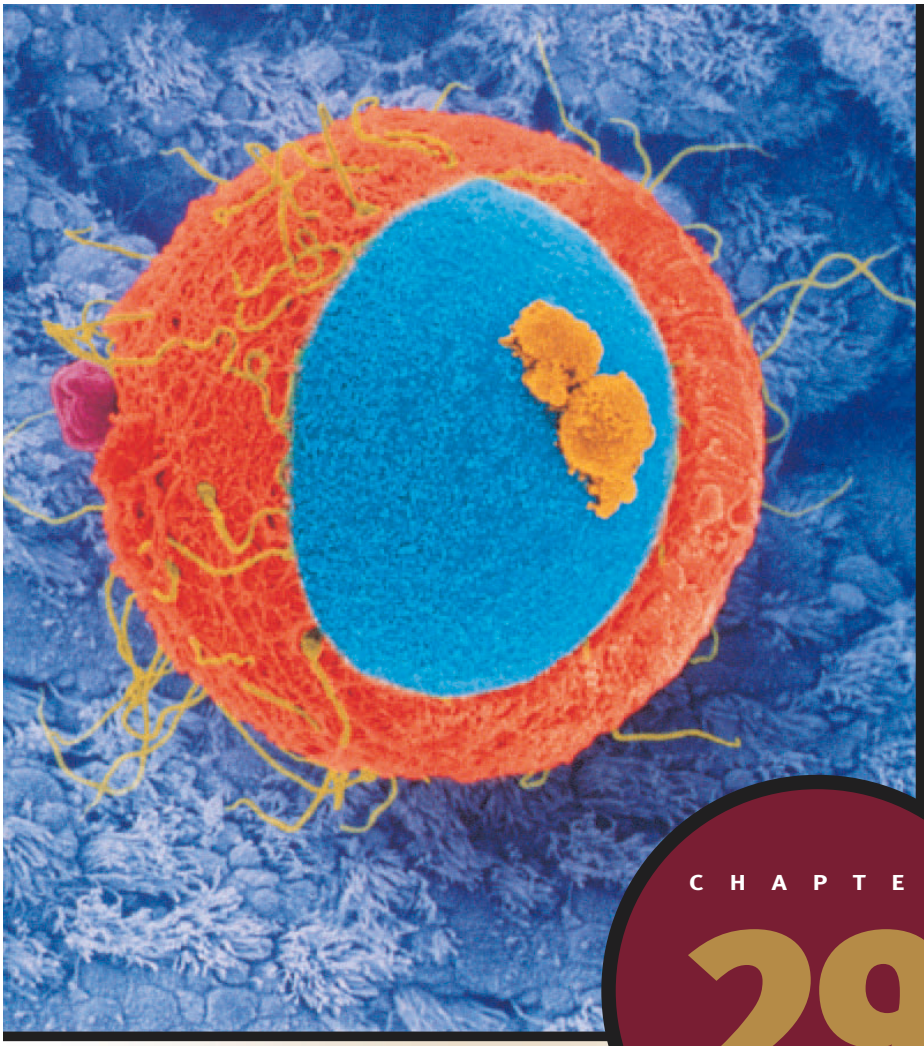


Colorized SEM of an oocyte with sperm cells on the surface.

Development, Growth, Aging, and Genetics

CHAPTER 29

The stages of life and associated activities are issues of great interest in today's society. We tend to view life stages very differently today than we did just a few years ago. For example, in 1960, 20% of males and 12% of females graduating from high school attended college. Today, over half of all people 25 and older have attended some college. In addition, there are many more nontraditional college students than there were just a few years ago.

In 1900, only 5% of the U.S. population was over age 65. Today, about 16% of the population is over age 65, and by 2030 more than 20% will be older than 65. The average life expectancy in 1900 was about 47 years, in 1940 it was about 63 years, and today it is about 78 years. In 1900, nearly 70% of all males over age 65 were still working; today only about 20% are still working past age 65. Older people are healthier and more active than they have ever been.

The life span is usually considered the period between birth and death; however, the 9 months before birth are a critical part of a person's existence. What happens in these 9 months profoundly affects the rest of a person's life. Although most people develop normally and are born without defects, approximately three out of every 100 people are born with a birth defect so severe that it requires medical attention during the first year of life. Later in life, many more people discover previously unknown problems, such as the tendency to develop asthma, certain brain disorders, or cancer. This chapter discusses *prenatal development* (1062), *parturition* (1085), *the newborn* (1088), *lactation* (1090), the *first year after birth* (1092), *life stages* (1092), *aging* (1092), *death* (1094), and *genetics* (1094).

Prenatal Development

Objectives

- *List the prenatal periods, and state the major events associated with each.*
- *Describe the events of fertilization and early cell division.*
- *Describe the events during morula and blastocyst formation.*

The prenatal period is the period from conception until birth, and it is divided into three parts: (1) the **germinal period**—approximately the first 2 weeks of development during which the primitive germ layers are formed; (2) the **embryonic period**—from about the second to the end of the eighth week of development, during which the major organ systems come into existence; and (3) the **fetal period**—the last 30 weeks of the prenatal period, during which the organ systems grow and become more mature.

