



NOTES

SEXUAL DEVELOPMENT

DEVELOPMENT OF THE REPRODUCTIVE SYSTEM

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SEXUAL DIFFERENTIATION

- Series of events begins at conception, ends with sexual characteristics acquisition (designated biologically male/female)
- During first five gestational weeks
 - Gonadal ridge develops, later becomes differentiated gonads
- Week 6
 - Primordial germ cells start migrating from yolk sac towards gonadal ridge
- Week 7
 - Primordial germ cells promote gene expression contained in sex chromosomes
- Wolffian, Müllerian ducts: structures that will develop into rest of reproductive tract; remain undifferentiated until week 8

MALE DEVELOPMENT

Male gonadal development

- Embryo genetically male → gene expression in Sex-determining Region in **Y chromosome (SRY)** promoted
 - SRY-region genes promote **testis-determining factor production** → testis-determining factor acts on undifferentiated gonads → gonadal transformation into **testes**
 - Gonadal ridge becomes seminiferous tubules, rete testis, straight tubules
- Testes contain three functional cell types
 - **Germ cells**: produce spermatogonia → produce male gametes in puberty
 - **Sertoli cells**: synthesize anti-Müllerian hormone
 - **Leydig cells**: synthesize testosterone

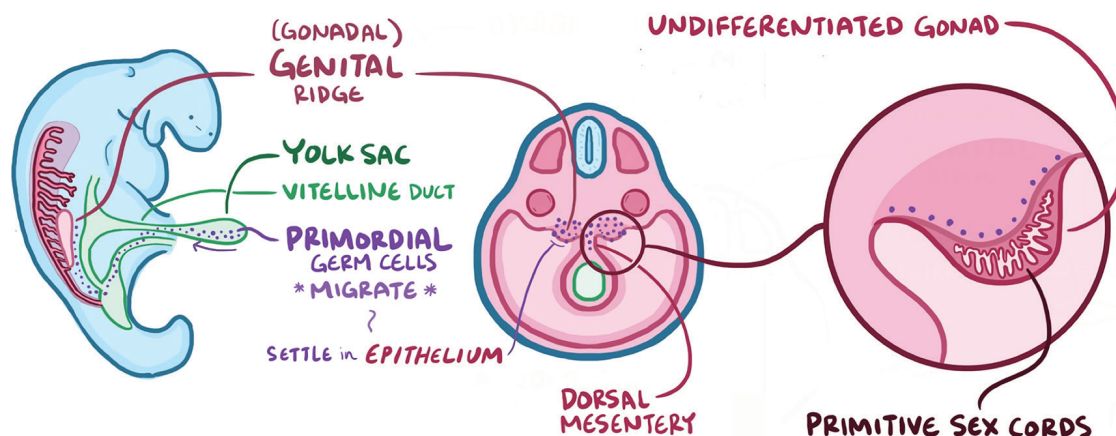


Figure 66.1 Illustration of the migration of primordial germ cells to the gonadal ridge in week 6. At this point, the gonad is undifferentiated, meaning that it can develop into ovaries or testes.

Male internal reproductive organ development

- Wolffian ducts give rise to male internal genitalia
 - AKA mesonephric duct/mesonephros
 - Meso = middle, in between; nephros = kidney
 - Two functions: connects primitive kidney to cloaca; develops into male genitalia
 - Growth, differentiation stimulated by testosterone
- Male internal reproductive organ development depends on Sertoli cells, Leydig cells, urogenital sinus
- Sertoli cells: synthesize, secrete anti-Müllerian hormone; AKA Müllerian inhibiting substance
 - Promotes Müllerian/paramesonephric-duct atrophy
- Leydig cells: synthesize, secrete testosterone → become internal male genitalia

- Promotes Wolffian/mesonephric-duct growth, differentiation

- Urogenital sinus: develops into external reproductive organs; undifferentiated until gestational week 9
 - Urethral folds → urethra (both)
 - Labioscrotal swellings → scrotum
 - Primordial phallus → penis

