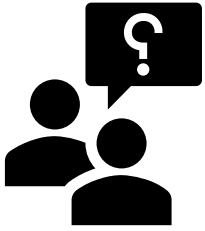


Discussion
Reproductive system lectures

Ebaa M Alzayadneh, PhD
Associate Professor
Department of Physiology and Biochemistry
The University of Jordan

Q1

- For in vitro fertilization, the female menstrual cycle is exogenously controlled utilizing several hormone treatments and assessments.
- A cycle begins by administering a receptor antagonist of Hormone 1, which stops the hypothalamic-pituitary gonadal axis for one week.
- During that week, there will be daily injections of Hormone 2, which stimulates the development of large antral ovarian follicles.
- During the next week, ultrasound is used to monitor follicular growth, and Hormone 3 is expected to increase.
- When several 18-mm follicles are seen, Hormone 4 is injected to induce oocyte maturation.
- Mature eggs are retrieved just before ovulation and mixed with, or injected with, sperm in vitro. The fertilized eggs are incubated for 3 days. During this time, the woman is injected daily with Hormone 5.
- After the embryos are transferred back to the uterus, Hormone 6 is monitored to confirm potential pregnancy. Which of the following are Hormones 1–6?

Q1

	Hormone 1	Hormone 2	Hormone 3	Hormone 4	Hormone 5	Hormone 6
A.	GnRH	FSH	E	hCG	E	hCG
B.	FSH	LH	P	E	P	P
C.	LH	GnRH	hCG	P	hCG	E
D.	GnRH	FSH	E	hCG	P	hCG
E.	FSH	LH	P	E	E	P

E: Estradiol; FSH: Follicle-stimulating hormone; GnRH: Gonadotropin-releasing hormone; hCG: Human chorionic gonadotropin; LH: Luteinizing hormone; P: Progesterone

Answer and Explanation

The correct answer is **D**. Here is the breakdown of why each hormone is used in this sequence:

1. **Hormone 1 (GnRH):** A **GnRH antagonist** is used to shut down the patient's natural hypothalamic-pituitary-gonadal axis. This prevents an "internal" LH surge that could cause premature ovulation before the eggs are ready for retrieval.
2. **Hormone 2 (FSH):** Daily injections of **FSH** are given to stimulate the "recruitment" and growth of multiple large antral follicles simultaneously, rather than just one dominant follicle.
3. **Hormone 3 (Estradiol/E):** As the follicles grow, the granulosa cells produce increasing amounts of **Estradiol**. Monitoring these levels via blood tests helps track follicular development alongside ultrasound.
4. **Hormone 4 (hCG):** Because **hCG** has the same biological activity as LH (binding to the same receptors), it is used as a "trigger shot" to simulate the **LH surge**, which induces the final maturation of the oocytes.
5. **Hormone 5 (Progesterone/P):** After egg retrieval, the natural corpus luteum may not function adequately due to the hormonal suppression used earlier. Therefore, **Progesterone** is administered to prepare and maintain the uterine lining (endometrium) for the embryo transfer.
6. **Hormone 6 (hCG):** This is the classic "pregnancy hormone." It is monitored after the transfer because its presence indicates that an embryo has successfully implanted and the trophoblast cells are secreting it.

Q2

- A young woman is given daily injections of a substance beginning on the sixteenth day of her normal menstrual cycle and continuing for 3 weeks. As long as the injections continue, she does not menstruate. The injected substance could be which of the following?

A) Testosterone

B) FSH

C) An inhibitor of progesterone's actions

D) A PGE2 inhibitor

E) LH

Answer and Explanation

The correct answer is E.

Here is the physiological reasoning:

- **The Luteal Phase Context:** By Day 16 of a standard 28-day cycle, the woman has already ovulated and is in the luteal phase. During this time, the [1] **corpus luteum** is responsible for secreting the estrogen and progesterone needed to maintain the uterine lining. [2]
- **The Trigger for Menstruation:** Normally, if pregnancy does not occur, the corpus luteum begins to involute (die) around Day 26 because of a lack of continued hormonal support. This causes a sudden drop in progesterone and estrogen levels, which leads to the shedding of the endometrium (menstruation).
- **The Role of LH:** The corpus luteum is maintained by **Luteinizing Hormone (LH)**. In a normal cycle, LH levels eventually decline, leading to the death of the corpus luteum.
- **Why LH prevents menses:** If you provide exogenous injections of **LH** (or a similar substance like hCG), you are essentially "rescuing" the corpus luteum. It will continue to produce progesterone and estrogen, which keeps the endometrial lining intact and prevents menstruation from occurring for as long as the injections continue.

