Chapter 28
The Female Reproductive System

Sex differentiation
the female reproductive tract develops from the mullerian duct system
develops because of the absence of testosterone and mullerian inhibiting
factor
does not require any positive action
can be disrupted by hormone influences during development
adrenogenital syndrome (AGS)
hypersecretion of androgens from the adrenal cortex
as in Cushing syndrome
children
enlargement of the clitoris and
premature onset of puberty

fetal development
1. enlargement of the clitoris to
resemble a penis
2. labia majora fuss and resemble a
scrotum
3. may be misidentified as boys

Anatomy of the female reproductive system
internal genitalia
ovaries
1. are primary reproductive organ of females
produce the gametes called egg or ova

2. produce sex hormones estrogen and
progesterone

3. located in the ovarian fossa, a depression of the
posterior pelvic wall
held in place by
1. ovarian ligament
2. broad ligament

4. about 3 cm long and 1.5 cm wide and 1 cm thick

5. are crudely divided into an outer cortex and a central
medulla
6. embedded in the connective tissue of the ovary cortex are bubble-like **ovarian follicles**
   each follicle consists of an immature egg called an oocyte surrounded by **follicle cells**, if one layer thick, or **granulosa cells** if more than one layer thick

**stages of follicular development**

1. **primordial follicle** simplest as only one layer of cells (**follicle cells**) surrounding the oocyte
2. **primary follicle** as two or more layers of **granulosa cells**
3. **secondary follicle** as a fluid-filled space called an **antrum**
4. **Graafian follicle** see the oocyte held by a stalk of granulosa cells in the antrum
5. Graafian follicle will rupture during ovulation and the remaining granulosa cells will form the **corpus luteum**
6. if not pregnant, corpus luteum becomes the **corpus albicans**

all these stages are not present in an ovary at one time

**female duct system or secondary sex organs**

1. **uterine tubes**
   the oocyte leaves the ovary and enters the uterine tube or Fallopian tube or oviduct
   is about 10cm long

   wall of the uterine tube has thick layer of smooth muscle, small number of secretory cells, and the epithelium is ciliated

   divided into three regions
   1. **infundibulum** funnel-shaped and as the feathery projections called **fimbriae** that drape over the ovary.
   2. **ampulla** middle regions and is site of fertilization
   3. **isthmus** is the narrowed region that empties into the uterus
the oocyte is moved along the oviduct aided by cilia and smooth muscle contraction (peristalsis)

the movement in the direction of the uterus helps move out infectious material
direction changes after intercourse to help move the sperm towards egg added by prostaglandins form semen

2. uterus
houses the embryo
provides the embryo nutrition
expels the fetus at after development

is 7 cm from top to bottom
is 4 cm at the widest point
is 2.5 cm thick
larger in women who have been pregnant

regions of the uterus
1. fundus is where the oviduct enters
   is the superior curvature
   typical sit of implantation
2. body is the main region
3. isthmus - narrow region between body and the cervix
4. cervix - narrow neck that projects into the vagina
   is open to the vagina by the cervical canal
   external os opens to the vagina
   internal os opens to the uterus

the cervical canal contains cervical glands that secrete mucus to plug the canal when not fertile
mucus becomes thinner at time of ovulation in response to estrogens

three layers of the uterine wall
1. perimetrium - the outermost layer which is part of the peritoneum
2. myometrium - thick middle layer of smooth muscle. Contracts during delivery
myometrium of cervix is mostly collagen

3. **endometrium** - the mucosal lining
site were embryo implants

contains numerous glands that secrete a nutritive substance for the embryo prior to implantation
uterine milk

undergoes cyclic changes in response to ovarian hormones

layers of the endometrium

**stratum functionalis**
is the superficial half and is shed during menstruation

**stratum basalis**
dereeper half and remains and regenerates a new functionalis in the next cycle

**Vagina**
extends from the cervix to the outside
also called the birth canal

allows discharge of menstrual fluid
receives the penis and semen during intercourse
is the passage for the baby during delivery

has no glands; lubrication is provided by transudation (vaginal sweating) and cervical mucous glands

the epithelial cells that line the vagina; store high amounts of glycogen which resident bacteria consume to produce lactic acid which lowers the pH and guards against other forms of infections but is a bad pH for sperm

