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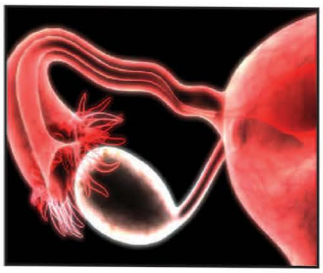
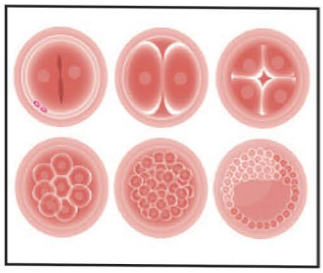
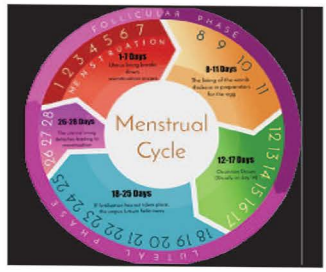
MCQs in Reproductive Endocrinology and Infertility



Based on Standard Textbook's
Speroff's Clinical Gynecologic Endocrinology and Infertility 8th edition; Yen and Jaffe's Reproductive Endocrinology 8th edition; David K Gardner Textbook of Assisted Reproductive Techniques: Laboratory Perspectives (Volume 1), 5th edition,Textbook of Assisted Reproductive Techniques: Clinical Perspectives (Volume 2), 5th edition; Anne M Jequier Infertility in the Male, 4th edition

Rashmi Vohra

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CHAPTER

3 Neuroendocrinology

Multiple Choice Questions

1. **Which of the following pituitary hormone is not under positive hypothalamic control unlike other hormones?**
   a. Prolactin b. Growth hormone
   c. FSH d. ACTH

2. **Which of the following is incorrect regarding GnRH?**
   a. A total of 24 forms of GnRH have been identified
   b. GnRH localized to the hypothalamus is GnRH-I
   c. GnRH is decapeptide
   d. GnRH-II is the main form found in the brain

3. **Prolactin gene expression is seen in all of the following tissues, *except:***
   a. Lactotropes of anterior pituitary gland
   b. Decidualised endometrium
   c. Hypothalamus
   d. Myometrium

4. **Which of the following is incorrect regarding prolactin?**
   a. Prolactin is highest in early morning hours
   b. Prolactin gene expression is stimulated by estrogen
   c. D2 type receptors are predominant in anterior pituitary gland
   d. TRH has stimulatory effect on prolactin secretion

5. **Mode of inheritance of Kallmann's syndrome:**
   a. X-linked
   b. Autosomal-dominant
   c. Autosomal-recessive
   d. All

6. **All of the following is true regarding GnRH secretion, *except:***
   a. Cells that produce GnRH originate from olfactory placode
   b. Arcuate nucleus is key locus for GnRH secretion
   c. GnRH is nonapeptide
   d. Half life of GnRH is 2-4 minutes

7. **Which of the following is true regarding feedback loops affecting GnRH secretion?**
   a. Long feedback loop is due to effects of target gland hormones on hypothalamus and pituitary
   b. Short feedback loop is due to effects of pituitary hormones on hypothalamus
   c. Ultrashort feedback is inhibition by hypothalamic releasing hormone on its own synthesis
   d. All

8. **Which of the following statement is correct regarding GnRH pulse frequency?**
   a. The measurement of LH pulses is used as an indication of GnRH pulsatile secretion
   b. Pulsatile secretion is more frequent but lower in amplitude during the follicular phase
   c. During the luteal-follicular transition, pulse frequency increases approximately 4.5-fold
   d. All

9. **Which of the following is incorrect regarding dopaminergic pathway?**
   a. Dopamine directly suppress gonadotropin secretion
   b. Dopamine directly suppress arcuate GnRH activity
   c. Dopamine directly suppress pituitary prolactin secretion
   d. Dopamine directly suppress melanocyte-stimulating hormone

10. **Which of the following is not true about major 'neurobiological brake'?**
    a. Facilitates gonadotropin secretion in absence of estrogen
    b. Neuropeptide Y is a peptide
    c. It stimulates appetite
    d. Stimulates pulsatile release of GnRH

11. **Which of the following is not true regarding intrapituitary autocrine paracrine system?**
    a. Activin and inhibin are peptide members of the transforming growth factor-b family

