**Objectives:**
1. Review male & female reproductive anatomy
2. Gametogenesis & steroidogenesis
3. Reproductive problems

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**Review of Male Reproductive Anatomy**

- Seminal vesicle
- Ejaculatory duct
- Prostate
- Bulbourethral gland
- Vas deferens
- Epididymis
- Testis
- Scrotum
- Corpus cavernosa penis
- Glans penis
- Prepuce (foreskin)
- Urethra
- Urinary bladder
- Symphysis pubis
- Ampulla of ductus deferens
- Anus
Male Reproductive anatomy and physiology.

Testes = paired gonads containing seminiferous tubules

Seminiferous tubules = tubules within testes where sperm and testosterone are produced.

3 cell types in seminiferous tubules:

1. Sertoli cells – assist in sperm production by responding to pituitary FSH.
2. Leydig cells – produce testosterone in response to pituitary LH.
3. Spermatogonia = primordial cells that undergo meiosis to produce mature sperm cells (spermatogonia).
**Epididymis** = structures on top of testes where sperm mature before entering vas deferens.

**Scrotum** = skin sacs holding testes outside of abdominal cavity. Keeps sperm ~3 °F cooler than body temp.

**Cremaster muscle** = Muscle that can lift or lower the testes within scrotum to regulate temperature

**Spermatic cord** = Connective tissue that wraps around cremaster, testes, & testicular nerve and blood vessels

**Inguinal ring** = Opening in inguinal ligament through which testes descend (around 7 months gestation).

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3 Sperm Transport Tubes:

1. **Vas deferens** = first and longest sperm transport tube. Meets with epididymis.  
2. **Ejaculatory duct** = sperm transport tube, which goes through prostate.  
3. **Urethra** = common passageway for either urine or semen.

**What is a vasectomy?**

Surgical cutting and clamping of the vas deferens as a permanent form of birth control.
3 Male Secretory Glands:

1. Seminal vesicles = large, paired glands that meet with vas deferens and contribute secretions to seminal fluid. 
   produce:
   - alkaline mucus (counteract vaginal acidity)
   - prostaglandin (cause uterine contractions)
   - fructose (energy source)

2. Prostate = gland under bladder which secretes mucus.

3. Bulbourethral gland =
   Gland that secretes lubricating Fluid, to lubricate head of penis, during sexual arousal.

The Prostate Gland

> Benign prostate hyperplasia (BPH)
   - Prostate grows with age.
   - non-cancerous growth of prostate.
   - Can block urine or semen transport.

Prostate cancer
   - Malignant
   - Detect with PSA = prostate-specific antigen. High levels in blood indicate possible prostate cancer.
   - Increased risk with mutation in BRCA gene (see later in powerpoint)
Corpus spongiosum = lower chamber surrounding urethra.
How an erection works:
See Clinical App

1. Arousal Causes nitric oxide (NO) release in arteries of corpus cavernosa.

2. NO causes production of a chemical messenger called cGMP).

3. cGMP causes arteries to relax & they open wide (vasodilate) allowing blood into spongy chambers.

4. Fluid pressure of blood causes erection.

5. When stimulation done, or after ejaculation, cGMP is broken down by enzyme (phosphodiesterase). Erection ends.

CLINICAL APPLICATIONS

Nitric oxide, released in the penis in response to parasympathetic nerve activation, enters the smooth muscle cells in the arterioles and stimulates the production of a second messenger, cyclic guanosine monophosphate (cGMP). The cGMP causes the smooth muscle cells to relax and the vessels to dilate, so that more blood can flow to the corpora cavernosa and produce erection. A particular cGMP phosphodiesterase enzyme then breaks down cGMP, ending the erection. Erectile dysfunction is now often treated with drugs such as sildenafil (Viagra), which block the cGMP phosphodiesterase enzyme. These drugs increase the cellular concentration of cGMP and thereby promote erection.
**How ED Drugs work (Viagra, Cialis, Levitra):**
(Click [HERE](#) to see my example writing assignment)

*Phosphodiesterase inhibitor* = a chemical that inhibits phosphodiesterase.

So ..., what would giving a phosphodiesterase inhibitor do to **cGMP** levels in the corpus cavernosa?

- Increases it (cGMP agonist)
- What would that do to arteries in the penis? **Vasodilation**
- What would that do w/respect to an erection? **Cause it to happen**

Viagra, Cialis, & Levitra are **phosphodiesterase inhibitors**.