Male external reproductive organ development

- Male external genitalia differentiation from urogenital sinus depends on testosterone presence
 - 5 alpha reductase in target tissues converts testosterone → more potent dihydrotestosterone
 - Dihydrotestosterone: responsible for masculinizing external genitalia

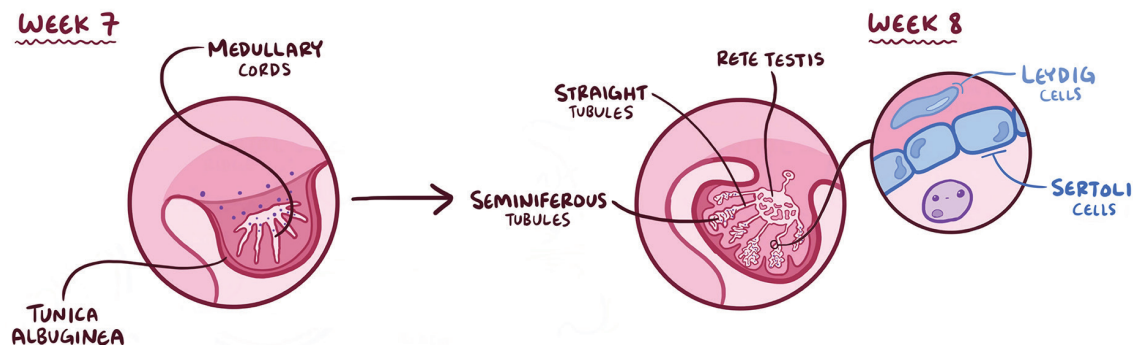


Figure 66.2 Biologically male sexual differentiation, week 7: genes in Sex-determining Region of Y chromosome (SRY) code for testis-determining factor (which initiates development of testes). Primitive sex cords → medullary cords that carry primitive germ cells deeper into mesoderm. The surface epithelial layer of each gonad thins out → tunica albuginea. Later, medullary cords → seminiferous tubules, straight tubules, rete testis. The primordial germ cells settle in seminiferous tubules mature into dormant spermatogonia. During puberty, spermatogonia start dividing → sperm (male gametes). During week 8, some cells in the seminiferous tubule walls differentiate into Sertoli cells, and cells between the seminiferous tubules differentiate into Leydig cells.

FEMALE DEVELOPMENT

Female gonadal development

- Without functional SRY gene
 - Week 9: ovaries begin developing
 - Week 10: ovarian cortex, inner medulla distinguishable
- Ovaries contain three functional cell types
 - Germ cells: produce oögonia; located in ovarian cortex (oögonia—haploid cells that remain arrested in prophase 1 of meiosis until ovulation)
 - Granulosa cells: synthesize estradiol
 - Theca cells: synthesize progesterone
- Ovarian follicle: oögonium surrounded by granulosa cells, connective tissue

Female internal reproductive organ development

- Müllerian duct → female genitalia
 - AKA paramesonephric duct/paramesonephros
 - Para = on the side of; meso = middle, in between; nephros = kidney
- Female internal reproductive organ development primarily depends on testes absence

- Lack of testosterone induces Wolffian duct degeneration
- Lack of anti-Müllerian hormone promotes Müllerian ducts persistence → develop into fallopian tubes, uterus, upper ⅓ of vaginal canal
- Rest of female reproductive organs arise from urogenital sinus

Female external reproductive organ development

- Urogenital sinus develops into external reproductive organs; undifferentiated until gestational week 9
 - Urethral folds → urethra (both ♂), labia minora
 - Labioscrotal swellings → labia majora, mons pubis
 - Primordial phallus → clitoris
- Female external genitalia differentiation
 - Androgen absence-dependent (testosterone, dihydrotestosterone)
- Phenotypic differentiation complete at week 12 → earliest ultrasound-based sex-determination date