**Vulva**
External genitalia of the female are collectively called the vulva

1. **Mons pubis**
Mound of adipose tissue overlying the pubic symphysis

2. **Labia majora**
3. Labia minora
   Enclose an area called the vestibuule
   Structures of the vestibuule
   1. urinary orifice
   2. vaginal orifice

3. Clitoris
   Miniature penis
   Contains a pair of corpora cavernosa
   No urinary role
   Entirely sensory
   Center of erotic stimulation

4. Vestibule glands (Bartholin)
   Pea-sized glands on each side of the vagina
   Are homologous to the bulbourethral glands
   Moisten the vulva and provide most of the lubrication for intercourse

Puberty
   Starts at age 9 to 10
   About 2% of girls it starts around age 3

   There is racial variation
   27% of black girls start by 7
   7% of white girls start by 7

   triggered by a rise in gonadotropin releasing hormone (GnRH)
   triggers release of LH and FSH
   triggers the ovaries to release estrogens, progesterone, and small amounts of androgens

   earliest signs (in order of appearance)
   thelarche
   development of breasts
   induced by estrogens

   pubarche
   growth of pubic and axillary hair
   sebaceous and apocrine glands
   induced by androgens from ovaries and adrenal cortex
   androgens also stimulate libido
menarche
first menstrual period
average age is 12 years old
must have 17% body fat
must have fat for pregnancy
is delayed in thin girls like athletes
first year the menstrual period is anovulatory

is induced by estrogens and progesterone

other effects of estrogens
secondary sex characteristics
growth of reproductive organs
stimulates release of growth hormone
increase in height
widening of pelvis
stimulates fat deposition resulting in feminine physique

Climacteric
Changes on sex hormone production
Occurs at midlife

Ovaries have fewer remaining follicles
Those left become less responsive to FSH and LH

Results in a drop of estrogens and progesterone
effects
Uterus vagina breasts will atrophy
Vagina becomes thinner and drier
Painful intercourse and more infections

Blood vessels constrict and dilate in response to shifting hormone levels
Results in hot flashes

Changes in hormone levels can result
Mood changes
Rise in cholesterol
Decline in bone mass

Menopause
A main effect is the cessation of menstrual cycle
Results form low sex hormone levels
Normally occurs around 45 to 55
Average is 52 which as increased
Oogenesis

males start to produce sperm at puberty
once started this is a continuous process generating new sperm
daily for the life of the man

females are born with all the immature egg cells they will have (1,000,000
--only need 400 to 500)
only a single egg matures per month once reaching puberty
process stops after menopause

1. the female and the male germ cells arise form tissue within the yolk sac of the embryo
2. this tissue migrates to and colonizes the gonadal ridges in the first 5 weeks of development
3. in the female, once the cells reach the gonadal ridge they development into oogonia
4. the oogonia divide by mitoses until the fifth month producing 6 to 7 million oogonia
5. some of these oogonia are surrounded by follicular cells then enter a growth phase and store up nutrients
they enter meiosis I but freeze in prophase I
most oogonia degenerate by a process called atresia
6. these cells are called primary oocytes
7. the primary oocytes together with the cells that surround them are called primordial follicles
8. at birth the child will have about 1 million primordial follicles each containing a primary oocyte frozen in meiosis I

12 years later

9. starting at puberty and continuing until menopause each month a small number of primordial follicles will begin to develop under the influence of FSH. They are now called primary follicles. They still contain a primary oocyte.
10. the granulosa cells of the follicle become active and divide and starts to produce estrogen and progesterone
11. the primary follicle continues to grow by mitoses and is now called the secondary follicle. Under the influence of LH the primary oocyte inside will complete meiosis I process producing 2 cells