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**4. Gametogenesis and Steroidogenesis in Males and Females**

*Gametogenesis* = production of gametes (eggs & sperm).

- *Spermatogenesis* = production of sperm within testes.

- *Oogenesis* = production of eggs within ovaries.

*Steroidogenesis* = production of sex steroids (estrogen, progesterone, testosterone).
**Spermatogenesis:**

- **Spermatogonia** (2n) = cells that undergo meiosis to make sperm.
  
  $\xrightarrow{\text{Meiosis 1}}$
  
  **Primary spermatocyte** (2n)
  
  $\xrightarrow{\text{Meiosis 2}}$
  
  **Secondary spermatocytes** (1n)
  
  $\xrightarrow{\text{Meiosis 3}}$
  
  **Spermatids** (1n) = immature sperm cells.
  
  $\xrightarrow{\text{Meiosis 4}}$
  
  **Spermatozoa** = mature sperm cells.

The **Ovaries** have **follicles** that contain a developing egg (oocyte). Once a month one follicle & egg mature. A **secondary oocyte** is ovulated. The remaining follicle becomes the **corpus luteum** & produces **progesterone**.

**mittelschmertz**

1. Primary follicle contains oogonium.

2. Secondary follicle contains primary oocyte.


5. Graafian follicle remains in ovary & becomes corpus luteum (CL) making progesterone.

4. Secondary oocyte ovulated

6. If no fertilization CL disintegrates.
Oogenesis:

- **Oogonium (2n)**
  - **Primary oocyte (2n)**
  - Meiosis 1
  - Meiosis 2 starts at puberty

Eggs in stasis as primary oocyte (2n) in ovaries from time a fetus to just before puberty.

Secondary oocyte (1n) within a "Graafian follicle"

- 2° oocyte is "ovulated" once/month
- Graafian follicle becomes corpus luteum
- "CL" produces progesterone ~14 days

**Progesterone** = hormone released from CL that maintains uterus in pregnancy-friendly state. Prevents egg development and ovulation.

Progesterone = hormone released from CL that maintains uterus in pregnancy-friendly state. Prevents egg development and ovulation.
review – Hypothalamus endocrine function:

> communicates between nervous and endocrine systems
> Secretes “releasing hormone” to stimulate gonads = GnRH
> This stimulates anterior pituitary to secrete LH & FSH
> FSH stimulates sperm or egg maturation
> LH stimulates testosterone production in testes, and estrogen production, ovulation, and corpus luteum formation in ovaries.

Steroidogenesis

Hypothalamic neurons secrete “releasing hormone” GnRH

Anterior pituitary responds to GnRH by secreting LH & FSH:

**QUESTIONS:** How does hormonal birth control work??

Answer = rising blood estrogen & progesterone inhibit hypothalamic GnRH, and pituitary LH & FSH. Egg doesn’t mature nor ovulate.

**Testes**

LH – make testosterone
FSH – stim. sperm develop.

**Ovaries**

LH – make estrogen & ovulate egg
FSH – stim. egg development.
**Clinical Applications**

About 60 million women worldwide currently use oral contraceptives (birth control pills). These contain a synthetic estrogen combined with synthetic progesterone, which are taken each day for 3 weeks after the last day of the menstrual period. Placebo pills are taken for the fourth week, to cause a fall in the blood levels of estrogen and progesterone so that menstruation can occur. The birth control pills immediately produce high blood levels of estrogen and progesterone, mimicking the luteal phase and causing negative feedback inhibition of FSH and LH. Thus, no follicles grow and ovulate (so fertilization is prevented), and no corpus luteum can be formed. The newer contraceptive pills have other benefits: they may reduce the risk of endometrial and ovarian cancer, as well as osteoporosis. However, they may also increase the risk of breast cancer, and possibly cervical cancer. Each woman should consult with a physician to weigh the potential benefits and risks in light of her own medical situation and family history.

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**Review**

**Male reproductive anatomy & physiology**
- male sexual structures
- physiology of an erection
- reproductive problems (ED, BPH)

**Gametogenesis**
- spermatogenesis
- oogenesis

**Steroidogenesis**
- Hypothalamic-pituitary-gonadal axis
- negative feedback inhibition of steroidogenesis
5. Female Reproductive Anatomy & Physiology.

