain is indicated in patients with a low/normal FSH, high prolactin, or visual field defects (eg, hemianopsia) to evaluate hypothalamic and pituitary causes (eg, sellar mass).

Educational objective:

(Choice A) Testosterone and dihydrotestosterone levels are used to diagnose 5-alpha-reductase deficiency and androgen insensitivity syndrome (AIS). In 5-alpha-reductase deficiency, genotypic males (46,XY) appear phenotypically female until puberty; elevated testosterone levels at puberty then cause virilization (eg, clitoromegaly) and lack of breast development, which are not seen in this patient. In AIS, genotypic males appear phenotypically female through puberty and have breast development. In contrast to this patient, those with AIS have no/minimal acne or pubic hair development due to an abnormal androgen receptor.

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(Choice C) Hymenal incision is performed in patients with imperforate hymen, which causes primary amenorrhea. Patients have a uterus and a blue-tinged vaginal mass due to accumulated menstrual blood (ie, [hematocolpos](#)).

(Choices D and F) TSH and prolactin levels are ordered in women with primary amenorrhea who have a uterus and low/normal FSH. MRI of the brain is indicated in patients with a low/normal FSH, high prolactin, or visual field defects (eg, hemianopsia) to evaluate hypothalamic and pituitary causes (eg, sellar mass).

Educational objective:

Müllerian agenesis causes primary amenorrhea due to the failed development of the uterus, cervix, and upper 1/3 of the vagina. Urogenital development is from a common embryologic source; therefore, renal malformations are common and patients require evaluation with a renal ultrasound.

References

- [ACOG Committee opinion: no. 728: Müllerian agenesis: diagnosis, management, and treatment.](#)
- [Mayer-Rokitansky-Küster-Hauser syndrome: complications, diagnosis and possible treatment options: a review.](#)

Obstetrics & Gynecology
Subject

Female Reproductive System & Breast
System

Amenorrhea
Topic

(Choice A) Testosterone and dihydrotestosterone levels are used to diagnose 5-alpha-reductase deficiency and androgen insensitivity syndrome

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A 34-year-old woman, gravida 1 para 1, comes to the office for infertility evaluation. She has been trying to conceive for the past year, but her cycles have become increasingly irregular, with the last menstrual period more than 3 months ago. Menses previously occurred every 27 days and lasted 4 days. The patient feels fatigued and has been waking up at night due to feeling too warm. She has been married for 6 years and has a 4-year-old daughter who was delivered vaginally without complications. The patient has hypothyroidism, for which she takes levothyroxine. She has no previous surgeries. The patient smokes a pack of cigarettes a day but does not use alcohol or illicit drugs. Both of her parents have type 2 diabetes mellitus. BMI is 24 kg/m². Vital signs are normal. Pelvic examination shows normal external genitalia, a small mobile uterus, and normal bilateral ovaries. TSH is normal and a pregnancy test is negative. Which of the following would most likely be seen in this patient?

- | | GnRH | FSH | Estrogen |
|--------------------------|--------|--------|----------|
| <input type="radio"/> A. | ↓ | ↓ | ↓ |
| <input type="radio"/> B. | ↑ | ↑ | ↓ |
| <input type="radio"/> C. | ↑ | Normal | ↑ |
| <input type="radio"/> D. | Normal | Normal | Normal |
| <input type="radio"/> E. | ↓ | ↓ | ↑ |

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	GnRH	FSH	Estrogen
<input type="radio"/> A. (15%)	↓	↓	↓
<input checked="" type="radio"/> B. (76%)	↑	↑	↓
<input type="radio"/> C. (0%)	↑	Normal	↑
<input type="radio"/> D. (3%)	Normal	Normal	Normal
<input type="radio"/> E. (4%)	↓	↓	↑

Omitted

Correct answer

B



76%

Answered correctly



03 secs

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05/09/2020

Last Updated

	GnRH	FSH	Estrogen
Hypothalamic hypogonadism	↓	↓	↓
Primary ovarian insufficiency	↑	↑	↓
Polycystic ovary syndrome	↑	Normal	↑
Normal ovulation	Normal	Normal	Normal
Exogenous estrogen use	↓	↓	↑