1. one cell is small and is called the first polar body
   eventually undergoes meiosis II (produces 2 smaller cells)
   it contains mostly unwanted genetic material
usually the first polar body dies

2. second cell is larger and has almost all the cytoplasm -- this is called the **secondary oocyte** and the follicle is now called a **graafian follicle**

12. **secondary oocyte** in the graafian follicle will arrest in meiosis II and is ovulated
   ---only if penetrated by sperm will meiosis II be completed
   this produces second polar body
   and the large **mature ovum**

end result 3 polar bodies and one functional gamete

hormones and the female reproductive cycle
more complicated then in males
must coordinate the **ovarian cycle** (events in the ovaries mainly follicle maturation) with the **uterine cycle** (events in the uterus mainly formation of the stratum functionalis and its activity)

**ovarian cycle**
is two cycles that occur consecutively
   follicular phase or the development of the follicle
   luteal phase or hormone release from the corpus lutum

**follicular phase**
starts with beginning of menstruation end with ovulation

**hormonal changes during ovarian cycle**
(28 day cycle)

day 1 of the cycle is the first day of menstrual flow
rising levels of GnRH cause LH and FSH to start slowly rising.
   The release of GnRH is at a low pulse rate (one pulse every 60 to 90 minutes) this has a greater effect on FSH release so LH levels stay fairly low and constant

   The rising FSH will stimulate follicular growth and maturation
   20 or so **primordial follicles** begin grows to a **primary follicle**
The FSH stimulates estrogen secretion from the follicles so estrogen levels will rise for the next two weeks.

By day 9-10 the single graafian follicle forms estrogen levels rise steeply causing GnRH release pulses every 30 to 60 minutes this stimulates LH secretion while inhibiting FSH.

By day 12-13 days have very high levels of estrogen this results in the pituitary becoming more sensitive to GnRH this along with the rapid pulse release of GnRH stimulates a spike in the release of more LH and a small spike of FSH.

**Results in:**
- The rising LH also stimulates the primary oocyte to complete meiosis I to resulting in a secondary oocyte (first polar body) in the graafian follicle. The secondary oocyte freezes in meiosis II and awaits fertilization
- The burst of LH increases the blood flow to the follicle causing the follicle to swell rapidly and burst (ovulation) this occurs about 34 to 38 hours after the peak in LH which is typically on day 14 of a 38 day cycle
- Follicle expels the secondary oocyte surrounded by the **corona radiata** (a layer of granulosa cells)

LH and FSH rapidly drop because the burst has depleted their stores the damage to the follicle cells during ovulation temporally reduces the release of estrogens.

**Luteal phase:**
after ovulation the ruptured follicle collapses
due to the previously high LH levels the remaining granulosa cells
increase in size and form a endocrine gland called the corpus luteum
secretes progesterone
so progesterone levels rise quickly while estrogen levels
slowly drop but do remain somewhat elevated
progesterone is the major hormone of the luteal phase and
it functions to continue the preparation of the uterus for pregnancy
CL degenerates after 10 days if not pregnant
now called the corpus albicans
results in drop of estrogen and progesterone
this remove the feedback on GnRH so LH and FSH
start it increase
starts the cycle over
the crash in estrogen and progesterone triggers the uterus to shed the endometrium and menstrual flow starts
day 1
if pregnant the CL remains until placenta takes over
endocrine role (3 months)

uterine or menstrual cycle
is a cycle of the endometrium of the uterus that occurs each month (28 days) in response to changes in levels of hormones
consists of a buildup of the endometrium followed by its breakdown and vaginal discharge
is closely coordinated with the phases of the ovarian cycle so that the uterus is ready for embryo implantation at the time that the female is fertile
four phases

