Chapter 28: The Reproductive Systems
Male reproductive system

- **Gonads – testes**
  - Produces sperm and secretes hormones

- **System of ducts – transport and stores sperm, assists in their maturation, and conveys them to the exterior**
  - Epididymis, ductus deferens, ejaculatory ducts, and urethra

- **Accessory sex glands – adds secretions to semen**
  - Seminal vesicles, prostate, and bulbourethral glands

- **Supporting structures**
  - Scrotum supports testes and penis delivers sperm into female reproductive tract
Male reproductive organs
Scrotum

- Supporting structure for testes
- Raphe – external median ridge
- Scrotal septum – internally divides scrotum into two sacs, each with a single testis
  - Made up of subcutaneous layer and dartos muscle
- Associated with each testis is the cremaster muscle
- Normal sperm production requires a temperature 2-3°C below core body temperature
  - Cremaster and dartos muscle contracts or relaxes
The Scrotum

Anterior view of scrotum and testes and transverse section of penis

Internal oblique muscle
Aponeurosis of external oblique muscle (cut)
Fundiform ligament of penis
Suspensory ligament of penis
Transverse section of penis:
Corpora cavernosa penis
Spongy (penile) urethra
Corpus spongiosum penis
Scrotal septum
Cremaster muscle
External spermatic fascia
Dartos muscle
Skin of scrotum
Spermatic cord
Superficial (cutaneous) inguinal ring
Cremaster muscle
Inguinal canal
Ductus (vas) deferens
Autonomic nerve
Testicular artery
Lymphatic vessel
Pampiniform plexus of testicular veins
Epididymis
Tunica albuginea of testis
Tunica vaginalis (peritoneum)
Internal spermatic fascia
Raphe

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Testes or testicles

- Paired oval glands in the scrotum
- Develops near kidney and descends through inguinal canals near 7\textsuperscript{th} month of fetal development
- Tunica vaginalis partially covers testes
- Tunica albuginea – internal to tunica vaginalis
  - Extends inward forming septa that divide testis into lobules
- Each of 200-300 lobules contains 1-3 seminiferous tubules
  - Sperm produced here through spermatogenesis
Internal and external anatomy of a testis

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Seminiferous tubule cells

- **Spermatogenic cells – sperm-forming cells**
  - Spermatagonia (stem cell) develop from primordial germ cells that arise in yolk sac and enter testes in 5th week of development
  - Primary spermatocytes → secondary spermatocytes → spermatids → sperm cells → lumen

- **Sertoli cells or sustenacular cells – support cells**
  - Tight junction form blood-testis barrier – prevents immune response against sperm cell surface antigens
  - Nourish spermatocytes, spermatids and sperm, phagocytize excess spermatid cytoplasm, control movements of spermatogenic cells, release sperm into lumen, produce fluid for sperm transport, secrete inhibin, regulate effects of testosterone and follicle-stimulating hormone (FSH)

- **Leydig (interstitial) cells** found in spaces between seminiferous tubules
- Secrete testosterone
Seminiferous tubules and stages of sperm production

(a) Transverse section of several seminiferous tubules

(b) Transverse section of a portion of a seminiferous tubule

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Spermatogenesis

- Takes 65-75 days
- Begins with spermatogonia – diploid (2n)
  - Stem cells undergo mitosis to replace themselves and some continue development
- Primary spermatocytes – diploid (2n)
  - Each duplicates its DNA and meiosis begins
- Meiosis I – homologous pairs line up, crossing over occurs
  - Secondary spermatocytes (haploid or n)
    - 2 cells at end of Meiosis I
    - Each chromosome made up of 2 chromatids attached at centromere
  - Meiosis II – 2 chromatids separate
    - Spermatids – 4 haploid cells at end of meiosis II
- Cells remain attached to each other by cytoplasmic bridges
- Spermiogenesis – development of spermatids into sperm
  - Spherical spermatids transform into elongated sperm
  - Acrosome and flagella form, mitochondria multiply
  - Sertoli cells dispose of excess cytoplasm
  - Spermiation – release from connections to Sertoli cells
  - Not yet able to swim
Events in spermatogenesis