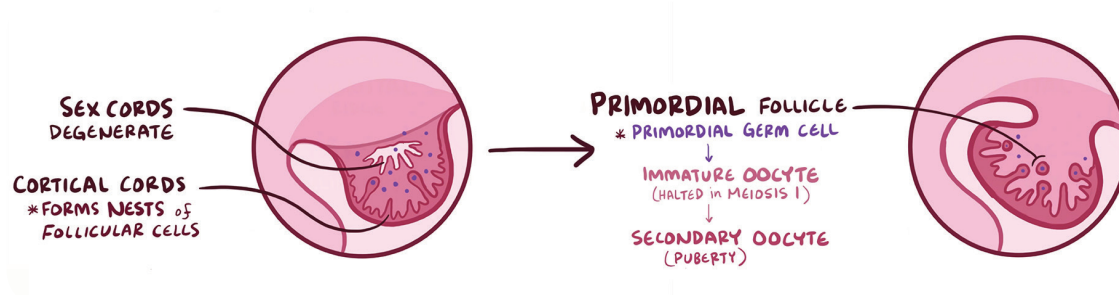


Figure 66.3 Biologically-female sexual differentiation. Since there is no Y chromosome to secrete Testis-determining factor, the undifferentiated gonads develop into ovaries. The rest of the reproductive tract acquires female characteristics in the absence of testosterone.

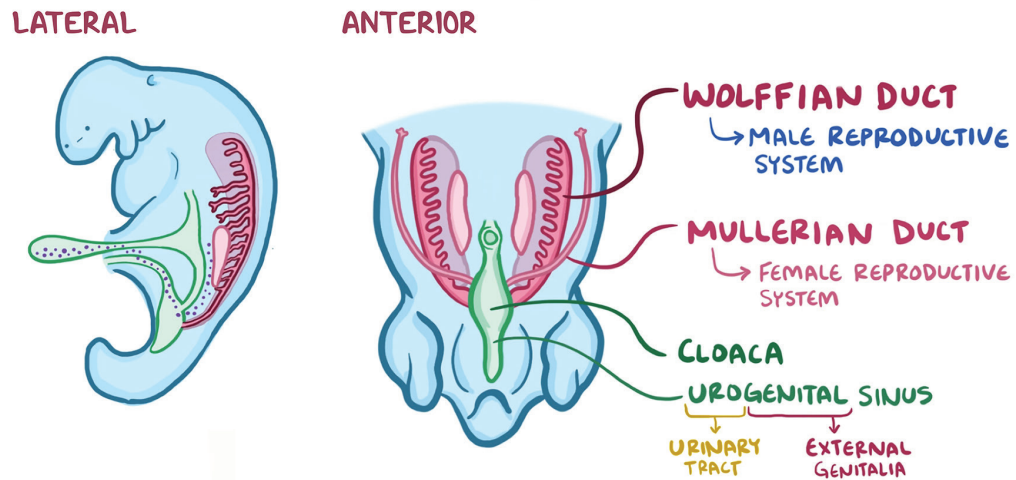
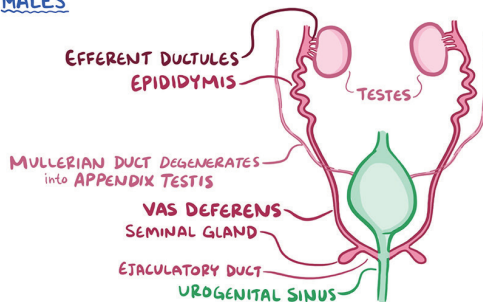


Figure 66.4 The genital ducts are initially undifferentiated, tubular structures that run down the embryo's back inside the two nephrogenic cords on either side of the embryo. The Wolffian and Müllerian ducts start in the thoracic and upper lumbar region and continue down the embryo's back until they open into the part of the cloaca called the urogenital sinus.

