Sexual Development

Stages of Development

- Development passes through distinct stages, the first of which is fertilization, when one sperm enters one ovum.
- To enter an ovum, a sperm must undergo the processes of capacitation and acrosome reaction.
- Enzymes from the ovum close its surrounding zona pellucida, so that no other sperm may enter.
6.3 Fertilization and production of the conceptus (Part 1)

- The second meiotic division occurs in the ovum, creating two pronuclei that, in turn, divide to make a 2-celled organism called a conceptus.

First polar body

Second polar body

At ovulation, the secondary oocyte halts in metaphase of meiosis II. Sperm have already completed meiosis II.

At fertilization, the secondary oocyte resumes meiosis II. Sister chromatids are pulled apart at anaphase.

One set of chromatids is discarded as the second polar body. The other becomes the female pronucleus. Meiosis II is complete. The sperm head becomes the male pronucleus.

6.3 Fertilization and production of the conceptus (Part 2)

DNA replication
Now each chromosome again consists of two sister chromatids.

The pronuclear membranes break down, and a spindle forms. This is metaphase of the first mitotic division of the zygote.

Anaphase
Sister chromatids are pulled apart. Cytoplasm starts to divide.

A 2-celled conceptus is formed. Each cell is diploid, possessing maternal and paternal versions of homologous chromosomes.
6 Stages of Development (cont’d)

• The conceptus undergoes additional cell division—a 16-cell stage (a morula (D)) and a 32-cell stage (a blastocyst (E)); the blastocyst implants itself in the wall of the uterus and begins to secrete the hormone human chorionic gonadotropin (hCG).

• The inner cell mass of the blastocyst becomes the amnion, which contains amniotic fluid in which the embryo/fetus lives throughout the pregnancy.
Stages of Development (cont’d)

• There are three kinds of cells in the embryo: the ectoderm (which becomes skin and the nervous system); the endoderm (which becomes the lungs and the lining of the gut and other organs); and the mesoderm (which becomes the cardiovascular and musculoskeletal systems).

• The placenta and umbilical cord also develop from these cells.

Stages of Development (cont’d)

• The embryonic phase is complete by about 7 weeks, at which point the embryo is termed a fetus; the development of the fetus involves growth and functional maturation of body systems.

• The fetus moves, sucks its thumb, responds to loud sounds, drinks amniotic fluid, voids urine, wakes, and sleeps.

• Minutes after birth, newborns reorganize their circulatory system according to the adult pattern.
Determination of Genetic Sex

- With few exceptions, any embryo that possesses at least one Y chromosome develops as a male, meaning that the father determines its sex.
- However, without the sex-determining region of the Y chromosome (SRY), the fetus will develop as female, the default pathway.
- Undifferentiated genital ridges develop into ovaries and testes; SRY must be present to cause cells to become Sertoli cells which, in turn, cause gonads to become testes.

6.8 The genetic basis of sex determination
• *DAX-1* is a gene located on the X chromosome; in XX embryos, *DAX-1* turns genital ridges into ovaries.

• Primordial germ cells (sperm and ova) migrate from the yolk sac into the gonads and develop either into primary oocytes in the ovary or into stem cells that give rise to sperm.

• To preserve balanced gene expression in the two sexes, each cell present in the female conceptus at the time of X inactivation picks one of its two X chromosomes to inactivate.

• The presence or absence of Barr bodies, formed by the genes on the inactivated X chromosome, offers a simple method of determining chromosomal sex.
Development of Internal Reproductive Tracts and External Genitalia

- Two sets of structures, the Wolffian ducts and the Müllerian ducts, are precursors of the male and female reproductive tracts; both sexes have a pair of both of these ducts early in development.

- Because the female developmental process is the default pathway, nothing extra is required to rid the embryo of the Wolffian ducts; the Müllerian ducts persist and become oviducts, uterus, and the deeper part of the vagina.

Development of Internal Reproductive Tracts and External Genitalia (Cont’d)

- The male developmental process involves two hormones —the anti-Müllerian hormone (AMH) secreted by Sertoli cells to suppress Müllerian duct development, and testosterone secreted by Leydig cells to stimulate Wolffian duct development.

- The remaining Wolffian ducts become the epididymis, vas deferens, ejaculatory ducts, and seminal vesicles.
6.12 Development of the male and female reproductive tracts (Part 2)

Female and male external genitalia consist of homologous structures.

Female external genitalia develop by default; in male fetuses, testosterone and dihydrotestosterone (DHT) are required for normal development of the external genitalia.
• Androgen receptors express the enzyme reductase, which converts testosterone to DHT for the formation of the penis and the scrotum.

• Ovaries descend into the pelvis after birth and end up on either side of the uterus.