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Sperm

- Each day about 300 million sperm complete spermatogenesis
- Head
  - Nucleus with 23 chromosomes (haploid or n)
  - Acrosome – vesicle filled with oocyte penetrating enzymes
- Tail
  - Neck – contains centrioles forming microtubules that comprise remainder of tail
  - Middle piece – contains mitochondria
  - Principal piece – longest portion of tail
  - End piece – terminal, tapering portion of tail
- Once ejaculated, sperm do not survive more than 48 hours in female reproductive tract
Parts of a sperm cell

- Acrosome
- Nucleus
- Neck
- Mitochondria
- Middle piece
- Principal piece
- End piece

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Hormonal control of testes

- At puberty, secretion of gonadotropin-releasing hormone (GnRH) increases.
- Stimulates anterior pituitary to increase secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH).
- LH stimulates Leydig cells to secrete testosterone:
  - Synthesized from cholesterol mainly in testes.
  - Suppresses secretion of LH and GnRH via negative feedback.
  - Enzyme 5 alpha-reductase converts testosterone into dihydrotestosterone (DHT) in external genitals and prostate.
- FSH acts indirectly on spermatogenesis:
  - FSH and testosterone act on Sertoli cells to stimulate secretion of androgen-binding protein (ABP).
  - ABP binds testosterone keeping concentration high.
  - Testosterone stimulates spermatogenesis.
  - Sertoli cells release inhibin which inhibits FSH.
Hormonal control of spermatogenesis

- Testosterone decreases release of GnRH and LH.
- Inhibin decreases release of FSH.
- LH stimulates testosterone secretion.
- Together with testosterone, FSH stimulates spermatogenesis.

Key:
- LH
- LH receptor
- FSH
- FSH receptor
- Testosterone
- Androgen receptor

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Androgens (testosterone and DHT)

- Prenatal development
  - Testosterone stimulates male pattern of development or reproductive system ducts and descent of testes
  - DHT stimulates development of external genitalia
- Development of male sexual characteristics
  - At puberty, they bring about development of male sex organs and development of male secondary sexual characteristics
- Development of sexual function
  - Androgens contribute to male sexual behavior, spermatogenesis and sex drive (libido)
- Stimulation of anabolism
  - Stimulate protein synthesis – heavier muscle and bone mass in men
Negative feedback regulates testosterone production

Some stimulus disrupts homeostasis by increasing the blood level of testosterone.

Cells in the hypothalamus that secrete GnRH:
- Input: Decreased GnRH in portal blood
- Output: Decreased LH in systemic blood

Anterior pituitary gonadotrophs:
- Control center

Leydig cells in the testes:
- Decrease in blood level of testosterone

Return to homeostasis when response brings blood level of testosterone back to normal.

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Reproductive system ducts in males

- **Ducts of testis**
  - Pressure generated by fluid produced by Sertoli cells push sperm along seminiferous tubules into straight tubules, rete testis, efferent ducts in epididymis and then ductus epididymis

- **Epididymis**
  - Consists of tightly coiled ductus epididymis
  - Stereocilia are microvilli that reabsorb degenerated sperm
  - Site of sperm maturation – acquire motility and ability to fertilize
  - Can store sperm for several months
  - Continues as ductus (vas) deferens

- **Ductus (vas) deferens**
  - Conveys sperm during sexual arousal through peristaltic contractions
  - Can also store sperm several months
Male reproductive system ducts

- **Spermatic cord**
  - Ascends out of scrotum
  - Consists of ductus deferens as it ascends through scrotum, testicular artery, veins that drain testes and carry testosterone, autonomic nerves, lymphatic vessels, and cremaster muscle
  - Spermatic cord and ilioinguinal nerve pass through inguinal canal

- **Ejaculatory ducts**
  - Formed by union of duct from seminal vesicle and ampulla of ductus deferens
  - Terminate in prostatic urethra
  - Eject sperm and seminal vesicle secretions just before release of semen into urethra