MALES



DESCENT of TESTES ~ by week 12

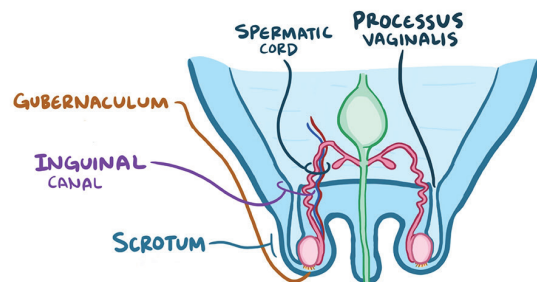
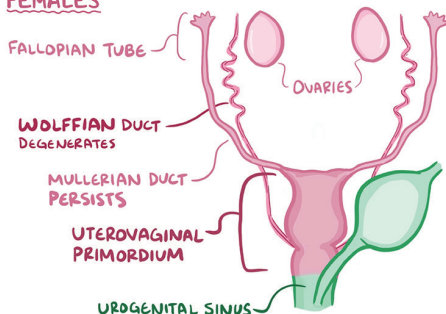


Figure 66.5 Male internal reproductive organ differentiation and descent of gonads.

FEMALES



DESCENT of OVARIES

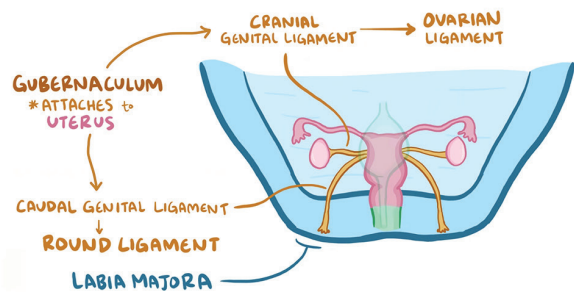


Figure 66.6 Female internal reproductive organ differentiation and descent of gonads.

SEX VS. GENDER

- Gender
 - Socially-constructed characteristics/ behaviors associated with biologically male/female people
 - E.g. norms, roles, relationships between individuals
- Genetic sex
 - Individual's chromosomal composition
 - XY: males
 - XX: females
 - Established by oocyte, sperm cell fusion
- Gonadal sex
 - Individual's reproductive organs
 - Male: testes
 - Female: ovaries
- Phenotypic sex

Internal, external reproductive organ structure

- Male genitalia
 - **Internal:** prostate, seminal vesicles, vas deferens, epididymis
 - **External:** penis, scrotum
- Female genitalia
 - **Internal:** fallopian tubes, uterus, upper $\frac{1}{3}$ vaginal canal
 - **External:** clitoris, labia majora, labia minora, lower $\frac{2}{3}$ vaginal canal

