Settings

1
2
3
4

Item 1 of 4
Question Id: 11888

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 23-year-old woman, gravida 2, para 1, comes to the labor and delivery unit at 39 weeks gestation with abdominal discomfort and regular contractions. The patient had an uncomplicated first pregnancy that resulted in a spontaneous vaginal delivery at full term 3 years ago, and the current pregnancy has been uncomplicated. She takes a prenatal vitamin daily and no other medications. In response to increasing estrogen levels, the myometrial cells start to express genes that encode connexin-43 and the oxytocin receptor. These molecular changes would result in increased formation of which of the following?

- A. Adherens junctions
- B. Desmosomes
- C. Fenestrae
- D. Gap junctions
- E. Hemidesmosomes
- F. Tight junctions

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Block Time Remaining: 00:00:02
TUTOR

12 | Feedback | Suspend | End Block

2:19 PM
2/10/2019

Settings

1
2
3
4

Item 1 of 4
Question Id: 11888

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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- A. Adherens junctions [10%]
- B. Desmosomes [8%]
- C. Fenestrae [6%]
- ✔ D. Gap junctions [62%]
- E. Hemidesmosomes [3%]
- F. Tight junctions [9%]

Omitted
Correct answer
D

62%
Answered correctly

4 Seconds
Time Spent

08/25/2018
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Explanation

Cell junctions

Block Time Remaining: 00:00:04
TUTOR

12 | Feedback | Suspend | End Block

2:19 PM
2/10/2019

Explanation

Cell junctions		
Type	**Proteins**	**Function**
Gap junction	Connexins	Intercellular communication
Tight junction	Claudins, occludin	Paracellular barrier
Adherens junction	Cadherins	Cellular anchor
Desmosomes	Cadherins (eg, desmogleins, desmoplakin)	
Hemidesmosomes	Integrins	

Initiation of labor requires a series of biochemical changes in the uterus and cervix mediated by endocrine changes. **Cell junctions** are multiprotein complexes that allow contact between adjacent cells or between a cell and the extracellular matrix. Communicating (gap) junctions

Initiation of labor requires a series of biochemical changes in the uterus and cervix mediated by endocrine changes. **Cell junctions** are multiprotein complexes that allow contact between adjacent cells or between a cell and the extracellular matrix. Communicating (gap) junctions are especially important during labor and delivery, which require coordination and synchronization of individual myometrial cells. Gap junctions permit diffusion of molecules between neighboring cellular cytoplasms through a connexon (cylinder with a central channel composed of 6 connexin proteins).

Immediately prior to delivery, **estrogen** stimulates upregulation of **gap junctions** between individual myometrial smooth muscle cells. An increase in gap junction density at delivery heightens **myometrial** excitability. Gap junctions consist of aggregated **connexin** proteins (eg, connexin-43) that allow passage of ions between myometrial cells.

Estrogen also increases expression of uterotonic (eg, oxytocin) receptors, which mediate calcium transport through ligand-activated calcium channels. The combination of an increase in gap junction density and uterotonic receptors results in coordinated, synchronous labor contractions.

(Choices A and B) Both adherens junctions and desmosomes are composed of cadherins and are involved in intercellular adhesion. The cytoplasmic anchor of adherens junctions is the actin filament, whereas the cytoplasmic anchor of desmosomes is the intermediate filament. Autoantibodies against desmoglein, a cadherin protein for desmosomes, are found in **pemphigus vulgaris**.

(Choice C) Fenestrae are gaps between endothelial cells that allow for paracellular transport. Swollen fenestrae in renal glomerular capillary endothelial cells are implicated in preeclampsia (presents with new-onset hypertension and proteinuria or end-organ dysfunction at ≥20 weeks gestation).

(Choice E) Hemidesmosomes link cells to the basement membrane via integrins, the transmembrane anchor proteins. Autoantibodies to these proteins cause **bullous pemphigoid** and **pemphigoid gestationis**.

(Choice F) Tight junctions are comprised of claudins and occludin and serve as paracellular barriers to water and solutes. The enterotoxin from *Clostridium perfringens*, a common cause of food poisoning, binds claudin and interferes with tight junctions in the intestinal barrier. Water loss from the tissue to the intestinal lumen results in watery diarrhea.

channels. The combination of an increase in gap junction density and uterotonic receptors results in coordinated, synchronous labor contractions.

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Educational objective:
Gap junctions facilitate communication and coordination between cells and play an important role in labor contractions. Connexins are proteins that assemble into gap junctions and their density increases in the uterus before delivery in response to rising estrogen levels.