Q3

A professional athlete in her mid-20s has not had a menstrual cycle for 5 years, although a bone density scan revealed normal skeletal mineralization. Which fact may explain these observations?

A) She consumes a high-carbohydrate diet
B) Her grandmother sustained a hip fracture at age 79 years
C) Her blood pressure is higher than normal
D) Her plasma estrogen concentration is very low
E) **She has been taking anabolic steroid supplements or 5 years**

Answer and Explanation

The correct answer is E.

Here is why this explains both the lack of a cycle and the normal bone density:

- **Suppression of the Cycle:** Anabolic steroids are synthetic versions of testosterone (androgens). In a female, high levels of exogenous androgens exert **strong negative feedback** on the hypothalamus and anterior pituitary. This inhibits the release of [1] **GnRH, FSH, and LH**, which are necessary to stimulate the ovaries. Without these triggers, the ovarian and menstrual cycles stop completely, leading to long-term amenorrhea.
- **The Bone Density "Clue":** Normally, if a woman stops menstruating because of low natural estrogen (like in menopause or extreme over-exercise), her bone density would decrease because estrogen is needed to inhibit bone resorption . However, this athlete has **normal bone density**.
- **Why the bones stay strong:** Anabolic steroids, like testosterone, have a direct **protein anabolic effect** on the body, including the bones . They stimulate bone matrix formation and mineralization. Therefore, even though her natural estrogen levels are likely low due to the shut-down of her cycle, the steroids she is taking are "substituting" for that protective effect on her skeleton.

Q4

- Drug X causes abortion if it is administered before or soon after implantation. What is the specific effect of X?

A) It binds to LH receptors, stimulating the secretion of progesterone from the corpus luteum

B) It blocks progesterone receptors

C) It blocks the secretion of FSH by the pituitary

D) It blocks the effects of oxytocin receptors in the uterine muscle

Answer and Explanation

The correct answer is B.

Here is why this drug is so effective at inducing abortion:

- **The Necessity of Progesterone:** Progesterone is often called the "hormone of pregnancy." Its primary job in the first few weeks is to maintain the **decidua** (the nutrient-rich lining of the uterus) and to **decrease the contractility of the uterus** to prevent the expulsion of the embryo .
- **Mechanism of the Drug:** If a drug blocks **progesterone receptors**, the uterus can no longer "sense" the progesterone that is being produced by the corpus luteum . This causes the uterine lining to break down and the muscle to start contracting, leading to the termination of the pregnancy.
- **Why the other options are wrong:**
  - **A:** Stimulating progesterone would actually **support** the pregnancy rather than end it .
  - **C:** FSH is responsible for **follicle growth** in the ovaries; by the time implantation has occurred, FSH is already naturally suppressed by pregnancy hormones .
  - **D:** Oxytocin is primarily responsible for **labor contractions** at the end of pregnancy; blocking its receptors early on would not typically cause an abortion .

Q5

- If a woman has a tumor that is secreting large amounts

of estrogen from the adrenal gland, which of the following will occur?

- A) Progesterone levels in the blood will be very low
- B) Her LH secretion rate will be totally suppressed
- C) She will not have normal menstrual cycles
- D) Her bones will be normally calcified
- **E) All the above**

Answer and Explanation

The correct answer is E.

Here is the breakdown of why every single one of those statements is true:

- **Suppression of LH (B):** Under normal circumstances, high levels of estrogen (except for the brief pre-ovulatory peak) exert strong **negative feedback** on the anterior pituitary and hypothalamus. This suppresses the secretion of LH and FSH. [1] [2]
- **Lack of Normal Menstrual Cycles (C):** A normal cycle requires the rhythmic rise and fall of hormones. If a tumor is constantly pumping out high levels of estrogen, the feedback loops are disrupted, and the hormonal triggers for ovulation and menstruation do not occur, leading to an **anovulatory state**.
- **Low Progesterone (A):** Progesterone is primarily produced by the **corpus luteum**, which only forms after ovulation occurs. Since the high estrogen levels have suppressed the LH surge needed for ovulation, no corpus luteum is formed, and progesterone levels remain very low.
- **Bone Calcification (D):** Estrogen is a major regulator of bone metabolism. It stimulates bone growth and inhibits osteoclasts (the cells that break down bone). Therefore, even with an abnormal reproductive cycle, her bones will be well-calcified due to the abundance of estrogen.