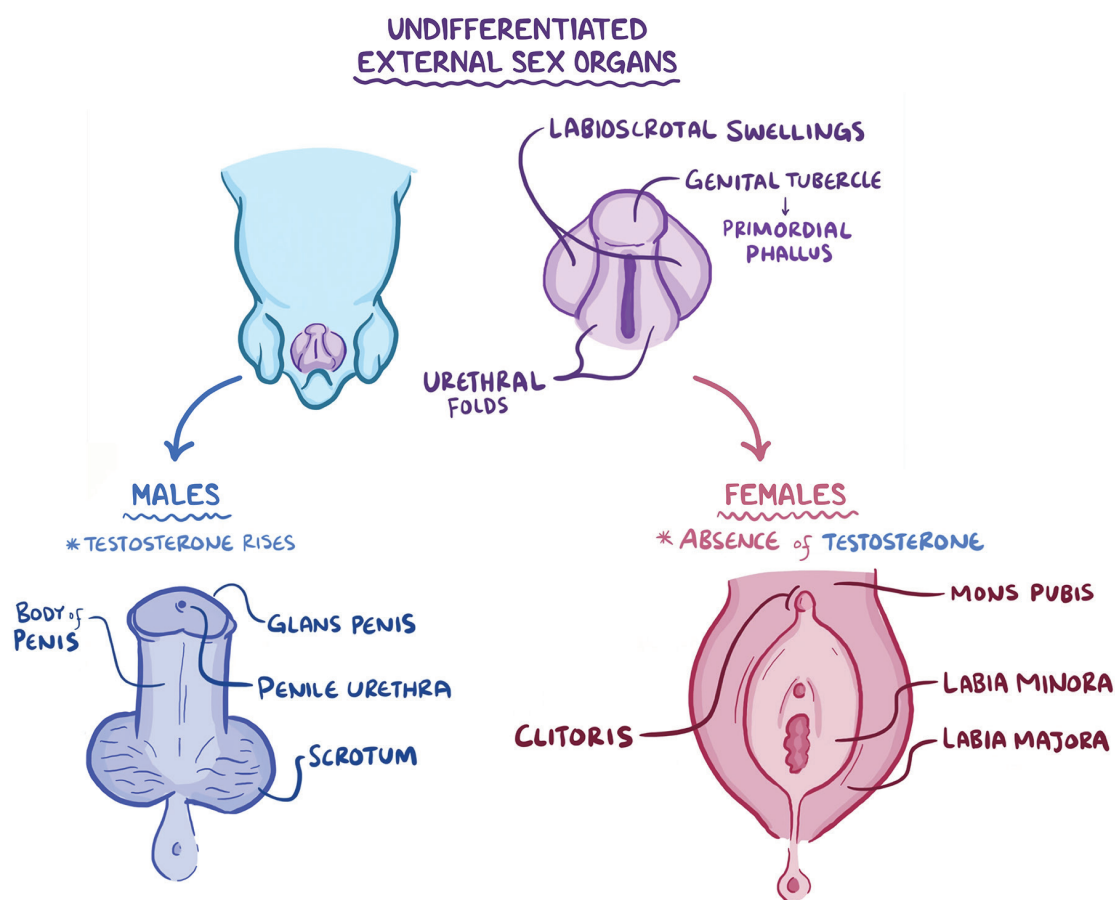


Figure 66.7 Male and female external sex organs. Phenotypic differentiation is complete at week 12.

PUBERTY & TANNER STAGING

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PUBERTY

- Sexual maturation process involving endocrine, physical changes; controlled by hypothalamic-pituitary-gonadal axis
- Begins between ages 10–14 in females; between age 12–16 in males

GnRH secretion

- Pulses from hypothalamus regulate luteinizing hormone (LH), follicle-stimulating hormone (FSH) secretion from anterior pituitary → development of sexual characteristics
 - Primary sex characteristics: genitals (organs directly involved in sexual reproduction)
 - Secondary sex characteristics: sex-specific physical characteristic not necessary involved in sexual reproduction (e.g. pubic hair—both sexes, voice changes—males, breast development—females)

Gamete production

- Oocytes (females); sperm (males)
- Males: LH acts on Leydig cells → produces testosterone; FSH acts on Sertoli cells → produces sperm
- Females: LH acts on ovarian follicles → produces progesterone, androstenedione (converted into estrogen)
 - Estrogen, progesterone levels vary according to menstrual cycle phases

Gonadal steroid production

- Testosterone (males), estradiol (females) secretion → ↑ circulating sex hormones
- Secondary sexual characteristics develop
- Stimulate bone growth, ossification
- Involved in growth hormone production → growth spurt

EVENTS OF PUBERTY

Gonadarche

- Gonadal activation by FSH, LH

Adrenarche

- ↑ adrenal androgen production by adrenal cortex

Thelarche

- Breast tissue appears
 - Ovarian estradiol-guided

Menarche

- First menstruation occurs
 - Ovarian estradiol-guided
 - First menstrual cycles tend to be anovulatory

Spermarche

- First sperm production occurs
 - FSH, LH, testosterone-guided
 - Nocturnal sperm emissions, sperm appears in urine

Pubarche

- Pubic hair appears
 - Adrenal androgens-guided
 - Association: body hair; acne; apocrine sweat glands activation