References

- Alterations in gap junction connexin43/connexin45 ratio mediate a transition from quiescence to excitation in a mathematical model of the myometrium.
- Glomerular endothelium: a porous sieve and formidable barrier

Settings

1
2
3
4

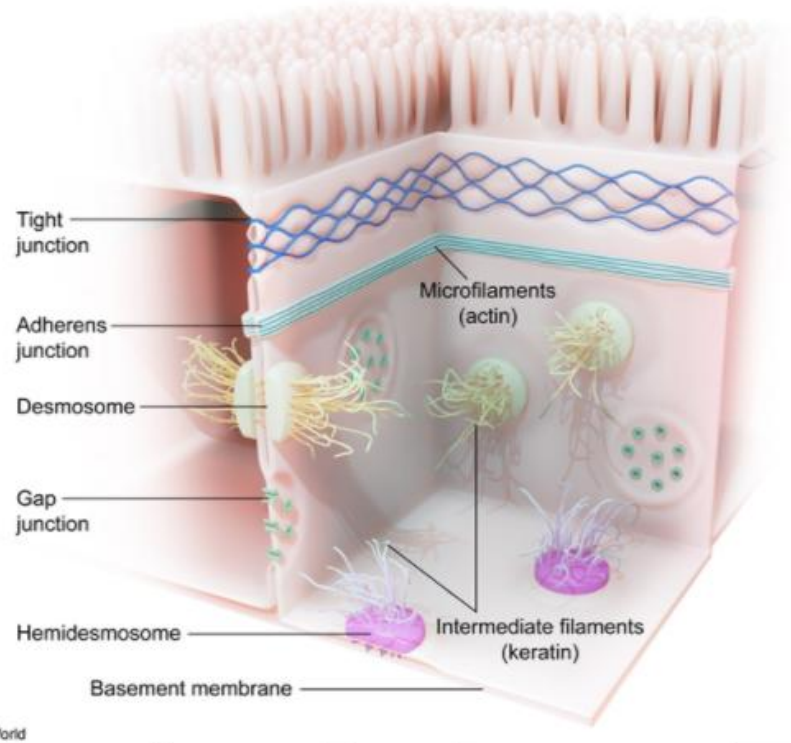
Item 1 of 4
Question Id: 11888

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Desmosomes	(eg, desmoglein)	Cellular anchor

Exhibit Display

Cell junctions



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12 | Feedback | Suspend | End Block

2:20 PM
2/10/2019

Settings

1
2
3
4

Item 2 of 4
Question Id: 1957

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 42-year-old woman, gravida 4, para 4, comes to the clinic due to heavy and painful menstrual bleeding over the past 3 months. Her last menstrual period was 4 weeks ago. Menarche was at age 10, and menstrual periods last for 3-5 days and occur every 30 days. She is sexually active with her husband and does not have pain with intercourse. The patient had a bilateral tubal ligation 3 years ago after the birth of her last child. She takes no medications and has no allergies. BMI is 24 kg/m^2. Vital signs are normal. On bimanual examination, the uterus is uniformly enlarged. Urine β-hCG is negative. Biopsy shows secretory endometrium. Which of the following is the most likely cause of this patient's symptoms?

A. Benign myometrial smooth muscle cell proliferation
B. Blastocyst implantation in the fallopian tube
C. Deficiency of von Willebrand factor
D. Endometrial tissue in the myometrium
E. Greater increase in endometrial gland proliferation compared to stroma
F. Hyperplastic growth of tissue from endometrial surface

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Block Time Remaining: 00:00:10
TUTOR

12 | Feedback | Suspend | End Block

2:20 PM
2/10/2019

Settings

1
2
3
4

Item 2 of 4
Question Id: 1957

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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A. Benign myometrial smooth muscle cell proliferation [12%]
B. Blastocyst implantation in the fallopian tube [2%]
C. Deficiency of von Willebrand factor [0%]
✔ D. Endometrial tissue in the myometrium [43%]
E. Greater increase in endometrial gland proliferation compared to stroma [18%]
F. Hyperplastic growth of tissue from endometrial surface [23%]

Omitted
Correct answer
D

43%
Answered correctly

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10/30/2018
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Explanation