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b. Follistatin is secreted by granulosa cells
c. Inhibin and activin are secreted by granulosa cells
d. Activin stimulates follistatin production

12. Opiate production is regulated by gene transcription and the synthesis of precursor peptides. Which of the following is not the precursor peptide for opiates?
a. Proopiomelanocortin (POMC)
b. Proenkephalin A and B
c. Prodynorphin
d. All

13. How stress affects reproductive function?
a. CRH directly inhibiting GnRH secretion
b. Cortisol inhibits pituitary responsiveness to GnRH
c. None of the above
d. Both of the above

14. Which of the following is not correct for neuroendocrine hormones involved with reproduction?
a. High levels of progesterone are responsible for the FSH surge at midcycle
b. Lower GnRH pulse frequencies favor FSH secretion, and higher GnRH pulse frequencies favor LH secretion
c. High levels of estrogen induce the LH surge at midcycle
d. Pineal is the source of gonadal inhibiting substances

15. Catecholamines stimulating secretion of GnRH from hypothalamus:
a. Dopamine
b. Serotonin
c. Norepinephrine
d. Prostaglandins

16. Which of the following statement does not hold true for inhibin?
a. Composed of two dissimilar peptides linked by covalent bonds
b. Inhibin B peaks in follicular phase
c. Inhibin A peaks is not detectable before puberty
d. Inhibin has no effect on growth hormone, ACTH and prolactin production

17. Which of the following statement does not hold true for activin?
a. Composed of two subunits identical to beta subunits of inhibin A and B
b. Inhibin potentiates activin activity
c. Activin inhibits growth hormone, ACTH and prolactin responses
d. Derived from granulosa cells

18. A glycopeptide secreted by gonadotrophs, also called FSH—suppressing protein inhibiting FSH synthesis, secretion and FSH response to GnRH:
a. Follistatin
b. Inhibin A
c. Inhibin B
d. IGF-1

19. What is true regarding differential control of FSH and LH secretion?
a. LH secretion is primarily regulated by GnRH, without involvement of the inhibin-activin-follistatin system
b. Activin enhances and follistatin suppress GnRH activity
c. Inhibin may enhance LH activity
d. All

20. Which is incorrect regarding endogenous opioids and their effects on GnRH?
a. Endorphins promote GnRH release
b. B endorphins are 5-10 times more potent than morphine
c. Ovarian sex steroids increase endorphin secretion
d. Endorphin levels peak in luteal phase with nadir during menses

21. How does hyperprolactinemia affects female reproductive function?
a. Disrupts normal follicular development
b. Premature destruction of corpus luteum
c. Inhibiting aromatase enzyme
d. All

22. FSH is essential for follicular growth. Which of the following event is not related to FSH in menstrual cycle?
a. Selection and maturation of dominant follicle
b. Aromatization within granulosa cells
c. Induction of LH surge
d. Induction of FSH and LH receptors on granulosa cells

23. Luteinizing hormone should be present at concentrations within the LH window, which is over the threshold level and beneath the ceiling value. Which of the following effects is result of LH levels above ceiling value?
a. Follicular premature luteinization
b. Inadequate androgen and estrogen biosynthesis
c. Absent paracrine signaling between granulosa and theca
d. Optimum oocyte maturation

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24. Which are the hormones not secreted by anterior pituitary?
a. Prolactin
b. FSH
c. ACTH
d. GnRH

25. Following is associated with corpus luteum of menstruation but not with corpus luteum of pregnancy:
a. Corpus albicans
b. hCG
c. Estrogen
d. Prolactin

26. Persistent high levels of which of the following hormone leads to positive feedback loop in hypothalamo-pituitary-ovary axis?
a. Estradiol
b. Estrone
c. Testosterone
d. Progesterone

27. Which of the following hormones stimulate growth of primary follicles?
a. Activin
b. Estrogen
c. FSH
d. Progesterone

28. Which of the following hormone produced by corpus luteum is low in follicular phase and maximal in luteal phase?
a. Progesterone
b. Estradiol
c. LH
d. Inhibin

29. Peptide hormone produced by testes responsible for suppression of FSH:
a. Inhibin A
b. Inhibin B
c. Activin A
d. Activin B