1. proliferative phase:
is the rebuilding phase that occurs before ovulation
occurs from day 6 through day 14 of the ovarian cycle
estrogens from follicles stimulate mitosis of the stratum basalis
so generate a **stratum functionalis**

estrogens also stimulate the endometrium to produce progesterone receptors

2. **secretory phase:**
   begins immediately after ovulation- day 15 until day 26
   the endometrium continues to thicken but due to fluid accumulation
   prepares the endometrium for implantation
   after ovulation the corpus luteum secretes mainly progesterone
      effects of progesterone
         stimulates endometrial glands to accumulate glycogen and secrete a glycogen fluid
         inhibits smooth muscle contraction

3. **premenstrual phase**
   period of endometrial degeneration
      is the last two days of the cycle (26-28)
      corpus luteum atrophies and progesterone levels fall sharply
      low progesterone results in spasmodic contractions of the arteries of the stratum functionalis
      causes ischemia
      tissue of functionalis becomes necrotic and falls away form the uterine wall
      tissue with blood mixes forming **menstrual fluid**

4. **menstrual phase:**
   is day one of the ovarian cycle
   lasts till day 5
   is the period in which the endometrial tissue is discharged from the vagina
   menstrual flow
      typically about 40 ml of blood and 35 ml of serous fluid
Pregnancy and childbirth

Adjustments of the woman’s body to pregnancy

Basics on prenatal development

Fertilization must occur in the distal half of the uterine tube

Unfertilized egg want last until uterus

Fertilized egg divides five or six times before it reaches the uterus

Fertilized egg is called a blastocyst for first two weeks and an embryo from 3 to 8 weeks and a fetus from 9 weeks to birth

Once the blastocyst reaches the uterus it contains an inner cell mass with will be the embryo and it contains an outer cell mass called the trophoblast which as several supporting roles like attachment to the endometrium and hormone production

Hormones of pregnancy

Human chorionic gonadotropin (HCG)

Is secreted by the trophoblast

Is basis for pregnancy test

Can detect by 8 or 9 days after conception

Stimulates the corpus luteum to grow and continue production progesterone and estrogen

Estrogens

Secretion increases to 30 times normal amounts by the end of gestation

Early source is corpus luteum (first 12 weeks)

Latter source is placenta

Effects of estrogens

Stimulates tissue growth in fetus and mother

Makes pubic symphysis more elastic and sacroiliac joints more limber so pelvis widens during pregnancy

Breast enlargement

Progesterone
Both placenta and corpus luteum are early sources of effects.

Together with estrogen they suppress release of FSH and LH preventing follicles from developing during pregnancy, which is basis for the “pill.”

Suppresses uterine contractions so not to expel the fetus.

Supports proliferation and secretion of the endometrium.

Also stimulates breast enlargement in mother.

**Human chorionic somatomammotropin**

Secreted during pregnancy several times higher in all hormones combined but function poorly understood.

Source is the placenta around week five.

As placenta grows release increases.

**Known function**

In other mammals it stimulates lactation.

Not so in humans.

Works as a week growth hormone.

Decreases insulin sensitivity and glucose usage and promotes release of free fatty acids from mothers adipose so he has alternative energy source. Results in leaving more glucose in the blood for the fetus.

**Parathyroid hormone**

Increased release from mother to release calcium from bone for fetal use.

**Thyroid hormone**

HCG elevates t4/t3 release.

Increases metabolic rate of mother and fetus.

**ACTH**

Levels increase by HCG.

Increases Glucocorticoids.

Mobilizes amino acids for fetal use.
Increased aldosterone
Increased blood volume
Can increase blood pressure

**Relaxin**
Produced by corpus luteum and placenta
Once thought to relax pubic symphysis but not so

Softens the cervix in preparation for childbirth

**Adjustments to pregnancy**

**Changes in the digestive system, nutrition and metabolism**
- **Morning sickness**
  - Thought to be a result of reduced intestinal motility caused by steroid hormones of pregnancy
- **Constipation**
  - Reduced intestinal motility
- **Heartburn**
  - Enlarging uterus pressing on the stomach
  - Results in acid reflux