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TUTOR

12 | Feedback | Suspend | End Block

2:20 PM
2/10/2019

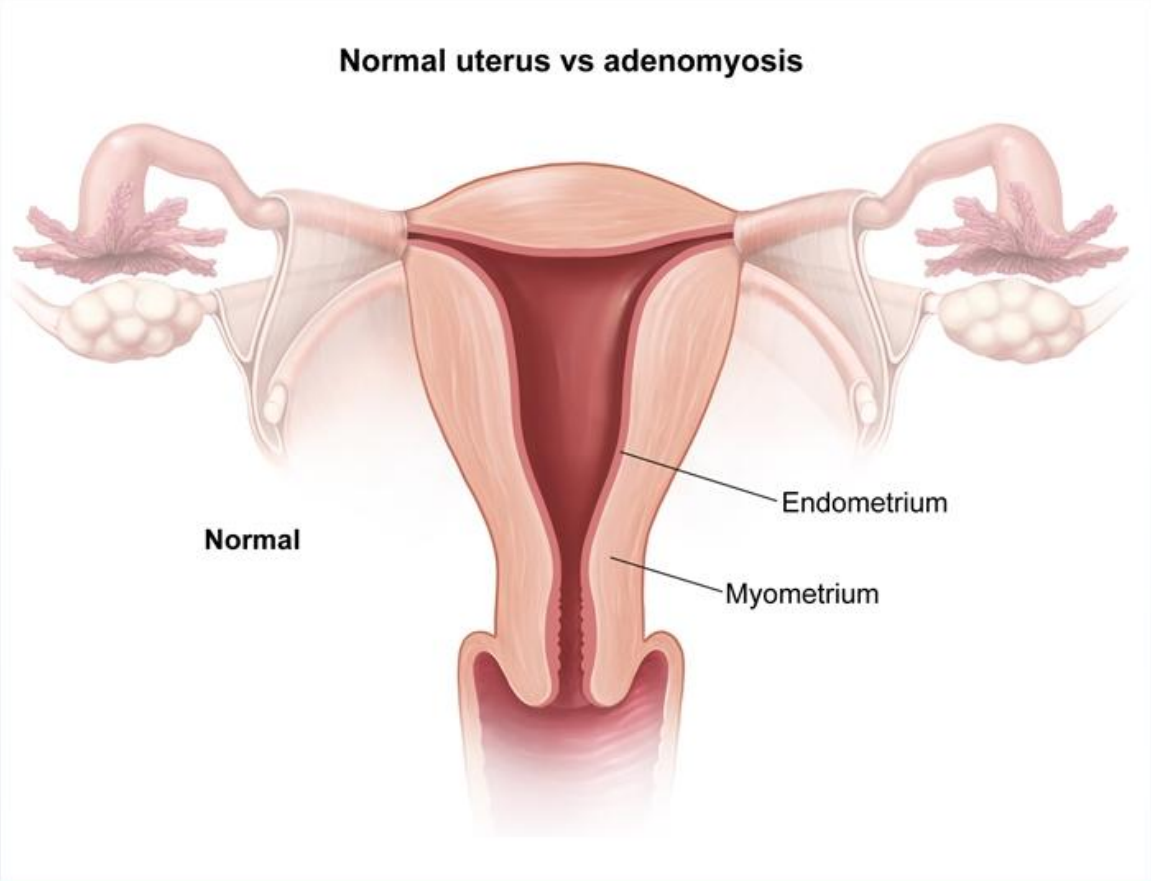
Settings

- 1
- 2
- 3
- 4

Item 2 of 4
Question Id: 1957

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Explanation



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2:20 PM
2/10/2019

Settings

1
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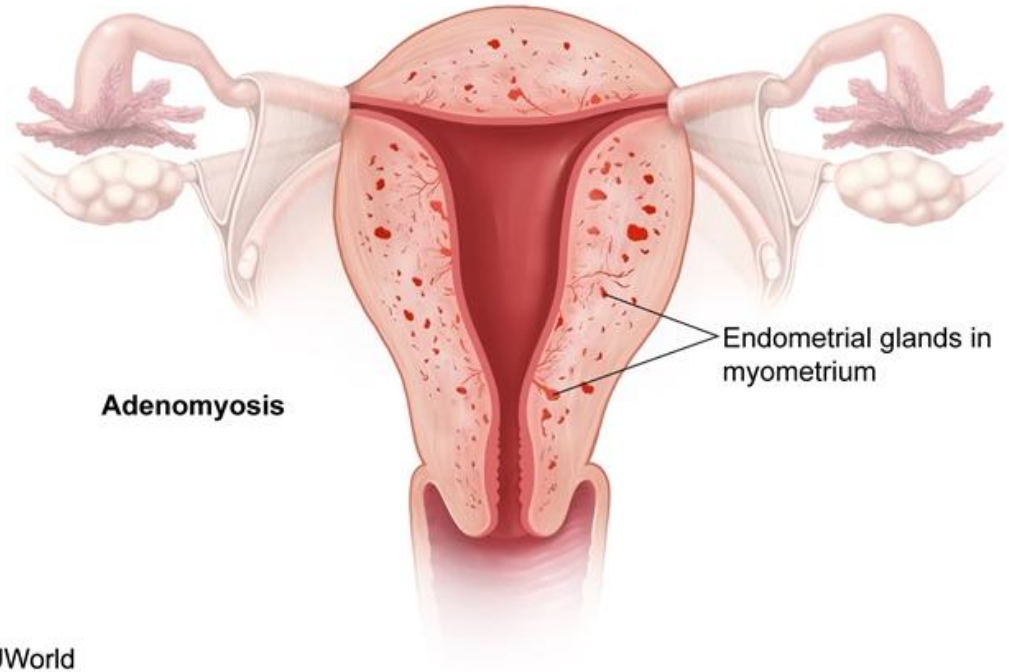
Item 2 of 4
Question Id: 1957

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom



Adenomyosis is the presence of **endometrial glandular tissue** within the **myometrium**. The condition is relatively common in middle-aged parous females. Symptoms include **heavy menstrual bleeding**, which is due to an increased endometrial surface, and **dysmenorrhea**, which results from endometrial tissue growth in the confined myometrial space. Physical examination classically shows a **uniformly enlarged uterus** (as seen in this patient). Uterine enlargement results from hormonal stimulation of endometrial glandular tissue in the myometrium. An endometrial biopsy is a sample of the tissue in the endometrial lining, and therefore, this patient's biopsy result of secretory endometrium is a

Block Time Remaining: 00:00:12
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12 | Feedback | Suspend | End Block

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2/10/2019

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(Choice A) Leiomyomas (also known as fibroids) are caused by proliferation of myometrial smooth muscle cells. Fibroids may cause heavy menstrual bleeding, but the uterus is usually irregularly enlarged.

(Choice B) The fallopian tube is the most common location for an **ectopic pregnancy**. Patients with extrauterine blastocyst implantation typically have amenorrhea with or without acute lower abdominal pain and a positive urine pregnancy test.