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Answer with Explanations

1. a. Prolactin

Ref: Kamini A Rao 2nd/ed p19

- Hypothalamus has peptidergic neural cells that secrete releasing and inhibitory hormones.
- These cells resemble both neurons and endocrine gland cells; respond to signals in the bloodstream, as well as to neurotransmitters within the brain in a process known as **neurosecretion**.
- These neurotransmitters are secreted at the nerve terminal.
- Neuroendocrine agents originating in the hypothalamus have positive stimulatory effects on growth hormone, TSH, ACTH, as well as gonadotropins.
- An exception to the overall pattern of positive influence of hypothalamus on pituitary is the control of prolactin secretion.
- Stalk secretion and transplantation cause release of prolactin from the anterior pituitary, implying a negative, inhibitory hypothalamic control. Furthermore, cultures of anterior pituitary tissue release prolactin in the absence of hypothalamic tissue or extracts.

2. d. GnRH-II is main form found in the brain

Ref: Speroff 8th/ed p 160

- GnRH-I is the main form found in the brain, whereas GnRH-II is widely distributed in other organs.

Gonadotropin Releasing Hormone

- Human GnRH-II expression is highest outside the brain.
- An analysis of the evolution of GnRH indicates three major forms:
  1. Localized to the hypothalamus—GnRH-I
  2. Forms in midbrain nuclei and outside the brain—GnRH-II
  3. Forms in several fish species—GnRH-III
- A total of **24 forms** of GnRH have been identified in multiple species, but GnRH-I and GnRH-II are the primary GnRHs in mammals.

3. c. Hypothalamus

Ref: Yen & Jaffe's 8th/ed p 46

Prolactin gene expression occurs in:

- The lactotropes of the anterior pituitary gland
- Decidualized endometrium
- Myometrium

The decidual mRNA is indistinguishable from pituitary prolactin mRNA except for four silent nucleotide differences and the decidual prolactin gene is 150 nucleotides longer in the 5' untranslated region.

4. a. Prolactin is highest in early morning hours

Ref: Speroff 8th/ed p 162

Prolactin levels are highest during sleep.

Association of hyperprolactinemia with the elevation in TRH secretion that occurs with hypothyroidism is an important clinical manifestation.

5. d. All

Ref: "Clinical genetic testing for Kallmann syndrome". JCEM. 98 (5): 1860-2

The following inheritance pattern is documented:

- X-linked
- Autosomal-dominant
- Autosomal-recessive

The 5–7-fold increased frequency in males indicates that X-linked transmission is the most common.

6. c. GnRH is a nonapeptide

Ref: Textbook of assisted reproductive techniques, Vol 2, 5th/ed p 513

GnRH

- GnRH is a **decapeptide** that is synthesized as part of a much larger precursor peptide, the **GnRH-associated peptide**, that has a 56-amino acid sequence.
- The structure of GnRH is common to all mammals, including humans, and its action is similar in both males and females.
- GnRH is a single-chain peptide comprising 10 amino acids.
- In humans, the pulsatile release frequencies ranges from the shortest interpulse frequency of approximately 71 minutes in the late follicular phase to an interval of 216 minutes in the late luteal phase.
- Native GnRH has a short plasma half-life and is rapidly inactivated by enzymatic cleavage.

7. d. All

Ref: Speroff 8th/ed p 164

The **long feedback loop** refers to the feedback effects of circulating levels of target gland hormones, and this occurs both in the hypothalamus and the pituitary.

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The **short feedback loop** indicates a negative feedback of pituitary hormones on their own secretion, presumably via inhibitory effects on releasing hormones in the hypothalamus.

The **ultrashort feedback** refers to inhibition by the releasing hormone on its own synthesis.

8. d. All

Ref: Yen & Jaffe's 8th/ed p 9

- Pulsatile GnRH secretion is absolutely required for long-term stimulation of gonadotropin synthesis and secretion.
- More frequent exposure to GnRH pulses can reduce gonadotropin responses to GnRH; continuous GnRH receptor stimulation leads to **desensitization** of gonadotropin synthesis and secretion.
- The measurement of LH pulses is used as an indication of GnRH pulsatile secretion as the long half-life of FSH precludes its use for this purpose.

