







- Germ cells become gametes (sperm and ova) in the gonads via meiosis.
- Ova and sperm are fused in fertilization.
- The new individual progresses from zygote → embryo → fetus.





#### Sex Chromosomes

- Females have two X chromosomes. – Mom always passes on an X chromosome.
- Males have an X and a Y chromosome.
   Dad can pass on *either* an X or a Y chromosome.
  - The sex of a child is determined by the contributing sperm.

#### Sex Chromosomes

- X and Y look different and have different genes.
  - X has 1,090 genes while Y has only 80 genes.
  - The Y chromosome has many testis-specific genes.



#### Sex Chromosomes

- In females, one of the two X chromosomes is inactive.
  - This produces a visible Barr Body.
  - This is an easy way to visually determine the sex of a cell.





#### Formation of Testes

- Soon after the production of TDF in XY embryos, the seminiferous tubules form.
  - Germinal cells and Sertoli cells differentiate 45–50 days after fertilization.
  - The Leydig cells (those that make testosterone) appear around day 65.

#### Formation of Testes

- The Leydig cells begin making large amounts of testosterone ~8 weeks after fertilization.
  - This stimulates the development of the rest of the male reproductive organs.
- As the testes develop, they descend into the scrotum.

#### Formation of Ovaries

- Without TDF, XX embryos do not develop testes.
- Follicular cells do not appear until the second trimester.



#### Formation of Accessory Sex Organs

- Between days 25 and 50, both male and female embryos have two systems of ducts:
  - Wolffian ducts: can become male tract
  - Mullerian ducts: can become female tract

#### Formation of Accessory Sex Organs

- In the growing testes, the Sertoli cells secrete Mullerian-inhibiting factor.
  - This makes the Mullerian duct regress.
  - Testosterone from the Leydig cells stimulates the development of the Wolffian duct (epididymis, ductus deferens, seminal vesicle).
  - Without this inhibition and stimulation, the Mullerian ducts develop into fallopian tubes and a uterus.

#### Formation of External Genitalia

- Identical in males and females for first 6 weeks of life
  - Both sexes have a urogenital sinus, labioscrotal swelling, genital tubercle, and urethral fold.
  - Testosterone masculinizes these into the scrotum, prostate gland, and penis.
  - Without testosterone, these become the labia and clitoris.





# Developmental Timetable

Approximate Time After Fertilization			Developmental Changes		
Days	Trimester	Indifferent	Male	Female	
19	First	Germ cells migrate from yolk sac.			
25-30		Wolffian ducts begin development.			
44-48		Müllerian ducts begin development.			
50-52		Urogenital sinus and tubercle develop.			
53-60			Tubules and Sertoli cells appear.		
			Müllerian ducts begin to regress.		
60-75			Leydig cells appear and begin testosterone production.	Formation of vagina begins.	
			Wolffian ducts grow.	Regression of wolffian ducts begins.	
105	Second			Development of ovarian follicles begins.	
120				Uterus is formed.	
160-260	Third		Testes descend into scrotum.	Formation of vagina is complete.	
			Growth of external genitalia occurs.		

#### **Disorders of Sexual Development**

- Hermaphroditism: Both ovarian and testicular tissue exist in the body.
  - Some people have an ovary on one side and a testis on the other, while others have fused ovotestes.
  - Due to a problem in zygotic mitosis, not every cell receives the full Y chromosome.

#### **Disorders of Sexual Development**

- Pseudohermaphroditism: The individual has ovaries *or* testes, but accessory structures are not complete or are inappropriate for the genetic sex.
  - Female pseudohermaphroditism: may be due to excessive secretion of adrenal androgens in a female = congenital adrenal hyperplasia.
  - Both Mullerian and Wolffian duct derivatives and male external genitalia

#### **Disorders of Sexual Development**

- Male pseudohermaphroditism: may be due to testicular feminization syndrome whereby testes make testosterone but testosterone receptors don't work.
  - Female external genitalia form, but there is no uterus or fallopian tubes because the Mullerian duct still degenerated.
  - There is no male tract either because the Wolffian duct was not stimulated.

#### **Disorders of Sexual Development**

Male pseudohermaphroditism: may also occur because of inability to make the enzyme 5<sup>α</sup>-reductase, which converts testosterone into DHT in target cells.
 This is required for masculinization of external genitalia.