(Choice C) Von Willebrand disease is a commonly inherited coagulopathy. A deficiency or dysfunction in von Willebrand factor causes ineffective hemostasis, resulting in long-standing, heavy menstrual and peripartum bleeding. This patient's heavy menstrual bleeding started recently, and she delivered 4 children without bleeding complications.

(Choice E) Endometrial hyperplasia is characterized by a greater increase in endometrial gland proliferation as compared to stroma. It often presents with irregular, but not painful, menstrual bleeding.

(Choice F) Endometrial polyps are a common cause of abnormal uterine bleeding. They are usually benign projections from the uterine lining resulting from hyperplastic growth of endometrial glands and stroma. They do not cause uterine enlargement.

Educational objective:
Adenomyosis is the presence of endometrial glandular tissue within the myometrium. Menorrhagia and dysmenorrhea are common presenting symptoms. Patients have a uniformly enlarged uterus with normal-appearing endometrial tissue on biopsy.

Settings

1
2
3
4

Item 3 of 4
Question Id: 11890

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 34-year-old woman comes to the office with bleeding from the right nipple. The patient has noticed blood staining her undergarments on several occasions over the past week but has no fever or breast pain. She has no significant medical problems and does not take any medications. Breast examination shows no palpable masses or skin changes. Thin, blood-tinged discharge is expressed from the right nipple. There are no enlarged lymph nodes. Which of the following is the most likely histopathologic finding in this patient's right breast?