9. a. Dopamine directly suppress Gonadotropin secretion

Ref: Speroff 8th/ed p 168

- Dopamine is a neurohormone as it is directly secreted into the portal blood.
- It does not exert a direct effect on gonadotropin secretion by the anterior pituitary; this effect is mediated through GnRH release in the hypothalamus.
- Prolactin delivered to the intermediate lobe of the pituitary suppresses melanocyte-stimulating hormone release.

10. a. Facilitates gonadotropin secretion in absence of estrogen

Ref: Yen & Jaffe's 8th/ed p 16

- Neuropeptide Y is considered as major **neurobiologic brake**.

In absence of estrogen, it inhibits gonadotropin secretion, while otherwise in presence of estrogen, it potentiates gonadotropin response to GnRH.

11. b. Follistatin is secreted by granulosa cells

Ref: Speroff 8th/ed p 172

- Follistatin is a peptide secreted by a variety of pituitary cells, including the gonadotropes.
- Its main action: inhibition of FSH synthesis and secretion and the FSH response to GnRH, by binding to activin and in that fashion decreasing the activity of activin.
- Activin stimulates follistatin production, and inhibin prevents this response.

12. d. All

Ref: Kamini A Rao 2nd/ed p 23

Opiate production is regulated by gene transcription and the synthesis of precursor peptides and at a post-translational level where the precursors are processed into the various bioactive smaller peptides.

The endogenous opioids are three related families of naturally occurring substances produced in CNS that represent the natural ligands for opioid receptors.

- *Proopiomelanocortin (POMC)*: The source of endorphins.
- *Proenkephalin A and B*: The source of several enkephalins.
- *Prodynorphin*: Yields dynorphins.

13. d. Both of the above

Ref: Speroff 8th/ed p 177

Corticotropin-releasing hormone (CRH) affects GnRH secretion by:

1. Directly inhibiting hypothalamic GnRH secretion
2. Augmenting endogenous opioid secretion.

Besides the CRH-induced inhibition of GnRH release, the increase in cortisol generated by CRH stimulation of pituitary ACTH secretion also contributes to the suppression of reproduction; cortisol directly inhibits pituitary responsiveness to GnRH.

14. a. High level of progesterone are responsible for the FSH surge at midcycle

Ref: Yen & Jaffe's 8th/ed p 18

- Late follicular rise in progesterone begins approximately 12 hours before the LH surge may be important for the full expression of the midcycle gonadotropin surge.
- Progesterone receptor antagonist mifepristone can delay the surge.
- Low levels of progesterone acting at the level of the pituitary gland enhance the LH response to GnRH and are responsible for the FSH surge at midcycle.
- Pineal gland is the source of gonadal inhibiting substances.

15. c. Norepinephrine

Ref: Kamini A Rao 2nd/ed

Catecholamines like norepinephrine, dopamine, serotonin and transmitters like opiates and prostaglandins appear to influence secretion of GnRH from hypothalamus.

Norepinephrine seems to stimulate GnRH release, whereas dopamine, serotonin, endogenous opioids, and CRH appear capable of inhibiting or suppressing GnRH.

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16. a. Composed of two dissimilar peptides linked by covalent bond

Ref: Kamini A Rao 2nd/ed p 23

- Inhibin is composed of two dissimilar peptides linked by **disulfide bonds**.

There are two forms of inhibin which are composed of one of the two inhibin beta subunits and a closely related alpha subunit to form inhibin A or inhibin B.

17. b. Inhibin potentiates activin activity

Ref: Kamini A Rao 2nd/ed p 23

Activin

- Derived from granulosa cells and pituitary gonadotrophs.
- Composed of two subunits identical to the b subunits of inhibin A and B.
- Augment FSH secretion but inhibit prolactin, ACTH, and growth hormone responses.
- Effects of activin are blocked by inhibin and follistatin.

18. a. Follistatin

Ref: Kamini A Rao 2nd/ed p 23

Follistatin

- Glycopeptide.
- Secreted by gonadotrophs.
- Also called FSH-suppressing protein involved in inhibiting FSH synthesis, secretion and FSH response to GnRH, by binding to and decreasing activity of activin.
- Activin stimulates follistatin production.