#### Sex Hormone Secretion

- The testes stop making testosterone by the third trimester, and the ovaries don't make embryonic sex hormone.
- Sex hormone secretion does not occur again in either sex until the gonads are stimulated at puberty.
- At this time, the anterior pituitary begins releasing gonadotropic hormones.

#### **Gonadotropic Hormones**

- Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are produced in both males and females with three effects:
  - 1. Stimulation of spermatogenesis or oogenesis
  - 2. Stimulation of gonadal hormone secretion
  - 3. Maintenance of the structures of the gonads

#### Regulation of FSH and LH

- Release of FSH and LH is controlled by the release of gonadotropin-releasing hormone (GnRH) from the hypothalamus.
- Regulated by a negative-feedback loop where rising levels of gonadal hormone:
   Inhibit GnRH release
  - Inhibit pituitary response to GnRH

#### Regulation of FSH and LH

- Aside from the usual gonadal hormones (testosterone, estrogen, and progesterone), the gonads also secrete inhibin.
  - Secreted by Sertoli cells in testes
  - Secreted by granulosa cells of ovarian follicles
  - Specifically inhibits release of FSH (no effect on LH)

#### **Regulation of Hormones**

- Similar in males and females, but male secretion is constant while female secretion is cyclical.
- At one point in the female cycle, estrogen has a positive effect on LH release.



#### Puberty

- Secretion of FSH and LH is elevated at birth and stays high for the first 6 months of postnatal life.
  - This declines to almost nothing until puberty.
- Puberty begins with a release of LH.
  - This results in increases in testosterone or estrogen secretion.
  - These hormones produce secondary sex characteristics.

#### Secondary Sex Characteristics

- In girls: growth spurt, breast development, menarche (first menstrual flow)
- In boys: occurs later; body, muscle, penis, and testis growth
- In both sexes: body hair is stimulated by androgens from adrenal gland at puberty



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able 20.2   Development of Secondary Sex Characteristics and Other Changes That Occur During Puberty in Girls					
Characteristic	Age of First Appearance	Hormonal Stimulation			
Appearance of breast buds	8-13	Estrogen, progesterone, growth hormone, thyroxine, insulin, cortisol			
Pubic hair	8-14	Adrenal androgens			
Menarche (first menstrual flow)	10-16	Estrogen and progesterone			
Axillary (underarm) hair	About 2 years after the appearance of pubic hair	Adrenal androgens			
Eccrine sweat glands and sebaceous glands; acne (from blocked sebaceous glands)	About the same time as axillary hair growth	Adrenal androgens			

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able 20.3   Development of S hat Occur During Puberty in E	econdary Sex Characteristics and C Boys	)ther Changes
Characteristic	Age of First Appearance	Hormonal Stimulation
Browth of testes	10-14	Testosterone, FSH, growth hormon
ubic hair	10–15	Testosterone
lody growth	11–16	Testosterone, growth hormone
arowth of penis	11–15	Testosterone
frowth of larynx (voice lowers)	Same time as growth of penis	Testosterone
acial and axillary (underarm) hair	About 2 years after the appearance of pubic hair	Testosterone
ccrine sweat glands and sebaceous glands; acne (from blocked sebaceous glands)	About the same time as facial and axillary hair growth	Testosterone

### Onset of Puberty

- Depends on activity levels and amount of body fat
  - Leptin secreted by adipose cells is required for the onset of puberty.
  - Exercise may inhibit GnRH secretion.
  - More active, slimmer girls begin puberty later.
  - Melatonin from the pineal gland may play a role, but this is not proven in humans.

#### Human Sexual Response

- · Four phases:
  - 1. Excitation: characterized by increased muscle tone, vasocongestion of sexual organs; also called arousal
  - 2. Plateau: continued vasocongestion
  - 3. Orgasm: contraction of the uterus/vagina and male ejaculatory organs
  - 4. Resolution: body returns to pre-excitation condition
    - Men experience a refractory period.