Basal metabolic rate increases 15 due to thyroid release
- Require only 300 extra calories per day even at last trimester
  - Placenta will store nutrients in the first and second trimester with are used in the last trimester

**Circulatory system**
- Full term placenta requires 625 ml of blood per minute from the mother
  - Maternal blood volume increases about 30% by fluid retention and hemopoiesis
  - Will have 1 to 2L more blood by term

Pressure of the fetus on the large pelvic blood vessels can block venous return and result in varicose veins and hemorrhoids and swelling of the legs

**Respiratory system**
- Oxygen demands increase about 20%
  - Due to increased metabolism

Ventilation increases 50% during pregnancy
- Increases more then demand due to pressure on the diaphragm making rapid shallow breathing necessary
End of term the expansion of the pelvis allows the fetus to drop and removes some pressure so breathing is easier.

**Urinary system**
Glomerular filtration rate increased 50% and urine output is elevated. Allows the disposal of both mother’s and fetus’s wastes.

Pressure of the fetus compresses the bladder. Frequent urination and leakage called incontinence.

**Childbirth or parturition**
The fetus is forced out by contractions of the uterus and the abdominal muscles of the mother.

Weak uterine contractions before labor are called **Braxton Hicks contractions**. Are very week becoming stronger near term. Result in false labor.

Strong contractions are called **labor contractions**.

**Initiation of labor contractions**
High levels of progesterone inhibit contractions but progesterone levels decline after second trimester the rising estrogens stimulate irritability of the uterus.

Near full term the **fetus** releases cortisol which:

- Stimulates the uterus to expresses increasing levels of oxytocin receptors
- Triggers the posterior pituitary to releases oxytocin
- Oxytocin act to stimulate the uterine muscle to contract and stimulate the fetal membranes to secrete prostaglandins with increase uterine contractions. This results in the fetus pushing on the cervix which has numerous stretch receptors.

**Labor contractions**
Positive feedback
First contractions = cervical stretching = oxytocin secretion = uterine contraction = cervical stretching

Uterine stretching by the growing fetus is also involved in initiating labor
Triggers the release of oxytocin
Twins are born 19 days earlier

**Stages of labor**

**Dilation stage**
- Longest 8 to 24 hours
- Dilation of the cervix
- Effacement or thinning of the cervix

Is the stage were the fetal membranes rupture

**Expulsion stage**
- About 30 minutes
- Starts with baby’s head entering the vagina and lasts until expelled

**Placental stage**
- Uterus continues to contract expelling the placenta and other fetal membranes

**Postpartum**

**Involution**
- Shrinkage of the uterus
- By 4 weeks it is near pregnancy weight
- Achieved by autolysis or self digestion

Breast-feeding speeds involution by inhibiting estrogen release and stimulating oxytocin release

**Lactation**
- Worldwide average is to feed until 4.2 years of age
- Can continue indefinitely as long as stimulated by feeding

Development of the mammary glands during pregnancy
- High **estrogens** stimulate ducts to grow and branch
- Helped by growth hormone insulin Glucocorticoids and prolactin
**Progesterone** stimulates the budding of an acini which is the site of milk production once the duct forming is complete.

**Colostrum**

By late pregnancy the acini are distended with a secretion called colostrum,

Similar to breast milk but 1/3 less fat and contains immunoglobulins that resist digestion and can be absorbed by the small intestine by pinocytosis

Give the child systemic immunity

This will be produce for 1 to 3 days postpartum

**Milk synthesis**

Is promoted by prolactin

Levels start to rise by week 5 of pregnancy but affect is inhibited by high levels of estrogen and progesterone

There droop after birth allows prolactin to stimulate milk synthesis

Milk production also requires growth hormone, insulin cortisol and parathyroid hormone to mobilize the necessary amino acids fatty acids glucose and calcium

**Milk ejection**

Controlled by a neuroendocrine reflex or suckling reflex

Stimulates release of oxytocin from posterior pituitary

Oxytocin stimulates myoepithelial cells that surround the acini so milk is pushed out