A. Atypical cells infiltrating the nipple skin
B. Cysts lined by metaplastic apocrine cells
C. Liquefactive necrosis of adipocytes with hemorrhage
D. Papillary cells with fibrovascular core
E. Stromal proliferation compressing the ducts to slits

Submit

Block Time Remaining: 00:00:13
TUTOR

12 | Feedback | Suspend | End Block

2:20 PM
2/10/2019

Settings

1
2
3
4

Item 3 of 4
Question Id: 11890

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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A. Atypical cells infiltrating the nipple skin [12%]
B. Cysts lined by metaplastic apocrine cells [8%]
C. Liquefactive necrosis of adipocytes with hemorrhage [11%]
✔ D. Papillary cells with fibrovascular core [55%]
E. Stromal proliferation compressing the ducts to slits [11%]

Omitted
Correct answer
D

55%
Answered correctly

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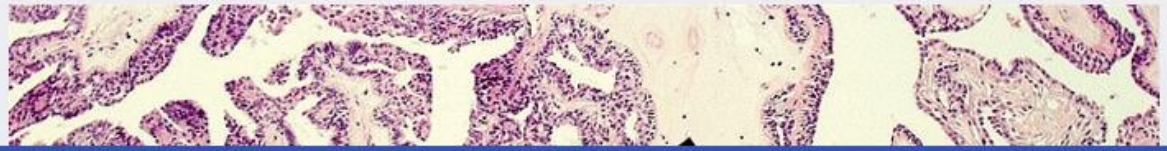
Explanation



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12 | Feedback | Suspend | End Block

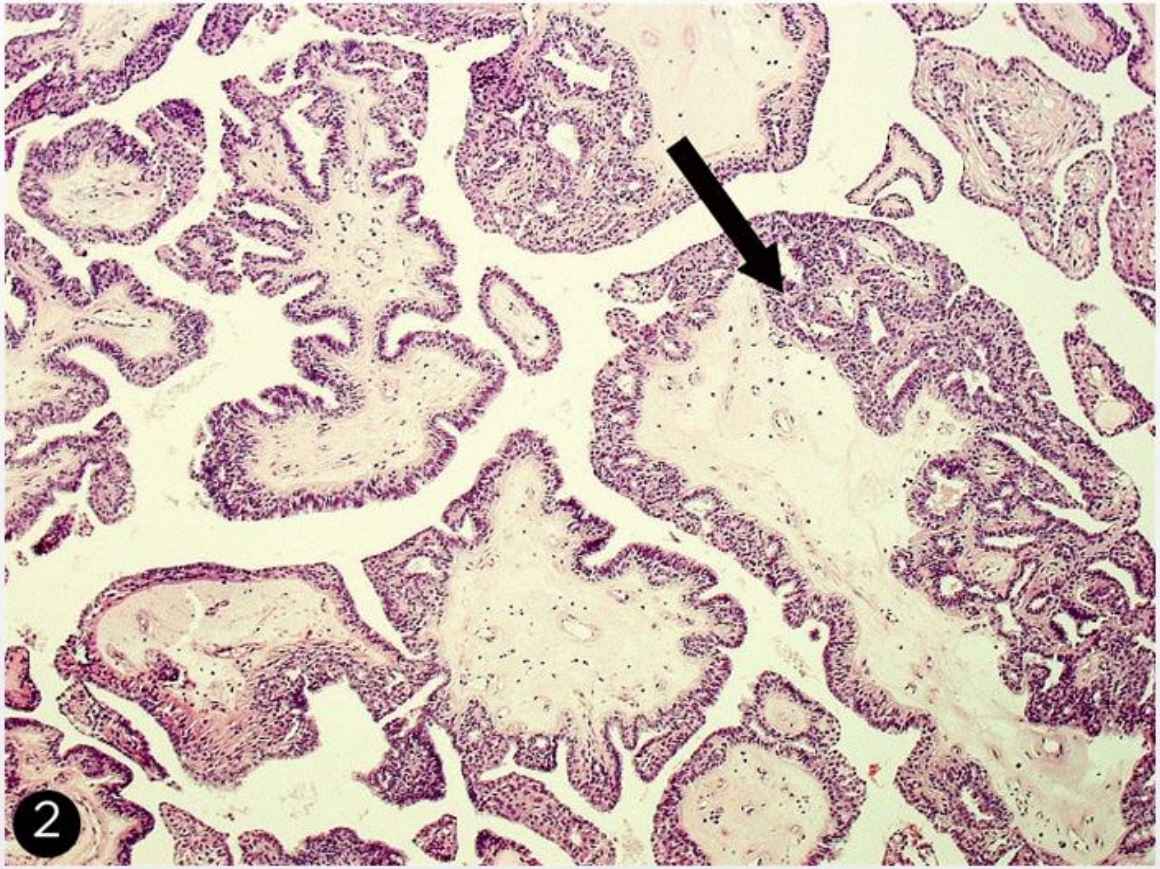
2:20 PM
2/10/2019

Settings

- 1
- 2
- 3
- 4

Item 3 of 4
Question Id: 11890

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom



Nipple discharge can be physiologic (bilateral, nonbloody, or milky without masses or skin changes) or pathologic (**bloody** or serosanguineous