**External genitalia**
- **Vulva** = labia major & minor
- **Clitoris** = erectile tissue with sensory nerves (similar to head of penis)

**Internal structures:**
- **Vagina** = copulatory & birth canal.
- **Uterus** = muscular sac capable of supporting developing fetus.
- **Fallopian tubes** = paired tubes that can transport fertilized egg from ovaries to uterus.
- **Cervix** = entryway into uterus from vagina.
- **Endometrium** = secretory layer of uterus.
- **Myometrium** = muscular layer of uterus, responds to oxytocin & prostaglandin.

**Ovaries** = paired gonads making eggs, estrogen & progesterone.

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**External Genitalia**
- **Clitoris** = equivalent of glans penis. Same sensory nerves & erectile tissue
- **Labia minor** = smaller inner labia
- **Labia major** = larger outer labia
- **Vestibule** = tissue surrounding urethral & vaginal openings. Prone to tearing during childbirth!

**Question:**
What is an episiotomy?

= Controlled incision into perineum to allow extra room for baby’s delivery

[Click the film strips below to see YouTube videos of the following:] delivery epidural C-sec episiotomy
The Uterus

- **Endometrium** – inner layer where implantation (attachment) of fertilized egg occurs
  - Sloughs off if no pregnancy occurs (menses)
- **Myometrium** — middle layer of smooth muscle = childbirth, sperm propulsion
- **Perimetrium** (visceral peritoneum)—outermost serous layer

Uterus wall has 3 layers:

Human uterus: normal Vs menstrual

Contracts in response to oxytocin
**Endometriosis** = when endometrial tissue of uterus wanders out of uterus to different locations. Still responds to progesterone by proliferating, and then shedding when progesterone declines each menstrual cycle. *Painful!

**Uterine Fibroids** = benign (noncancerous) growths of myometrium, which often appear during childbearing years.

Also called *leiomyomas* (lie-o-my-O-muhs) or *myomas*.

Are NOT associated with an increased risk of uterine cancer (almost never develop into cancer)

**Symptoms:**

- May have none
- Heavy menstrual bleeding
- Pelvic pressure / pain
- Backache
- Frequent/difficult urination
The majority of hysterectomies (surgical removal of the uterus) are performed because of uterine fibroids (leiomyomas). These are nonmalignant (noncancerous) neoplasms (growths) in the uterus that also include abundant extracellular matrix. Fibroids can be as small as 10 mm or as large as 20 cm, and produce such symptoms as pelvic discomfort and profuse menstrual bleeding. Uterine fibroids have receptor proteins for estradiol and progesterone, which can stimulate their growth. Because most fibroids are located within the uterine wall, they usually can be surgically removed only by a hysterectomy.

**The Fallopian Tubes**

**Ectopic Pregnancy** = pregnancy “out of place” (basically anywhere except within the uterus). Frequency of 2% among females.

Danger of an Out-of-place pregnancy = only uterus & its strong ligaments can support weight of growing fetus. Only endometrium capable of forming a fully functional placenta. All other tissues not compatible for pregnancy.

An ectopic pregnancy is NEVER viable for the embryo AND is life-threatening for the mother

HPV – human papilloma virus. Present in 50% of sexually active adult population. Can cause polyps and warts at site of contact. Can lead to increased risk for cancer.

Cervical warts

Cervical polyps

Cervical cancer stages

Vaginal warts

Penile warts

Oral/throat cancer?
**HPV Vaccine - 2006**

- Gardasil marketed by Merck & Cervarix by GlaxoSmithKline
- Both are set of 3 vaccinations given over a 6 month period.

**Only Gardasil is:**
- Effective against 4 strains HPV – 2 which cause cancer & 2 which cause warts
- Tested & recommended for 9-26 yr old girls AND boys
  (younger is better - before sexual exposure!)
- Can get up to 21-26 yrs but protection goes down w/sexual exposure.

**https://www.cdc.gov/hpv/parents/vaccine.html**

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The prevalence of human papillomavirus (HPV) infections in adolescent girls in the United States has declined significantly since the human papillomavirus vaccine (Gardasil, Merck) was introduced in 2006, a new study by the Centers for Disease Control and Prevention (CDC) estimates.

The study, published June 2013 in the *Journal of Infectious Diseases*, reveals that HPV prevalence decreased 56% among female adolescents aged 14 to 19 years since 2006, despite relatively low immunization rates.

Only about half of all girls in the United States received the first dose of the HPV vaccine, the CDC said in a statement. A series of 3 shots is recommended over the course of 6 months. In contrast, countries such as Rwanda and Australia have vaccinated more than 80% of their teenaged girls.