- **Urethra**
  - Shared terminal duct of reproductive and urinary systems
  - Subdivided into prostatic urethra, membranous urethra, and spongy (penile) urethra
  - Ends at external urethral orifice
Accessory reproductive organs in males
Accessory sex glands – secrete most of liquid portion of semen

- **Seminal vesicles** - About 60% of semen volume
  - Secrete alkaline, viscous fluid containing fructose, prostaglandins, and clotting proteins (different from blood)

- **Prostate** - About 25% of semen volume
  - Secretes milky, slightly acidic fluid containing citric acid, several proteolytic enzymes, acid phosphatase, seminalplasmin (antibiotic)

- **Bulbourethral glands**
  - Secrete alkaline fluid that protects passing sperm by neutralizing acids from urine in urethra
  - Mucus lubricates end of penis and lining of urethra
Semen and Penis

- **Semen**
  - Mixture of sperm and seminal fluid
  - Typical volume 2.5-5 mL with 50-150 million sperm/mL
  - Slightly alkaline pH of 7.2-7.7 due to seminal vesicle secretions
  - Provides transport medium, nutrients, and protection
  - Coagulates after ejaculation due to clotting proteins

- **Penis**
  - Contains urethra
  - Passageway for ejaculation of semen and excretion of urine
  - Body of penis – 3 cylindrical masses of tissue with erectile tissue
  - Glans penis – terminal opening is external urethral orifice
    - Prepuce or foreskin covers glans in uncircumcised men
  - Root of penis is attached portion
  - Erection – parasympathetic fibers release and cause local production of nitric oxide (NO) causing smooth muscle in arterioles to relax and dilate allowing large amounts of blood to enter penis
Internal structure of the penis
Female reproductive system

- Gonads – ovaries
- Uterine (fallopian) tubes or oviducts
- Uterus
- Vagina
- External organs – vulva or pudendum
- Mammary glands
Female organs of reproduction and surrounding structures
Ovaries

- Paired glands homologous to the testes
- Produce
  - Gametes – secondary oocytes that develop into mature ova (eggs) after fertilization
  - Hormones including progesterone, estrogens, inhibin and relaxin
- Series of ligaments hold ovaries in place
  - Broad ligament – part of parietal peritoneum
  - Ovarian ligament – anchors ovaries to uterus
  - Suspensory ligament – attaches ovaries to pelvic wall
Relative positions of the ovaries, the uterus, and supporting ligaments

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Histology of ovary

- Germinal epithelium – covers surface of ovary
  - Does not give rise to ova – cells that arise form yolk sac and migrate to ovaries do
- Tunica albuginea
- Ovarian cortex
  - Ovarian follicles and stromal cells
- Ovarian medulla
  - Contains blood vessels, lymphatic vessels, and nerves
- Ovarian follicles – in cortex and consist of oocytes in various stages of development
  - Surrounding cells nourish developing oocyte and secrete estrogens as follicle grows
- Mature (graafian) follicle – large, fluid-filled follicle ready to expel secondary oocyte during ovulation
- Corpus luteum – remnants of mature follicle after ovulation
  - Produces progesterone, estrogens, relaxin and inhibin until it degenerates into corpus albicans
Histology of the ovary

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(c) Ovulation of a secondary oocyte

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Oogenesis and follicular development

- Formation of gametes in ovary
- Oogenesis begins before females are born
- Essentially same steps of meiosis as spermatogenesis
- During early fetal development, primordial (primitive) germ cells migrate from yolk sac to ovaries
- Germ cells then differentiate into oogonia – diploid (2n) stem cells
- Before birth, most germ cells degenerate – atresia
- A few develop into primary oocytes that enter meiosis I during fetal development
  - Each covered by single layer of flat follicular cells – primordial follicle
  - About 200,000 to 2,000,000 at birth, 40,00 remain at puberty, and around 400 will mature during a lifetime
Follicular development

