

## IN SUMMARY

### NORMAL MENSTRUAL CYCLE

#### **MENSTRUAL CYCLE OVERVIEW**

- Purpose: production of a fertilizable egg and development of appropriate uterus for implantation
- Controlled by hypothalamic pulse generator in arcuate nucleus
- Pulse generator signal = Gonadotropin releasing hormone (GnRH)

#### GnRH

- Release is pulsatile in nature, once every 75 minutes
- GnRH causes pituitary to release follicle stimulating hormone (FSH) and luteinizing hormone (LH)
- GnRH and LH one-to-one: each pulse of GnRH causes simultaneous pulse of LH
- FSH more complex, regulated by both GnRH and ovarian peptide inhibin

#### FOLLICULAR DEVELOPMENT

- Resting stage = primordial follicle
  - Consists of oocyte in meiosis I with single layer of granulosa cells
  - Maturation initially FSH and LH independent
- Follicular maturation characterized by increase in number of granulosa cells
- Almost all follicles undergo atresia due to lack of rescue by gonadotropins
  - Depends on number of FSH receptors
  - Contains no LH receptors until final development stage
- During menstrual cycle, several follicles will develop to be sensitive to FSH = “recruited,” but only one will gain dominance
  - Due to positive feedback within granulosa cells
  - FSH induces its own receptor
  - Estrogen dependent process (FSH → estradiol → FSH receptor)
- Estradiol is inhibitory to FSH release from pituitary
  - Deprives less mature follicles of FSH → only one dominant follicle is produced
- Note: in vitro fertilization administers excess FSH to produce multiple follicles for pregnancy enhancement

#### FOLLICULAR PHASE

- First half of menstrual cycle
- Estradiol levels increase 10-fold due to activity of dominant follicle
- Estradiol → increased LH synthesis, but inhibition of release → “reserve pool” is saturated → massive release of LH over 36-hour period = LH surge → trigger for ovulation (end of follicular phase)
- Estrogen → hypertrophy of endometrium (proliferative phase of endometrial cycle)
- Prior to LH surge, pulsatile release of LH acts on second ovarian cell type, the theca cell
- Theca cell synthesizes androstenedione → substrate for granulosa cell estradiol production via aromatization from aromatase enzyme
  - Aromatase activity induced by FSH action on granulosa cell
- LH receptor present at all time on theca cells; high levels of FSH on *granulosa* cells (a few days prior to LH surge) induces LH receptor
- LH surge typically occurs 14 days into menstrual cycle (counted from first day of bleeding), but can vary 9-17 days
- Second half of cycle, luteal phase, is more precise = 14 +/-2 days

#### OVULATION

- LH surge → proteases digest capsule of ovary → extrusion of oocyte and granulosa cells (cumulus oophorus)
- Oocyte proceeds to meiosis II, arrested until fertilization
- LH surge → partial 17 hydroxylase block by remaining theca and granulosa cells → progesterone production → yellow color of remaining dominant follicle → corpus luteum (yellow body)

LUTEAL PHASE

- Second half of menstrual cycle
- Estrogen *and* progesterone dominated
- Premenstrual breast tenderness, bloating, affective lability are progesterone induced
- Progesterone → convert endometrium into secretory pattern (secretory phase of endometrial cycle)
  - Day 21 abundant secretion, optimal for implantation of fertilized egg
- Without pregnancy, estrogen and progesterone production from corpus luteum declines → spasm of endometrial vasculature → breakdown of endometrium → menses
- In pregnancy, embryo produces human chorionic gonadotropin (hCG)
  - Identical first 121 amino acids to LH
  - Maintains corpus luteum → no menses

FUNDAMENTAL QUESTIONS
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1. What is the arcuate nucleus and what does it produce?
2. Describe the wave form of GnRH? LH?
3. What does inhibin do and where does it come from?
4. What is a dominant follicle?
5. How many follicles attempt maturation each month?
6. What is produced by the corpus luteum?
7. What is a basal body temperature and how does a patient go about measuring this?
8. Describe what happens in theca cells ? Granulosa cells?
9. When in the cycle does the LH surge occur?
10. Describe the process of mitosis, meiosis one, meiosis two.
11. At what point is there a reduction in the number of chromosomes?
12. What happens to the endometrium during the follicular phase? The secretory phase?
13. Why does the endometrium shed? What happens to the vessels underlying it?