#### III. Male Reproductive System

#### Testes

· Have two compartments:

- Seminiferous tubules: where spermatogenesis occurs
  - FSH receptors are found here, on Sertoli cells.
  - FSH influences spermatogenesis.
- Interstitial tissue: where Leydig cells make testosterone; also filled with blood and lymphatic capillaries
  - LH receptors found here on Leydig cells
  - Testosterone secreted in response to LH



# Gonadotropin Secretion

- LH secretion is controlled by rising testosterone secretion through negative feedback.
- FSH secretion is controlled by testosterone and inhibin secretion.
  - Inhibin is released from the Sertoli cells of the seminiferous tubules.



#### Testosterone in the Brain

- Testosterone is converted to its derivatives in brain cells.
  - Converted by 5<sup>α</sup>-reductase to DHT or to estradiol by aromatase enzyme
  - Estradiol is used to inhibit LH secretion.



#### Action of Testosterone Copyright © The McGraw-Hill Companies, Inc. F Table 20.4 | Actions of Androgens in the Male Action Growth and develo pment of wol velopment of urogenital sinus into pr ent of male external genitalia (penis t puberty: Completion of melotic div After puberty: Maintenance of spermatopenesis wth and m nce of accessory sex organ Growth of penis arowth of facial Body growth Protein synthesis and muscle growth Anabolic Effects Growth of bones Growth of other organs (including larynx) Erythropolesis (red blood cell forma







# Spermiogenesis

- Maturation of spermatids into functioning spermatozoa
  - Mature spermatozoa have a flagellum, head, midpiece, and acrosome cap.



#### Spermiogenesis and Sertoli Cells

- Sperm development requires Sertoli cells.
   Sertoli cells create a blood-testis barrier controlling what can enter the seminiferous tubules and preventing the immune system from developing antibodies against the sperm.
  - They also secrete FAS ligand, which binds to an FAS receptor on T cells, stimulating apoptosis.
    - This creates an immunologically privileged site.

#### Spermiogenesis and Sertoli Cells

- · Sertoli cells envelop the developing sperm.
  - They phagocytize some of the spermatid cytoplasm in spermiogenesis.
  - They secrete androgen-binding protein (ABP) into the seminiferous tubule lumen. This binds to testosterone and concentrates it in the tubule.
    - ABP production is stimulated by FSH.
    - Testosterone stimulates spermatogenesis and spermiogenesis.



#### Hormonal Control of Spermatogenesis

- Testosterone is required to stimulate meiosis and early spermatid maturation.
  - Testosterone is secreted by the Leydig cells after stimulation by LH.
  - FSH enhances spermatogenesis through the action of the Sertoli cells that are stimulated to make ABP, which concentrates the testosterone levels.
    - · FSH ensures optimal fertility

#### Male Accessory Sex Organs

- Spermatids move from the seminiferous tubules → rete testis → efferent ductules → epididymis.
- The epididymis is the site of sperm maturation and storage.
- In ejaculation, spermatozoa move from the epididymis → ductus deferens → ejaculatory duct → urethra.

#### Male Accessory Sex Organs

- The seminal vesicle and prostate gland add fluid to the sperm to form semen.
  - Seminal fluid: contains fructose (energy for sperm)
  - Prostate fluid: contains citric acid, calcium, and coagulation proteins





# Erection

- Nitric oxide serves as the neurotransmitter.
- Activates guanylate cyclase to produce cGMP → Closes Ca<sup>2+</sup> channels → Decreases cytoplasmic Ca<sup>2+</sup> levels →
  - Relaxes muscles
- Venous outflow of blood is partially blocked during an erection.



# Control of the Erection

- Controlled by the hypothalamus and the sacral region of the spinal cord
  - Can occur due to conscious sexual thought (hypothalamus → spinal cord → penis) or sensory stimulation (penis → spinal cord → penis)



#### Emission and Ejaculation

- Emission is the movement of semen into the urethra.
- Ejaculation is the forceful expulsion of semen from the urethra.
  - Both are under sympathetic nervous system control.
  - Contraction of smooth muscles in the tubules, seminal vesicle, prostate, and muscles at base of penis is involved in ejaculation.

# Male Fertility

- A sperm count < 20 million/ml semen is called oligospermia and is considered less fertile.
  - May be caused by heat, drugs, or anabolic steroids

Male F	ertility
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Characteristic	Reference Value
Volume of ejaculate	1.5-5.0 ml
Sperm count	40-250 million/ml
Sperm motility	
Percentage of motile forms:	
1 hour after ejaculation	70% or more
3 hours after ejaculation	60% or more
Leukocyte count	0-2,000/ml
рН	7.2-7.8
	150-600 mg/100 ml

# Vasectomy Most widely used and reliable form of male contraception The vas deferens is cut and tied to prohibit sperm transport. A vasectomy does not affect testosterone production or ejaculation.