- Each month from puberty to menopause, FSH and LH stimulate the development of several primordial follicles
  - Usually, only one reaches ovulation
- Primordial follicles develop into primary follicles
  - Primary oocyte surrounded by granulosa cells
  - Forms zona pellucida between granulosa cells and primary oocyte
  - Stromal cells begin to form theca folliculi
- Primary follicles develop into secondary follicles
  - Theca differentiates into theca interna secreting estrogens and theca externa
  - Granulosa cells secrete follicular fluid in antrum
  - Innermost layer of granulosa cells attaches to zona pellucida forming corona radiata
Ovarian follicles

(a) Primordial follicle

(b) Late primary follicle

(c) Secondary follicle

(d) Mature (granulosa) follicle

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Follicular development

- Secondary follicle becomes mature (graaffian) follicle
  - Just before ovulation, diploid primary oocyte completes meiosis I
  - Produces 2 unequal sized haploid (n) cells – first polar body is discarded and secondary oocyte
- At ovulation, secondary oocyte expelled with first polar body and corona radiata
- If fertilization does not occur, cells degenerate
- If a sperm penetrates secondary oocyte, meiosis II resumes
- Secondary oocyte splits into 2 cells of unequal size – second polar body (also discarded) and ovum or mature egg
- Nuclei of sperm cell and ovum unite to form diploid zygote
Oogenesis

During fetal development meiosis I begins.

After puberty, primary oocytes complete meiosis I, which produces a secondary oocyte and a first polar body that may or may not divide again.

The secondary oocyte begins meiosis II.

A secondary oocyte (and first polar body) is ovulated.

After fertilization, meiosis II resumes. The oocyte splits into an ovum and a second polar body.

The nuclei of the sperm cell and the ovum unite, forming a diploid (2n) zygote.
Summary of oogenesis and follicular development

**Table 28.1**
Summary of Oogenesis and Follicular Development

<table>
<thead>
<tr>
<th>Age</th>
<th>Oogenesis</th>
<th>Follicular development</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fetal period</strong></td>
<td>Oogonium</td>
<td>Primordial follicle</td>
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<tr>
<td></td>
<td>Mitosis</td>
<td></td>
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<td></td>
<td>Primary oocyte</td>
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<tr>
<td></td>
<td>Meiosis in progress</td>
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<tr>
<td><strong>Childhood (no development of follicles)</strong></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Primary oocyte (still in prophase I)</td>
<td>Primary follicle</td>
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<tr>
<td><strong>Puberty to menopause each month</strong></td>
<td></td>
<td>Secondary follicle</td>
</tr>
<tr>
<td></td>
<td>Primary oocyte</td>
<td></td>
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<tr>
<td></td>
<td>Meiosis I completed by one primary oocyte each month</td>
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<tr>
<td></td>
<td>First polar body</td>
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<tr>
<td></td>
<td>Meiosis II of first polar body may or may not occur</td>
<td></td>
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<tr>
<td></td>
<td>Second polar body</td>
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<tr>
<td></td>
<td>All polar bodies degenerate</td>
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<td>Ovulation</td>
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<td></td>
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<td>Mature (graafian) follicle</td>
</tr>
</tbody>
</table>
Uterine (fallopian) tubes or oviducts

- Provide a route for sperm to reach an ovum
- Transport secondary oocytes and fertilized ova from ovaries to uterus
- Infundibulum ends in finger-like fimbriae
  - Produce currents to sweep secondary oocyte in
- Ampulla – widest longest portion
- Isthmus – joins uterus
- 3 layers
  - Mucosa – ciliary conveyor belt, peg cells provide nutrition to ovum
  - Muscularis – peristaltic contractions
  - Serosa – outer layer
Relationship of the uterine tubes to the ovaries, uterus, and associated structures
Histology of the uterine (fallopian) tube

(a) Details of epithelium in sectional view

(b) Details of epithelium in surface view

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Uterus

- **Anatomy**
  - Fundus, body, isthmus, and cervix (opens into vagina)
  - Normal position is anteflexion – anterior and superior over bladder
  - Ligaments maintain position – broad, uterosacral, cardinal and round