Block Time Remaining: 00:00:15
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12 | Feedback | Suspend | End Block

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2/10/2019

Nipple discharge can be physiologic (bilateral, nonbloody, or milky without masses or skin changes) or pathologic (**bloody** or serosanguineous and **unilateral** with/without palpable masses and skin changes). **Intraductal papilloma** is the most common cause of alarming bloody or serosanguineous (eg, blood-tinged) nipple discharge. Affected patients typically have no associated breast mass or skin changes. Intraductal papilloma is caused by a proliferation of papillary cells (black arrow) in a duct or cyst wall with a fibrovascular core and may contain foci of atypia or ductal carcinoma in situ. The bloody discharge results from twisting of the vascular stalk of the papilloma in the duct.

(Choice A) Paget disease of the nipple is characterized by an **eczematous exudate** over the nipple and areola and is due to ductal spread of malignant cells (black arrow) to the **nipple surface**. Occasionally, bloody nipple discharge may be present.

(Choice B) Fibrocystic changes of the breast involve diffuse small **cysts (black arrow)** with or without metaplasia and frequently cause cyclic breast pain without nipple discharge.

(Choice C) **Fat necrosis** is preceded by localized trauma and typically presents as an irregular breast mass without nipple discharge. Histology shows liquefactive necrosis of adipocytes (black arrow) with hemorrhage (green arrow).

(Choice E) Fibroadenomas are small, firm, and mobile breast masses that occur due to proliferation of breast stroma and ducts, with stromal proliferation compressing the ducts to **slits (black arrow)** on microscopic examination.

Educational objective:
Intraductal papilloma is a proliferation of papillary cells in a cyst wall or duct that may contain focal atypia. It is the most common cause of bloody nipple discharge and typically presents without breast masses or skin changes.

References

- Evaluating nipple discharge.

Settings

- 1
- 2
- 3
- 4

Item 4 of 4
Question Id: 334

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 28-year-old woman, gravida 3 para 3, comes to the emergency department with severe abdominal pain in the left lower quadrant and vaginal bleeding. She is saturating a pad every 3-4 hours. Her last menstrual period was 6 weeks ago. Past surgical history is significant for 3 cesarean deliveries and permanent sterilization via a bilateral tubal ligation. A urine pregnancy test is positive, and an ultrasound shows a 2-cm mass in the left adnexa adjacent to the ovary and a thickened endometrial stripe. If a uterine curettage is performed, which of the following findings would be expected in this patient?

A. Atypical endometrial cells, disorganized glands, and multiple mitoses
B. Dilated, coiled endometrial glands and edematous stroma
C. Enlarged chorionic villi and avascular edematous stroma
D. Inflammatory infiltration of endometrial glands
E. Straight, short endometrial glands and compact stroma

Submit

Block Time Remaining: 00:00:16
TUTOR

12 | Feedback | Suspend | End Block

2:21 PM
2/10/2019

Settings

1
2
3
4

Item 4 of 4
Question Id: 334

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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- A. Atypical endometrial cells, disorganized glands, and multiple mitoses [10%]
- ✔ B. Dilated, coiled endometrial glands and edematous stroma [56%]
- C. Enlarged chorionic villi and avascular edematous stroma [25%]
- D. Inflammatory infiltration of endometrial glands [3%]
- E. Straight, short endometrial glands and compact stroma [3%]

Omitted
Correct answer
B

56%
Answered correctly

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01/25/2019
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Explanation