#### Female Accessory Reproductive Organs

- Ovaries: female gonads; site of oocyte and sex steroid production
- Fallopian tubes: have fimbriae that wrap around the ovaries and "catch" the oocyte after ovulation

- Most common site of fertilization







# **Ovarian Cycle: Oocytes**

- Toward the end of gestation, a female's oogonia begin meiosis to produce primary oocytes.
  - The ovaries of a newborn girl have 2 million primary oocytes.
  - By puberty, this number is cut to about 400,000.
  - Only about 400 of these will be ovulated in her lifetime.

# Ovarian Cycle: Follicles

- Primary oocytes are contained within primary follicles.
  - In response to FSH, some of the primary follicles grow to produce many layers of granulosa cells.
  - Some develop fluid-filled vesicles called secondary follicles.









# Ovarian Cycle: Oocytes

 As the Graafian follicle grows, the primary oocyte finishes meiosis I to become a secondary oocyte (plus a polar body, which soon degenerates).



### **Ovarian Cycle: Oogenesis**

- The secondary oocyte finishes meiosis if the cell is fertilized by a sperm.
- This produces an ovum and a second polar body, which degenerates.



#### Ovarian Cycle: Estrogen

- Aside from stimulating the development of the follicles, FSH stimulates estrogen production in the follicles.
  - The bigger the follicle, the more estrogen it releases.



#### Ovarian Cycle: Ovulation

- The surviving Graafian follicle becomes so big it bulges out of the ovary.
  - Hormones stimulate the follicle to burst and release the secondary oocyte.
  - If not fertilized, the oocyte will degenerate after a few days.



# Ovarian Cycle: Corpus Luteum

- After ovulation, the remaining follicle becomes a corpus luteum.
  - This secretes both estrogen and progesterone.
  - These hormones play a role in the menstrual cycle.

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# Menstrual Cycle

- Describes the 28-day cycle of endometrial buildup and sloughing in response to ovarian hormones
- Three phases:
  - Menstrual
  - Proliferative
  - Secretory
- Changes in the endometrium follow changes in the follicles of the ovaries.

#### Cyclic Changes in the Ovaries

- Follicular changes in the ovaries can be broken into three phases:
  - Follicular phase
  - Ovulation
  - Luteal phase

### **Ovarian Follicular Phase**

- Lasts from day 1 through 13 (variable)
- Primary follicles →
   Secondary follicles →
   Graafian follicle (one kept)
- Characterized by increasing levels of estrogen production, reaching a high around day 12

#### **Ovarian Follicular Phase**

- Initiated by FSH
- FSH also upregulates the number of FSH receptors on the follicles → sensitivity to FSH increases
- At the end of this phase, FSH and high levels of estrogen stimulate production of LH receptors in the Graafian follicle.
- Increased estrogen also stimulates the hypothalamus to release more GnRH → LH is released from anterior pituitary
   Called the LH surge

### Ovulation

- FSH causes the Graafian follicle to bulge out of the ovary wall.
- LH surge begins ~24 hours before ovulation.
  - Stimulates Graafian follicle to rupture, releasing secondary oocyte

#### Luteal Phase

- After ovulation, LH stimulates the ruptured follicle to become a corpus luteum.
  - This secretes estrogen and progesterone.
  - Progesterone peaks ~1 week after ovulation.

# 

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### Luteal Phase

- High levels of estrogen and progesterone feed back on the pituitary gland and inhibit FSH and LH secretion.
- There may also be inhibin production, which helps inhibit FSH.
- Shuts down follicle development to prevent further ovulation long enough to give the secondary oocyte a chance to be fertilized

# Luteal Phase

- Ends with the degeneration of the corpus luteum around day 28
- Decreasing levels of estrogen and progesterone stimulate the sloughing of the endometrium and menstruation.

#### Cyclic Changes in the Endometrium

- The menstrual cycle begins with menstruation at the end of the previous ovarian cycle.
- The development of the endometrium is regulated by secretion of estrogen and progesterone in the ovaries.