19. d. All

Ref: Speroff 8th/ed p 172

LH secretion is primarily regulated by GnRH, without involvement of the inhibin-activin-follistatin system, while FSH is controlled by other intrapituitary autocrine and paracrine system too apart from GnRH.

20. a. Endorphins promote GnRH release

Ref: Kamini A Rao 2nd/ed p 23

- Endorphins inhibit GnRH release within hypothalamus, resulting in inhibition of gonadotropin secretion but have no effect on pituitary response to GnRH.
- B endorphins are 5–10 times more potent than morphine
- Ovarian sex steroids increase central endorphin secretion, further depressing gonadotropin levels.
- Endorphin levels vary significantly throughout the menstrual cycle, with peak levels in the luteal phase and a nadir during menses.
- The dysphoria experienced by some women in the premenstrual phase of cycle may be related to a withdrawal of endogenous opiates.

21. d. All

Ref: Kamini A Rao 2nd/ed p 24

Effects of hyperprolactinemia on female reproductive function:

- Disrupts normal follicular development
- Atresia of dominant follicle
- Inhibits aromatase enzyme
- Inhibits progesterone synthesis by corpus luteum
- Premature destruction of corpus luteum
- Induces uterine adenomyosis

22. c. Induction of LH surge

Ref: Kamini A Rao 2nd/ed p 25

- LH surge is as a result of persistently raised estrogen levels.

Functions of FSH in menstrual cycle:

- Selection and maturation of dominant follicle
- Proliferation of granulosa cells
- Aromatization within granulosa cells
- Induction of FSH and LH receptors on granulosa cells
- Production of autocrine-paracrine factors- activin and inhibin
- FSH surge helps in ovulation
- Prevents germ cells from atresia in luteal- follicular transition

23. a. Follicular premature luteinization

Ref: Kamini A Rao 2nd/ed p 25, Textbook of assisted reproductive techniques, Vol 2, 5th/ed p 526

The amount of LH necessary to induce a response in the follicle varies from a minimum **"LH threshold"** to a maximum **"LH ceiling".**

This amount has not been determined, but it has been suggested that **less than 1%** of follicular LH receptors need to be occupied in order to produce a steroidogenic response.

The LH dependent phase of menstrual cycle proceeds normally only if LH is present at concentrations within the LH window, which is over the threshold level and beneath the ceiling value.

The impact of different concentrations of LH on menstrual cycle is shown in the following table:

Effects below LH threshold	Effects within LH window	Effects above LH ceiling
Absent paracrine signalling between granulosa and theca	Normal follicular growth and development	Suppression of granulosa proliferation
Inadequate androgen and estrogen synthesis	Adequate granulosa proliferation and functional maturation	Follicular premature luteinisation

Contd…

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Contd…

Effects below LH threshold	Effects within LH window	Effects above LH ceiling
Compromised oocyte maturation	Normal estrogen and androgen biosynthesis	Compromised oocyte development
	Optimum oocyte maturation	

24. d. GnRH

Ref: Textbook of assisted reproductive techniques, Vol 2, 5th/ed p 513

GnRH is secreted by hypothalamus, not anterior pituitary.

25. a. Corpus albicans

Ref: Kamini A Rao 2nd/ed p 35

Corpus luteum of nonpregnant cycle ultimately turns into corpus albicans.

26. a. Estradiol

Persistent high levels of estradiol are responsible for positive feedback loop in H-P-O axis leading to LH surge.

Low levels of estradiol inhibit FSH and LH.

27. c. FSH

Ref: Speroff 8th/ed p 202

FSH stimulates growth of primary follicle.

28. a. Progesterone

Ref: Speroff 8th/ed p 46

Progesterone is synthesized by corpus luteum.

Including the small contribution from the adrenal, the blood production rate of progesterone in preovulatory phase is less than 1 mg/day.

During luteal phase, production increases to 20–30 mg/day.

29. b. Inhibin B

Ref: Cambridge. Infertility in the male. 4th/ed p 23

- There is a reciprocal relationship between plasma FSH and inhibin B levels.

Inhibin is a glycoprotein hormone secreted by Sertoli cells composed of alpha subunit disulphide-linked to one of two beta subunits, to form inhibin A or B. Undetectable levels are seen in agonadal men and in men with testicular disorders, suggesting testicular origin.

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