Ectopic pregnancy with ruptured fallopian tube

Block Time Remaining: 00:00:17
TUTOR

12 | Feedback | Suspend | End Block

2:21 PM
2/10/2019

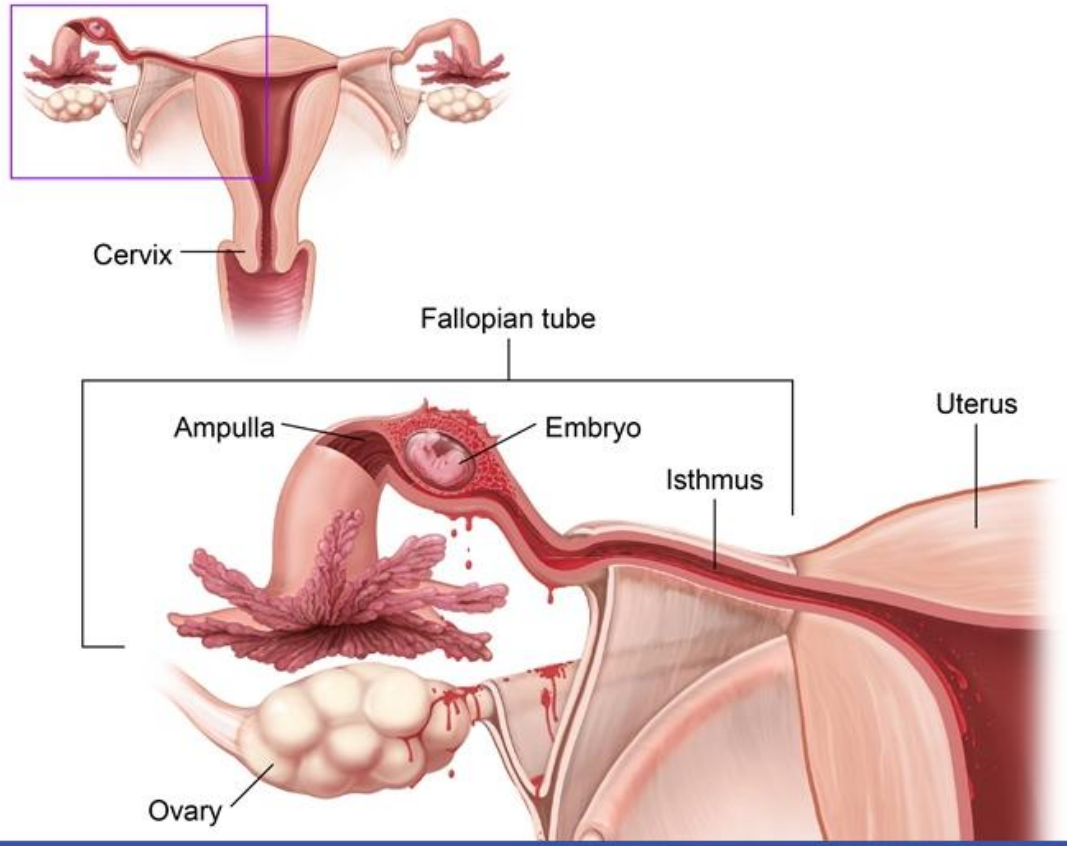
Settings

- 1
- 2
- 3
- 4

Item 4 of 4
Question Id: 334

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

Ectopic pregnancy with ruptured fallopian tube



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2:21 PM
2/10/2019

Settings

1
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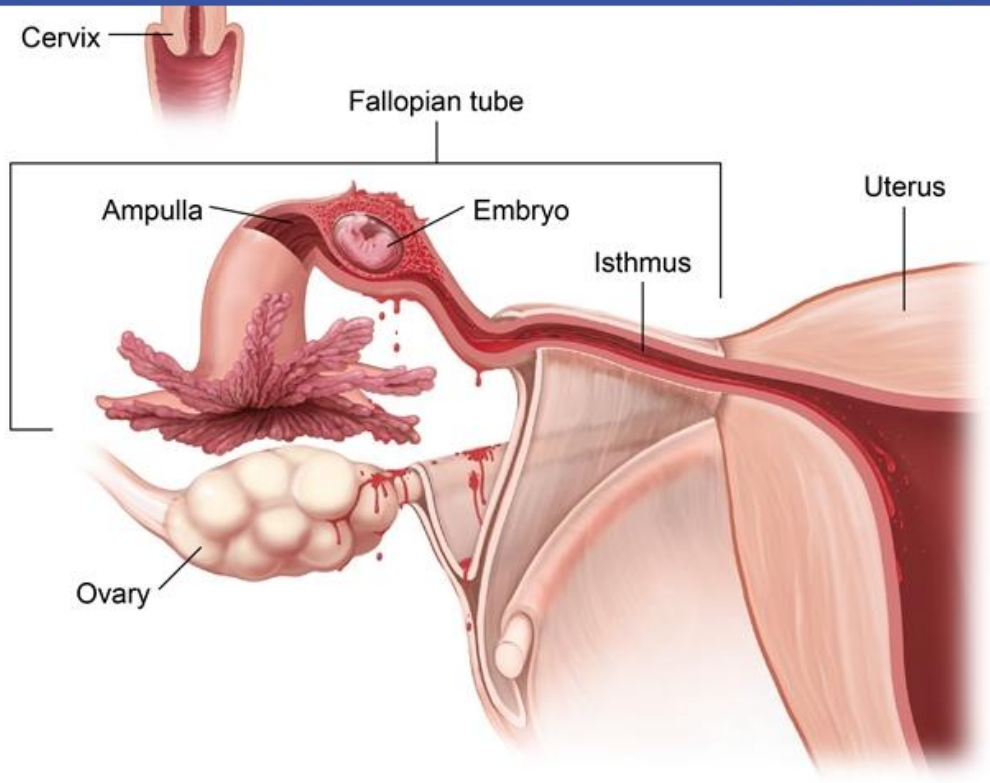
3
4