#### **Proliferative Phase**

- Occurs while ovary is in the follicular phase
- Increasing levels of estrogen stimulate the growth of the stratum functionale of the endometrium.
- The endometrium also becomes more vascular and develops LH receptors.

### Secretory Phase

- Occurs while the ovaries are in the luteal phase
- Secretion of progesterone stimulates the development of uterine glands, which store glycogen.
- The endometrium also becomes even thicker and more vascular.
- Endometrium is prepared to nourish a growing embryo if the oocyte is fertilized.

#### **Menstrual Phase**

- Occurs as a result of the fall in estrogen and progesterone when the corpus luteum degenerates
- Arteries in the endometrium constrict, cells in the stratum functionale die, and this region is sloughed.

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able 20.6   Phases of the Menstrual Cycle							
Phase of Cycle		Hormonal Changes		Tissue Changes			
Ovarian	Endometrial	Pituitary	Ovary	Ovarian	Endometrial		
Follicular (days 1-4)	Menstrual	FSH and LH secretion low	Estradiol and progesterone remain low	Primary follicles grow	Outer two-thirds of endometrium is shed with accompanying bleeding		
Follicular (days 5–13)	Proliferative	FSH slightly higher than LH secretion in early follicular phase	Estradiol secretion rises (due to FSH stimulation of follicles)	Follicles grow; graafian follicle develops (due to FSH stimulation)	Mitotic division increases thickness of endometrium; spiral arteries develop (due to estradiol stimulation)		
Ovulatory (day 14)	Proliferative	LH surge (and increased FSH) stimulated by positive feedback from estradiol	Estradiol secretion falls	Graafian follicle ruptures and secondary oocyte is extruded into uterine tube	No change		
Luteal (days 15–28)	Secretory	LH and FSH decrease (due to negative feedback from steroids)	Progesterone and estrogen secretion increase, then fall	Development of corpus luteum (due to LH stimulation); regression of corpus luteum	Glandular development in endometrium (due to progesterone stimulation)		







- menstruation).
- Controlled by leptin

# Contraceptive Pill

- Includes synthetic estrogen and progesterone
  - Acts like a prolonged luteal phase
  - Produces negative-feedback inhibition of GnRH, so ovulation never occurs
  - The endometrium still proliferates.
  - Placebo pills are taken for 1 week to allow menstruation.

#### Rhythm Method of Contraception

- Pregnancy is unlikely as long as a couple has sex more than 6 days before ovulation and more than 1 day after.
- A woman can time ovulation by taking her temperature.
- This is a pretty good indicator for when ovulation occurs but not a very reliable form of birth control.





- activity and menses – Due to changes in the ovaries, not to
- decreases in FSH and LH
- FSH and LH levels are actually elevated due to lack of negative feedback.
- Usually occurs after age 50

#### Menopause

- Symptoms are due to loss of estrogen.
   Hot flashes are produced by vasomotor disturbances.
  - The walls of the urethra and vagina atrophy, and vaginal glands no longer produce lubrication.
  - After menopause, risk for atherosclerosis and osteoporosis increases.

#### Menopause and Osteoporosis

- Estrogen is needed for bone deposition, so menopausal women are at increased risk for osteoporosis.
  - Adipose tissue does make a weak form of estrogen called estrone.
  - Heavier women have a reduced risk of osteoporosis.

VI. Fertilization, Pregnancy, and Parturition

#### Fertilization

- Over 300 million sperm enter the female at ejaculation.
  - Only about 100 of these live to enter the fallopian tube.
  - In order to fertilize the ovum, a sperm must become capacitated. This takes at least 7 hours after ejaculation.
  - The sperm follow chemical and thermal signals toward the oocyte.

### Fertilization

- Fertilization usually occurs in the fallopian tubes.
- The association between the acrosome cap and zona pellucida cells stimulates the release of acrosomal enzymes.
  - These enzymes allow the sperm to "digest" its way into the oocyte.











#### **Cleavage and Blastocyst Formation**

- Cleavage begins 30–36 hours after fertilization.
  - Characterized by rapid mitosis, which forms a hollow ball of cells called the blastocyst
- · The blastocyst has two parts:
  - Embryoblast will become the fetus.
  - Trophoblast will become the chorion → placenta.