Q6

- Men who take large doses of testosterone-like androgenic steroids for long periods are sterile (non fertile). What is the explanation for this finding?
- A) High levels of androgens bind to testosterone receptors in the Sertoli cells, resulting in overstimulation of inhibin formation
- B) Overstimulation of sperm cell production results in the formation of defective sperm cells
- C) **High levels of androgen compounds inhibit the secretion of GnRH by the hypothalamus, resulting in the inhibition of LH and FSH release by the anterior pituitary**
- D) High levels of androgen compounds produce hypertrophic dysfunction of the prostate gland

Answer and Explanation

The correct answer is C.

Here is the physiological explanation for why exogenous steroids lead to infertility:

- **Negative Feedback Loop:** The male reproductive system is regulated by a strict feedback loop. Normally, the hypothalamus secretes GnRH, which triggers the pituitary to release FSH and LH. [1] [2]
- **The Effect of Steroids:** When a man takes large doses of testosterone-like steroids, these compounds circulate in the blood and signal the brain that "enough" hormone is already present. This exerts **strong negative feedback** on the hypothalamus, inhibiting the secretion of **GnRH**.
- **Inhibition of Gonadotropins:** Without GnRH, the anterior pituitary stops releasing **FSH and LH**.
- **Spermatogenesis Failure:** This is the critical part for fertility. **FSH** is required to stimulate the Sertoli cells to support sperm production, and **LH** is required to stimulate the Leydig cells to produce the *local* high concentration of testosterone needed within the testes for sperm to mature. [3]
- **Sterility:** Because the external steroids have shut down the natural production of FSH and LH, the "machinery" for making sperm in the testes stops working, resulting in sterility.

Q7

A man who has been exposed to high levels of gamma radiation is sterile due to destruction of the germinal epithelium of the seminiferous tubules, although he has normal levels of testosterone. Which of the following would be found in this patient?

A) **A normal secretory pattern of GnRH**

B) Normal levels of inhibin

C) Suppressed levels of FSH

D) Absence of Leydig cells

Answer and Explanation

The correct answer is A.

Here is why this patient presents with this specific hormonal profile:

- **Understanding the Damage:** Gamma radiation specifically targets cells that are rapidly dividing. In the testes, the **germinal epithelium** (which produces sperm) is highly sensitive and easily destroyed, leading to sterility.
- **The "Intact" Cells:** The question states that the man has **normal levels of testosterone**. This tells us that the **Leydig cells**, which are located in the interstitium between the tubules and are responsible for secreting testosterone, were not destroyed by the radiation. Therefore, option D is incorrect.
- **The GnRH Pattern:** In males, the secretion of **GnRH** from the hypothalamus is primarily regulated by the negative feedback of **testosterone**. Since his testosterone levels are normal, the feedback loop to the hypothalamus remains functional and "happy," resulting in a normal secretory pattern of GnRH.
- **Why the other options are wrong:**
  - **B: Inhibin** is produced by the Sertoli cells within the seminiferous tubules. When the germinal epithelium is destroyed, Sertoli cell function is often compromised, or the signal to produce inhibin is lost, leading to **low** (not normal) inhibin levels.
  - **C:** Inhibin's primary job is to provide negative feedback to the pituitary to inhibit **FSH**. With low levels of inhibin, the "brakes" are removed, and FSH levels would actually be **elevated**, not suppressed.

Q8

A child raised as female presents at puberty with deepening voice and increased muscle mass. Karyotype is 46,XY. Testosterone level is normal/high. Internal male structures are present, and the prostate is small.

Which enzyme deficiency is most likely?