**http://jid.oxfordjournals.org/content/early/2013/06/18/infdis.jit192.abstract**
**Ovarian cycle**

Days:
1-13 = Follicle phase
Egg development from FSH

Day 14 = ovulation (LH high)

Days 15-28 - CL makes progesterone

**Menstrual cycle**

Days:
1-5 = menstruation
- progesterone low

5–14 = Estrogen ↑

15–28 =
- endometrium thickens
- progesterone↑

**If no fertilization:**
- Corpus luteum breaks down and stops progesterone secretion @day 28.
- Without progesterone, endometrium secretes prostaglandin, which cause uterine contractions to expel menstrual tissue.
- Menstrual flow – egg and lining shed
IF no fertilization:
- Corpus luteum breaks down and stops progesterone secretion @day 28.
- Without **progesterone**, endometrium secretes **prostaglandin**, which cause uterine contractions to expel menstrual tissue.
- Menstrual flow – egg and lining shed

IF fertilization:
- Embryo makes **hCG** within 1 week (*the hormone pregnancy tests detect*)
- hCG “rescues” corpus luteum – it keeps making progesterone ~ 1month (until placenta forms and takes over progesterone production).

**CLINICAL APPLICATIONS**

Because hCG is secreted by the cells of the chorionic membrane of the embryo, and not by the mother’s endocrine glands, all **pregnancy tests** assay (test) for hCG in urine or blood. Modern pregnancy tests detect the beta subunit of hCG (one of two different polypeptide chains that comprise the protein), which is unique to hCG and provides the least amount of cross-reaction with related hormones. Pregnancy tests use **monoclonal antibodies** (produced by lymphocyte clones; see chapter 11), which are specific for the beta subunit of hCG and are produced by animals such as rabbits injected with hCG. Home pregnancy tests, using monoclonal antibodies that react with hCG in urine, are generally accurate in the week following the first missed menstrual period.
**Polycystic Ovarian Syndrome** = follicles in ovary fill with fluid (cysts). Painful condition that decreases fertility.

**Treatment:**
- Hormonal birth control – it inhibits hypothalamic GnRH, which inhibits pituitary LH & FSH. Without FSH, no follicle and egg will mature. Keeps ovaries “quiet”.

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**Ovarian cancer**

**↑ risk factors include:**
- Genetics (close female relative had it)
- Have had more ovulations in life (never on hormonal birth control or been pregnant)
- Have mutation in the BRCA gene
- Polycystic ovarian syndrome
- Hormonal problems

**↓ risk factors include:**
- not have genetics
- no mutation in BRCA gene
- fewer ovulations in life (never on birth control, never pregnant)

**Question:** Why do you think having been on birth control lowers risk of ovarian cancer??

The fewer times you ovulated in your life, the fewer times the ovary had to repair itself, with mitosis, then the less the risk of cancer developing.
Ovarian and Breast Cancer and the BRCA Gene:

**BRCA Gene** = tumor suppressor gene that normally suppresses tumor growth (a good thing!)

**Mutation in BRCA Gene** – means the gene does not suppress tumors. Mutation in this gene associated with increased risk for ovarian & breast cancer. Can get blood test for it.

**CA-125 test** = cancer antigen 125 (a non-genetic test)
increased levels of this in blood associated with ↑ risk of ovarian cancer (separate from BRCA gene)

Cancer and the BRCA Gene:

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>General Population (No Mutation)</th>
<th>Individuals With Mutation</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>BRCA1</td>
</tr>
<tr>
<td>Breast</td>
<td>12%</td>
<td>50-80%</td>
</tr>
<tr>
<td>Ovarian</td>
<td>1-2%</td>
<td>24-40%</td>
</tr>
<tr>
<td>Male Breast</td>
<td>0.10%</td>
<td>1-2%</td>
</tr>
<tr>
<td>Prostate</td>
<td>15% (N. Europe Origin)</td>
<td>up to 30%</td>
</tr>
<tr>
<td></td>
<td>18% (African American)</td>
<td></td>
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<tr>
<td>Pancreatic</td>
<td>0.50%</td>
<td>1-3%</td>
</tr>
</tbody>
</table>
Click [HERE](#) for a YouTube video I made about my breast cancer story AND the BRCA gene mutation.

**Review**

Female reproductive anatomy & physiology
- reproductive structures
- ectopic pregnancy & endometriosis
- HPV, warts, cervical cancer, HPV vaccine, ovarian & breast cancer
- review of oogeneis
- menstrual & ovarian cycle
- role of hCG in rescuing corpus luteum in pregnancy