Primary ovarian insufficiency (POI), a form of **hypergonadotropic hypogonadism**, is the cessation of ovarian function at age <40. The condition is characterized by amenorrhea or oligomenorrhea and symptoms of decreased estrogen (eg, hot flashes, fatigue). Initial presentation is with irregular menses or **infertility**. Patients typically have a history of an autoimmune disorder (eg, hypothyroidism) or Turner syndrome. The decreased ovarian function results in **low estrogen levels**; this prevents the physiologic negative feedback mechanism, thereby causing **increased levels of GnRH and FSH** at the level of the hypothalamus and pituitary, respectively. Infertility treatment for POI consists of either in vitro fertilization or oocyte/embryo donation.

(Choice A) Hypothalamic hypogonadism is characterized by low GnRH secretion and resultant low levels of FSH and estrogen. Typical presentation is also with oligomenorrhea or amenorrhea, but the condition is more likely in the setting of relative caloric insufficiency from decreased caloric intake (eg, eating disorders) or strenuous exercise. Patients with hypothalamic hypogonadism do not have associated menopausal symptoms.

(Choice C) Polycystic ovary syndrome (PCOS) causes infertility by anovulation. Patients with PCOS have elevated GnRH, normal FSH, and elevated estrogen. In patients with PCOS, these occur due to increased peripheral conversion of androgens to estrone. This leads to persistently elevated (ie, continuous high-frequency pulses) GnRH levels at the hypothalamus, which causes a preference for LH production (and normal to decreased FSH levels) at the pituitary. These patients typically have a history of irregular menses, obesity, and signs of hyperandrogenism (eg, hirsutism, acne). Physical examination may show bilaterally enlarged ovaries.

Exogenous estrogen use

Primary ovarian insufficiency (POI), a form of **hypergonadotropic hypogonadism**, is the cessation of ovarian function at age <40. The condition is characterized by amenorrhea or oligomenorrhea and symptoms of decreased estrogen (eg, hot flashes, fatigue). Initial presentation is with irregular menses or **infertility**. Patients typically have a history of an autoimmune disorder (eg, hypothyroidism) or Turner syndrome. The decreased ovarian function results in **low estrogen levels**; this prevents the physiologic negative feedback mechanism, thereby causing **increased levels of GnRH and FSH** at the level of the hypothalamus and pituitary, respectively. Infertility treatment for POI consists of either in vitro fertilization or oocyte/embryo donation.

(Choice A) Hypothalamic hypogonadism is characterized by low GnRH secretion and resultant low levels of FSH and estrogen. Typical presentation is also with oligomenorrhea or amenorrhea, but the condition is more likely in the setting of relative caloric insufficiency from decreased caloric intake (eg, eating disorders) or strenuous exercise. Patients with hypothalamic hypogonadism do not have associated menopausal symptoms.

(Choice C) Polycystic ovary syndrome (PCOS) causes infertility by anovulation. Patients with PCOS have elevated GnRH, normal FSH, and elevated estrogen. In patients with PCOS, these occur due to increased peripheral conversion of androgens to estrone. This leads to persistently elevated (ie, continuous high-frequency pulses) GnRH levels at the hypothalamus, which causes a preference for LH production (and normal to decreased FSH levels) at the pituitary. These patients typically have a history of irregular menses, obesity, and signs of hyperandrogenism (eg, hirsutism, acne). Physical examination may show bilaterally enlarged ovaries.

(Choice D) Normal hormone levels would indicate ovulation, unlikely in a patient with irregular menses. Likely etiologies of infertility with normal laboratory values and normal menses are tubal blockage or male factor.

(Choice E) Exogenous estrogen use decreases GnRH and FSH levels through negative feedback, thereby preventing ovulation. This patient has signs of hypoestrogenism (eg, hot flashes), not hyperestrogenism (eg, breast tenderness).

Educational objective:

Primary ovarian insufficiency, cessation of ovarian function at age <40, may present with infertility, irregular menses, and menopausal symptoms. It is characterized by elevated gonadotropin-releasing hormone and FSH levels and a low estrogen level.

References