A. 17β-hydroxysteroid dehydrogenase deficiency
B. Aromatase deficiency
C. Side-chain cleavage enzyme deficiency
D. **5-α-reductase type 2 deficiency**
E. 11β-hydroxylase deficiency

Answer and Explanation

The correct answer is D.

This specific clinical presentation is a classic textbook case for understanding the difference between the roles of Testosterone and Dihydrotestosterone (DHT):

- **Role of Testosterone:** Testosterone is responsible for the development of **internal male structures** (like the epididymis and vas deferens). Since the patient has internal male structures and normal/high testosterone, we know the body is producing testosterone and responding to it internally. 1 2
- **Role of DHT:** Testosterone must be converted into **DHT** by the enzyme **5-α-reductase** to facilitate the development of **external male genitalia** and the **prostate** 3 . 3
- **The Deficiency:** In 5-α-reductase deficiency, the fetus has plenty of testosterone (so internal male parts grow), but almost no DHT. Without DHT, the external genitalia do not masculinize in utero, often resulting in a female appearance at birth.
- **Puberty Shift:** When puberty hits, the massive surge in testosterone is often enough to cause "virilization"—deepening the voice and increasing muscle mass—even without DHT. However, the prostate remains small because its growth is uniquely dependent on DHT.

Enzymes Functions.

- **17β-hydroxysteroid dehydrogenase:** This enzyme is responsible for the final step in testosterone synthesis (converting androstenedione to testosterone). A deficiency would result in low testosterone and high levels of weaker androgens . 1
- **Aromatase:** This enzyme converts androgens (like testosterone) into estrogens. A deficiency would lead to a lack of estrogen and potentially high levels of testosterone. 2 3
- **Side-chain cleavage enzyme:** This is the "gatekeeper" enzyme that converts cholesterol into pregnenolone, which is the very first step in making all steroid hormones . A deficiency here would mean a total lack of all adrenal and gonadal steroids .
- **5-α-reductase type 2:** This enzyme converts testosterone into the much more potent dihydrotestosterone (DHT) . DHT is specifically required for the development of the prostate and male external genitalia .
- **11β-hydroxylase:** This is an adrenal enzyme involved in making cortisol . A deficiency leads to Congenital Adrenal Hyperplasia (CAH), which often causes female fetuses to become "masculinized" because the body shunts hormone production toward androgens instead .

Q9

Milk is produced by a woman only after delivery, not before?

A) Levels of LH and FSH are too low during pregnancy to support milk production

B) **High levels of progesterone and estrogen during pregnancy suppress milk production**

C) The alveolar cells of the breast do not reach maturity until after delivery

D) Oxytocin is not secreted until the baby stimulates the nipple

E) Prolactin is not secreted until the baby is born

Answer and Explanation

The correct answer is B.

Here is why milk production only kicks in after the baby is born:

- **Preparation vs. Production:** During pregnancy, the very high levels of **estrogen and progesterone** actually do a lot of work preparing the breasts; they cause the ducts to grow and the milk-producing alveoli to develop .
- **The Inhibitory Effect:** However, these same hormones (estrogen and progesterone) have a powerful **inhibitory effect** on the actual secretion of milk . Even though prolactin levels are high throughout pregnancy, these "pregnancy steroids" prevent the breast tissue from actually responding to prolactin and producing milk .
- **The Post-Delivery Trigger:** Once the placenta is delivered, the source of these high hormone levels is gone, and estrogen and progesterone levels **drop precipitously** . This sudden removal of inhibition finally allows **prolactin** to stimulate the alveolar cells to begin milk production .

Q10

- The research laboratory of a fertility clinic investigates various biomolecules for their ability to induce sperm **Capacitation**. The molecules have most likely been isolated from the fluid of which of the following structures?
- A. Epididymis and sertoli
- B. Ovaries
- C. Seminal vesicles
- D. Seminiferous tubules
- **E. Uterus**

Answer and Explanation

The correct answer is E.