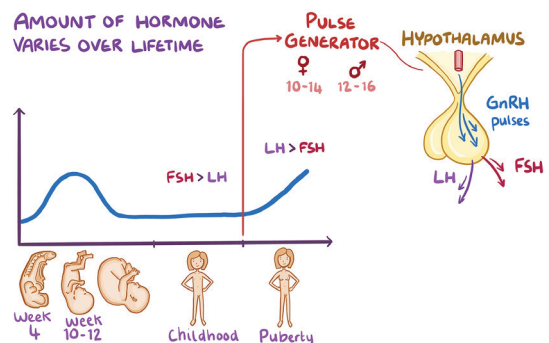


Figure 66.8 Puberty begins when pulse generator in hypothalamus begins secreting GnRH in pulses → pulsatile secretion of FSH and LH. In puberty, GnRH receptors in anterior pituitary become more sensitive to GnRH stimulation: small ↑ GnRH = large ↑ FSH, LH levels.

TANNER STAGING

- System for describing predictable steps during sexual maturation
- Centers on two, **independent criteria**
 - **Appearance:** **pubic hair** in males, females
 - **Genital development:** ↑ **testicular volume, penile growth** (males); **breast development** (females)

FIVE CATEGORIES OF TANNER STAGING

Stage 1: pre-pubertal

- ♂ No pubic hair present in either sex
- ♂ Small penis, testes
- ♀ Have flat-chest

Stage 2

- ♂ Soft pubic hair appears
- ♂ Measurable testes enlargement
- ♀ Breast buds appear

Stage 3

- ♂ Pubic hair becomes coarser
- ♂ Penis begins to enlarge in size, length
- ♀ Breast mounds form

Stage 4

- ♂ Pubic hair begins to cover pubic area
- ♂ Penis begins to widen
- ♀ Breast enlargement forms “mound-on-mound” breast contour

Stage 5: adult

- ♂ Pubic hair extends to inner thigh
- ♂ Penis, testes enlarged to adult size
- ♀ Breast takes on adult contour

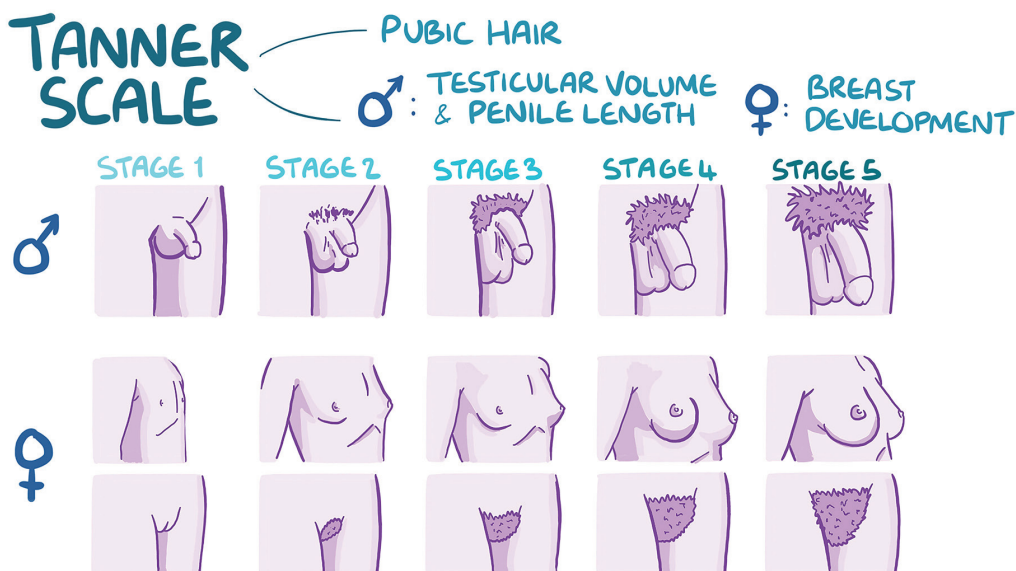


Figure 66.9 Illustration of the five stages of the Tanner scale in males and females.