Item 4 of 4
Question Id: 334

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom



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Ectopic pregnancy occurs when a **fertilized ovum implants outside of the uterus**. The most common site is the **ampulla** of the fallopian tube, which may appear as an adnexal mass on ultrasound. Risk factors include tubal pathology, such as from previous infection or surgery (eg, **tubal ligation**). Pregnancy after permanent sterilization is extremely rare, but one-third of cases are ectopic if implantation occurs. An ectopic

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A ruptured ectopic pregnancy is managed surgically by removing the pregnancy and achieving hemostasis. Dilation and curettage of the uterus may be performed either to stop uterine bleeding or confirm whether the pregnancy is intrauterine or ectopic. In an ectopic pregnancy, the uterine specimen would reveal **decidualized endometrium** only, consistent with **dilated, coiled endometrial glands** and **vascularized edematous stroma**. These changes occur in the luteal phase of the **menstrual cycle**, under the influence of **progesterone**, as the endometrium prepares for implantation. Embryonic and trophoblastic tissue will be absent from the uterus.

(Choice A) The finding of atypical endometrial cells that form glands would suggest **endometrial adenocarcinoma**, a malignancy that typically occurs in postmenopausal women and manifests with vaginal bleeding.

(Choice C) A molar pregnancy or spontaneous abortion may present with vaginal bleeding. Uterine curettage may show enlarged chorionic villi and avascular edematous stroma. In contrast, intrauterine chorionic villi are absent in an ectopic pregnancy.

(Choice D) An inflammatory endometrial infiltrate would suggest endometritis, an infection of the decidua, which presents with uterine tenderness, fever, and tachycardia. An ectopic pregnancy is not an infectious process.

(Choice E) Straight, short endometrial glands and compact stroma are found in the early **proliferative phase of the menstrual cycle**. This microscopic appearance would be observed 4-7 days after the onset of menses.

Educational objective:
An ectopic pregnancy is characterized by implantation outside of the uterus. Uterine curettage would reveal decidual changes in the endometrium due to progesterone secretion but no embryonic or trophoblastic tissue (eg, no villi).

Settings

1
2
3
4

Item 4 of 4
Question Id: 334

Mark | Previous | Next | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

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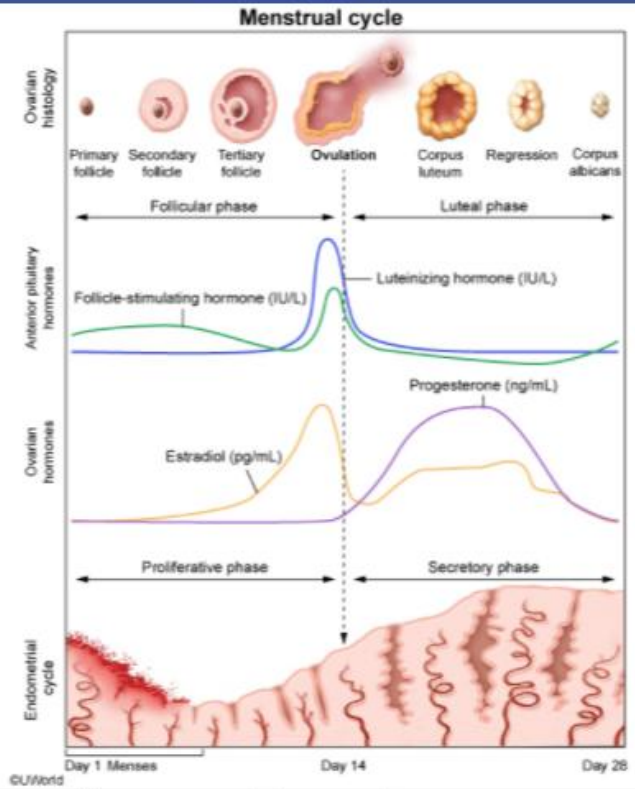

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