Here is why the uterus is the most likely source for these molecules:

- **Definition of Capacitation:** When sperm are first ejaculated, they are not yet capable of fertilizing an egg. They must undergo a process called **capacitation**, which involves the washing away of inhibitory factors and the weakening of the acrosomal membrane. [1]
- **The Environment:** Capacitation does **not** occur in the male reproductive tract. Instead, it is triggered by contact with the fluids in the **female genital tract** (the uterus and fallopian tubes).
- **The Mechanism:** Fluids in the uterus wash away inhibitory cholesterol from the sperm's head and change the permeability of the membrane to calcium, which gives the sperm the "hyperactivated" motility needed to penetrate the egg.
- **Why the other options are wrong:** Options A, C, and D are all part of the male system where sperm are produced, matured, or stored, but they do not induce capacitation. Option B (ovaries) is incorrect because sperm do not actually enter the ovaries; they meet the egg in the fallopian tube.

Q11

- In females, a drug formulated to prevent luteinizing hormone (LH) from binding to its receptor in luteal cells.

A. inhibits progesterone production by the corpus luteum

B. reduces estrogen level

C. induces ovulation

D. induces long menstruation

E. stimulates granulosa and theca cells secretion

Answer and Explanation

The correct answer is A.

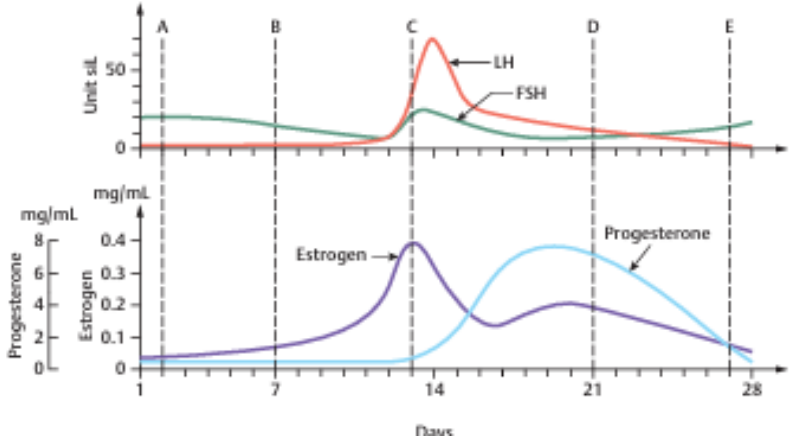
Here is why blocking LH at the luteal cell level has this effect:

- **The Role of Luteal Cells:** Luteal cells are the specific cells that make up the **corpus luteum** after ovulation has occurred. [1]
- **The Stimulus for Progesterone:** The primary function of the corpus luteum is to secrete large amounts of **progesterone** to prepare the uterus for potential pregnancy. However, the corpus luteum is "LH-dependent." It requires the constant binding of **LH** to its receptors to keep the cellular machinery for progesterone production running.
- **Effect of the Drug:** If you block the LH receptor, you cut off the "signal" telling the corpus luteum to work. As a result, the production and secretion of **progesterone** will be inhibited.
- **Why the other options are wrong:**
  - **B:** While the corpus luteum does produce some estrogen, its *primary* and most significant output is progesterone.
  - **C:** Ovulation is *caused* by a surge of LH; blocking LH receptors would **prevent** ovulation, not induce it.
  - **E:** Granulosa and theca cells are characteristic of the **follicular phase** before the corpus luteum is even formed.

Q12

- When is the woman most fertile?

A. A
B. B
C. C
D. D
E. E



Answer and Explanation

The correct answer is C.

Here is why this point on the graph represents the peak of fertility:

- **Understanding the Timeline:** In the graph, point **C** occurs around day 13 or 14 of the typical 28-day cycle. [1]
- **The Hormonal Markers:** At point **C**, we see two critical events: the **peak of estrogen** and the massive **LH surge**.
- **The Biological Event:** The LH surge is the direct trigger that causes the dominant follicle to rupture and release the egg—the process of **ovulation** [2][3]. [2][3]
- **Fertility Window:** Because the egg only lives for a short period after release (about 12–24 hours), the time immediately surrounding ovulation (point C) is when a woman is most fertile and fertilization is most likely to occur.
- **Why the other points are less fertile:**
  - **A and B:** These points occur during the **follicular phase** when the egg is still developing inside the follicle and has not yet been released.
  - **D:** This is the **luteal phase** (around day 21). While progesterone is high here, the egg has already been released days ago and, if not fertilized, is no longer viable.
  - **E:** This is the end of the cycle, just before menstruation begins.