• The testes descend into the pelvis at 6–7 months postconception; shortly before birth they enter the scrotum.
“True Hermaphrodite”

- Gonadal Intersexuality
  - Expression of female and male genitals
  - Both, ovate testes

- Turners Syndrome
  - X0
  - 1 out of every 2500 female births
  - Short stature
  - Lymphoedema (swelling) of the hands and feet
  - Broad chest (shield chest) and widely-spaced nipples
  - Low hairline, Low-set ears
  - Reproductive sterility
  - Rudimentary ovaries
  - absence of a menstrual period
  - Increased weight, obesity
  - Characteristic facial features
  - Webbing of the neck
  - Poor breast development
  - Horseshoe kidney
  - Visual impairments sclera, cornea, Glaucoma, etc.
  - Ear infections and hearing loss.
Turner’s and Klinefelter’s syndromes

- Klinefelter’s Syndrome
  - XXY, XXXY
  - 1/500
  - Small testes, reduced fertility
  - Gynecomastia – enlarged breasts
  - Feminized hips
  - Learning disabilities
  - Low sex drive

Androgen Insensitivity Syndrome

- AIS
  - androgen receptor sites don’t take androgen
  - 1/10,000
  - The XY body develops into a female expression
  - Sterile
  - Tests reside inside
  - Taller
Congenital Adrenal Hyperplasia

- CAH
  - 1/16,000
  - ambiguous genitalia (fused labia, large clitoris)
  - early pubic hair
  - precocious puberty or failure of puberty to occur (sexual infantilism: absent or delayed puberty)
  - excessive facial hair, virilization, and/or menstrual irregularity in adolescence
  - infertility, lack of menstruation
  - hypertension

Sexual Dimorphism Results from Hormone Exposure During Sensitive Periods

- The CNS contains sexually dimorphic structures such as groups of cells called nuclei.
- One such group of cells, the sexually dimorphic nucleus of the preoptic area (SDN-POA) is larger in male rats than in female rats.
- Female rats can develop a larger, male-sized SDN-POA if exposed to testosterone during perinatal development.
- Conversely, male rats can develop a smaller, female-sized SDN-POA when castrated early in development.
6.16 Sexual differentiation in the hypothalamus (Part 1)

(A) Male

A normal male rat shows a testosterone peak perinatally (just before and around birth)...

...and a second rise at puberty.

The male SDN-POA is large.

(B) Female

A normal female rat lacks both the perinatal and pubertal rises in testosterone levels...

...and her SDN-POA is small.

Conception \underline{Birth} \underline{Sensitive period} \underline{Adult}

6.16 Sexual differentiation in the hypothalamus (Part 2)

(C) Female

A female injected with testosterone at the time of the male perinatal surge...

...develops a large SDN-POA.

Testosterone

(D) Female

Injections at later times, such as at puberty...

...have no effect on the size of a female's SDN-POA.

Conception \underline{Birth} \underline{Sensitive period} \underline{Adult}
In rats, a group of cells known as the anteroventral periventricular nucleus, or AVPV, is larger in females than in males.

In humans, a cell group believed to be equivalent to SDN-POA, the third interstitial nucleus of the anterior hypothalamus (INAH3), is larger in men than in women.

Men’s brains produce more of the neurotransmitter serotonin than do women’s brains.

Hormone exposure during sensitive periods guides not only anatomical sex differences, but behavioral sex differences as well.

Exposure to hormones during sensitive periods in development helps to organize the formation of brain circuits that support behavioral sex differences.

Later exposure to hormones can then activate these brain circuits.

Genes continue to play a part in postnatal sexual development as they interact with the environment.
Puberty Marks Sexual Maturation

- During early infancy, the levels of circulating gonadotropins (LH and FSH) are high in both sexes, and testosterone is high in infant boys until from 6 to 9 months of age.
- Throughout most of childhood, there are no marked differences in sex hormone levels between boys and girls.
- The pubertal growth spurt begins at about age 11 for girls and age 13 for boys; girls develop wider hips and boys develop wider shoulders.

6.20 Growth velocity curves for boys and girls
Puberty Marks Sexual Maturation (cont’d)

• Puberty, which has been starting at progressively younger ages, marks the transition to adulthood as changes occur in the external genitalia, secondary sexual characteristics, internal reproductive tract, and gonads.

6.23 Puberty is starting earlier
Puberty Marks Sexual Maturation (cont’d)

- Puberty, perhaps triggered by the attainment of a critical body weight, is caused by a rise in circulating levels of adrenal and gonadal sex steroids and growth hormone. Girls experience the onset of menstruation; boys experience a first ejaculation.
  - breast development
  - pubic or underarm hair development
  - rapid height growth - a growth "spurt"
  - onset of menstruation
  - acne
  - "mature" body odor