# Embryonic Stem Cells and Cloning Embryoblast cells cultured in vitro are called embryonic stem cells and are pluripotent = able to become any type of cell in the body. These cells might be used therapeutically to treat diabetes type I, Parkinson disease, or spinal cord injury.

# Implantation

 On the sixth day after fertilization, the trophoblast cells secrete an enzyme that allows the blastocyst to "eat" into the endometrium.









#### **Blastocyst Development**

- The fetal part of the blastocyst becomes: – Endoderm: will become the gut organs
  - Ectoderm: will become the skin and nervous system
- The mesoderm develops later and will become the muscles, bones, and connective tissues.



# Blastocyst Development

- The syncytiotrophoblast secretes proteindigesting enzymes and creates blood-filled cavities in the endometrium.
- The cytotrophoblast sends villi into these pools of maternal blood, forming the chorion frondosum.



### **Placenta Formation**

- As the blastocyst develops, the endometrium also changes to form the decidua basalis.
  - This joins with the chorion frondosum to form the placenta.
  - By the end of the second trimester, the spiral arteries of the endometrium have become tubes lined in cytotrophoblast.

#### Amniotic Sac Formation

- Part of the chorion envelops the growing embryo.
- The fluid-filled space between becomes the amniotic sac.
- This fluid comes from isotonic secretion, urine from the fetus, and sloughed cells.



### Amniocentesis

- Samples from the amniotic fluid can help diagnose genetic abnormalities such as Down syndrome.
  - Samples are taken at week 16.





- Maternal blood is also delivered to/from the placenta.
- In this way, maternal and fetal blood do not mix.
- Molecules diffuse across tissues of the placenta for exchange.

#### Molecule Exchange

- Oxygen and nutrients diffuse from maternal blood to fetal blood.
- Carbon dioxide and wastes diffuse from fetal blood to maternal blood.
- The placenta degrades maternal molecules that may harm the fetus.



# Endocrine Functions of the Placenta

- The placenta secretes protein hormones:
   Chorionic gonadotropin: acts like LH in the ovary and as a thyroid-stimulating hormone
  - Chorionic somatomammotropin: acts similar to growth hormone and prolactin
  - They both work to increase lipolysis to increase blood fatty acid levels and glucosesparing to increase blood glucose levels.

# Endocrine Functions of the Placenta

- The placenta secretes steroid hormones:
  - Estrogen and progesterone
  - Cholesterol from maternal blood and enzymes from the fetus are needed to produce these hormones.





#### Labor and Parturition

- The powerful contractions needed to expel the fetus occur in response to oxytocin from the mother's hypothalamus and prostaglandins from the placenta.
- Labor is initiated by rising levels of corticotropin-releasing hormone (CRH) from the placenta.

#### Labor and Parturition

- CRH stimulates the secretion of ACTH from the pituitary → cortisol from the adrenal glands of both mother and child.
  - Cortisol has positive feedback on CRH secretion.
  - It stimulates the production of surfactant in the fetal lungs.
- ACTH also stimulates the secretion of DHEAS in the fetus.

#### Labor and Parturition

- DHEAS is converted to estrogen in the placenta.
  - Estrogen makes the myometrium more sensitive to oxytocin and prostaglandins as more receptors for each--and more gap junctions between muscle cells--are formed.
  - Oxytocin and prostaglandins stimulate the release of Ca<sup>2+</sup>, which stimulates muscle contraction.



#### Mammary Glands

- Mammary glands are composed of 15–20 lobes separated by adipose tissue.
- Each lobe is made up of lobules composed of glandular alveoli that secrete milk in lactation.
- Milk flows from secondary tubules → mammary ducts → the lactiferous duct → nipple.



# Mammary Glands in Pregnancy

- The mammary glands change during pregnancy.
  - Cortisol, thyroxine, and insulin make the mammary glands more sensitive to rising progesterone and estrogen levels.
  - Progesterone stimulates alveoli growth.
  - Estrogen stimulates tubule and duct growth.

#### Lactation

- Prolactin from the pituitary gland stimulates the production of milk proteins.
   – Casein and lactalbumin
- Prolactin is inhibited by PIH from the pituitary gland. PIH is stimulated by estrogen secretion.
  - When the placenta is shed at birth, estrogen levels drop, lifting inhibition on prolactin.