- **Histology – 3 layers**
  1. Perimetrium – outer layer
     - Part of visceral peritoneum
  2. Myometrium
     - 3 layers of smooth muscle
     - Contractions in response to oxytocin from posterior pituitary
Uterus

3. Endometrium – inner layer
   - Highly vascularized
   - Stratum functionalis – lines cavity, sloughs off during menstruation
   - Stratum basalis – permanent, gives rise to new stratum functionalis after each menstruation

   - Blood supply
     - Uterine arteries, arcuate arteries, radial arteries
     - Just before branches enter endometrium divide into
       - Straight arterioles supplying stratum basalis
       - Spiral arteries supplying stratum functionalis change markedly during menstrual cycle

   - Cervical mucus - produced by secretory cells of cervix mucosa
     - Water, glycoproteins, lipids, enzymes, and inorganic salts
     - More hospitable to sperm near ovulation – thinner, more alkaline
     - Supplements energy needs of sperm, protect sperm from phagocytes and hostile environment of tract
Histology of the uterus

(a) Transverse section through the uterus
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(b) Details of endometrium
Vagina

- Fibromuscular canal extending from exterior of body to uterine cervix
- Mucosa continuous with uterine mucosa
  - Decomposition of glycogen makes acidic environment hostile to microbes and sperm
  - Alkaline components of semen raise pH
- Muscularis – 2 layers of smooth muscle
- Adventitia – anchors vagina to adjacent organs
- Hymen – forms border around and partially closes vaginal orifice
Vulva or pudendum – external female genitalia

- Mons pubis – cushions pubic symphisis
- Labia majora – homologous to scrotum
- Labia minora – homologous to spongy (penile) urethra
- Clitoris – 2 small erectile bones and numerous nerves and blood vessels
  - Homologous to glans penis
- Vestibule – region between labia minora
  - External urethral orifice, openings of several ducted glands, and vaginal orifice
- Bulb of the vestibule – 2 elongates masses of erectile tissue on either side of vaginal orifice
Components of the vulva (pudendum)

(a) Inferior view

Mons pubis
Labia majora (spread)
Labia minora (spread exposing vestibule)
Hymen
Prepuce of clitoris
Clitoris
External urethral orifice
Vaginal orifice (dilated)
Anus

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Perineum

- Diamond-shaped area medial to thighs and buttocks of males and females
- Contains external genitalia and anus
Breast / Mammary glands

- Nipple has openings of lactiferous ducts
- Areola – pigmented area
- Mammary gland – modified sudoriferous gland that produces milk
  - 15-20 lobes divided into lobules composed of alveoli (milk-secreting glands)
The Female Reproductive Cycle

- Encompasses ovarian and uterine cycle, hormonal changes that regulate them, and related changes in breast and cervix
- Ovarian cycle – series of events in ovaries that occur during and after maturation of oocyte
- Uterine (menstrual) cycle – concurrent series of changes in uterine endometrium preparing it for arrival of fertilized ovum
Hormonal regulation

- **Gonadotropin-releasing hormone (GnRH)**
  - Secreted by hypothalamus controls ovarian and uterine cycle
  - Stimulates release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from anterior pituitary

- **FSH**
  - Initiate follicular growth
  - Stimulate ovarian follicles to secrete estrogens

- **LH**
  - Stimulates further development of ovarian follicles
  - Stimulate ovarian follicles to secrete estrogens
  - Stimulates thecal cells of developing follicle to produce androgens to be converted into estrogens
  - Triggers ovulation
  - Promotes formation of corpus luteum – produces estrogens, progesterone, relaxin and inhibin
Hormonal regulation

- Estrogens secreted by ovarian follicles
  - Promote development and maintenance of female reproductive structures and secondary sex characteristics
  - Increases protein anabolism including building strong bones
  - Lowers blood cholesterol
  - Inhibit release of GnRH, LH and FSH

- Progesterone
  - Secreted mainly by corpus luteum
  - Works with estrogens to prepare and maintain endometrium for implantation and mammary glands for milk production
  - Inhibits secretion of GnRH and LH
Hormonal regulation

- **Relaxin**
  - Produced by corpus luteum
  - Relaxes uterus by inhibiting contraction of myometrium
  - At end of pregnancy, increases flexibility of pubic symphysis and dilates uterine cervix

- **Inhibin**
  - Secreted by granulosa cells of growing follicles and by corpus luteum
  - Inhibits secretion of FSH and LH
Secretion and physiological effects of hormones in the female reproductive cycle
4 Phases

- Typical duration 24-35 days
- Assume a duration of 28 days
  1. Menstrual phase
  2. Preovulatory phase
  3. Ovulation
  4. Postovulatory phase
The female reproductive cycle

(a) Hormonal regulation of changes in the ovary and uterus

(b) Changes in concentration of anterior pituitary and ovarian hormones

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Menstrual phase or menstruation

- Roughly first 5 days of cycle
- First day of menstruation is day 1 of new cycle
- Events in ovaries
  - Under FSH influence, several primordial follicles develop into primary follicles and then into secondary follicles
    - Takes several months
    - Follicle that begins to develop in one cycle may not mature for several cycles later
- Events in uterus
  - Menstrual discharge occurs because declining levels of estrogens and progesterone stimulate release of prostaglandins causing uterine spiral arterioles to constrict
  - Cells deprived of oxygen begin to die
  - Only stratum basilis remains
Preovulatory phase

- More variable in length
- Lasts from days 6-13 in a 28 day cycle
- Events in ovaries
  - Some of secondary follicles begin to secrete estrogens and inhibin
  - Dominant follicle – one follicle outgrown all others
    - Estrogens and inhibin of dominant follicle decrease FSH causing other follicles to stop growing
    - Fraternal (nonidentical) twins result when 2 or 3 secondary follicles become codominant and are ovulated and fertilized at the same time
Preovulatory phase

- Normally, one dominant follicle becomes the mature (graffian) follicle
- In ovarian cycle, menstrual and preovulatory phases are termed follicular phase because follicles are growing

**Events in uterus**
- Estrogens stimulate repair of endometrium
- Cells of stratum basalis undergo mitosis to form new stratum functionalis
- Thickness of endometrium doubles
- In uterine cycle, preovulatory phase is the proliferative phase because endometrium is proliferating
Ovulation

- Rupture of mature (graffian) follicle and release of secondary oocyte
- Day 14 of 28 day cycle
- High levels of estrogens exert a positive feedback effect on cells secreting LH and GnRH
High levels of estrogens from almost mature follicle stimulate release of more GnRH and LH.

1. High levels of estrogens from almost mature follicle stimulate release of more GnRH and LH.
2. GnRH promotes release of FSH and more LH.
3. LH surge brings about ovulation.

Almost mature (graafian) follicle
Corpus hemorrhagicum (ruptured follicle)
Postovulatory phase

- Duration most constant of phases
- Lasts for 14 days in 28 day cycle (day 15-28)
- Events in one ovary
  - After ovulation, mature follicle collapses to form corpus luteum under the influence of LH
  - Secretes progesterone, estrogen, relaxin and inhibin
  - In the ovarian cycle, this is the luteal phase
Corpus luteum

- If oocyte not fertilized, corpus luteum lasts 2 weeks
  - Degenerates in corpus albicans
  - As levels of progesterone, estrogens and inhibin decrease, release of GnRH, FSH, and LH rise due to loss of negative feedback
  - Follicular growth resume as new ovarian cycle begins
- If oocyte is fertilized, corpus luteum lasts more than 2 weeks
  - Human chorionic gonadotropin (hCG) produced by chorion of embryo about 8 days after fertilization stimulates corpus luteum
Events in uterus

- Progesterone and estrogens produced by corpus luteum promote growth of endometrium
- Because of secretory activity of endometrial glands, this is the secretory phase of uterine cycle
- Changes peak about 1 week after ovulation when a fertilized ovum might arrive in uterus
- If fertilization does not occur, levels of progesterone and estrogens decline due to degeneration of corpus luteum
- Withdrawal of estrogens and progesterone causes menstruation
Hormonal interactions in the ovarian and uterine cycles
End of Chapter 28

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