The medical community in general uses the mother's **last menstrual period (LMP)** to calculate the **clinical age** of the unborn child. Most embryologists, on the other hand, use **postovulatory age** to describe the timing of developmental events. Postovulatory age is used in this book. Because ovulation occurs about 14 days after LMP and fertilization occurs near the time of ovulation, it's assumed that postovulatory age is 14 days less than clinical age.

Fertilization

Fertilization is the process by which a sperm cell attaches to a secondary oocyte, the sperm head enters the oocyte cytoplasm, and joins the oocyte pronucleus to form a new nucleus (figure 29.1). Only a few dozen sperm cells, of the several hundred million deposited in the vagina during sexual intercourse, reach the vicinity of the secondary oocyte in the ampulla of the uterine tube. The **corona radiata** is a barrier to the sperm cells reaching the oocyte. The sperm cells are propelled through the loose matrix between the follicular cells of the corona radiata by the action of their flagella. The **zona pellucida** is an extracellular membrane, comprised mostly of glycoproteins, between the corona radiata and the oocyte. One particular zona pellucida glycoprotein, called **ZP3,** is a species-specific sperm cell receptor, to which molecules on the acrosomal cap of the sperm cell bind. This binding initiates the **acrosomal reaction,** which results in the release of digestive enzymes, primarily hyaluronidase.

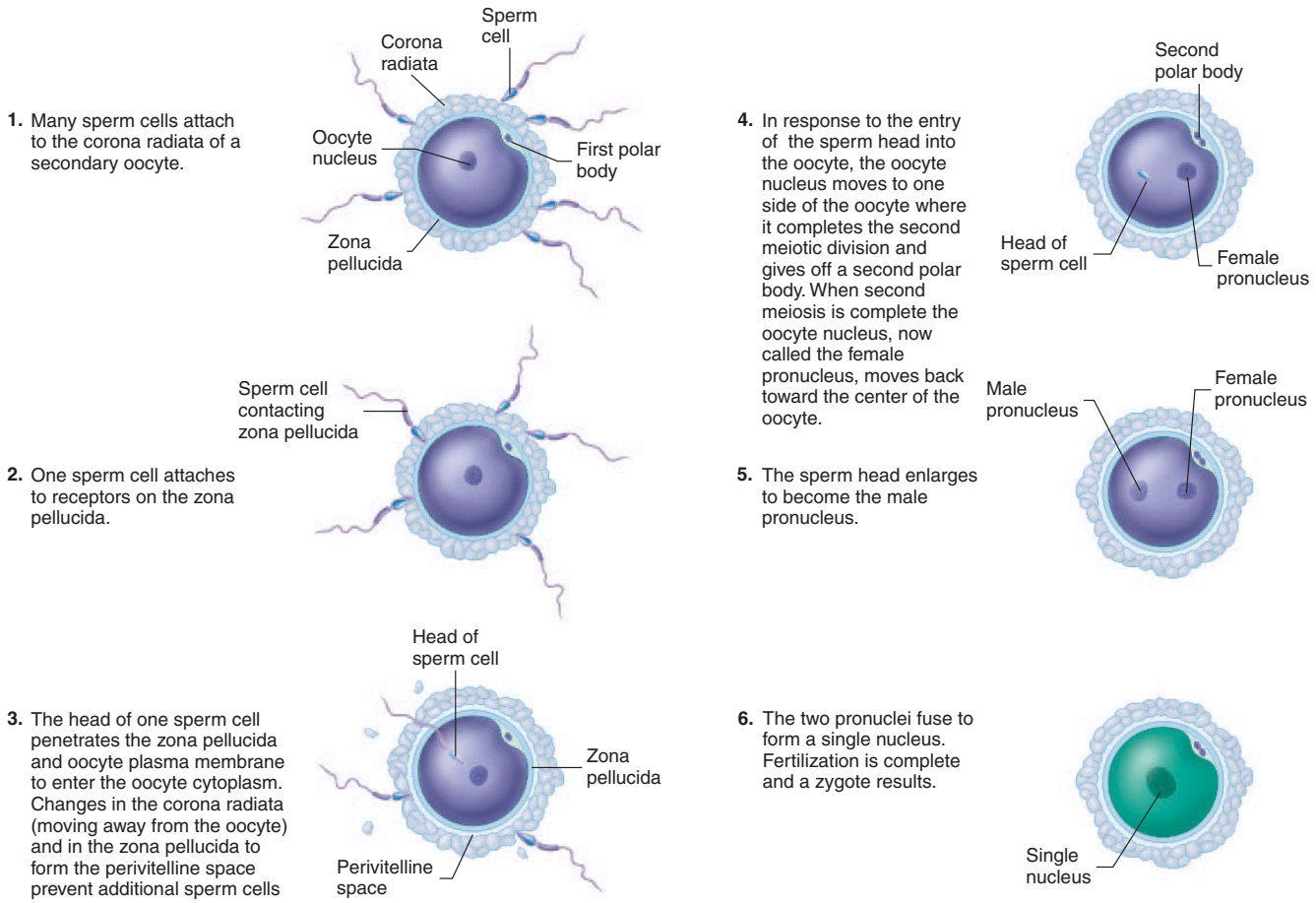


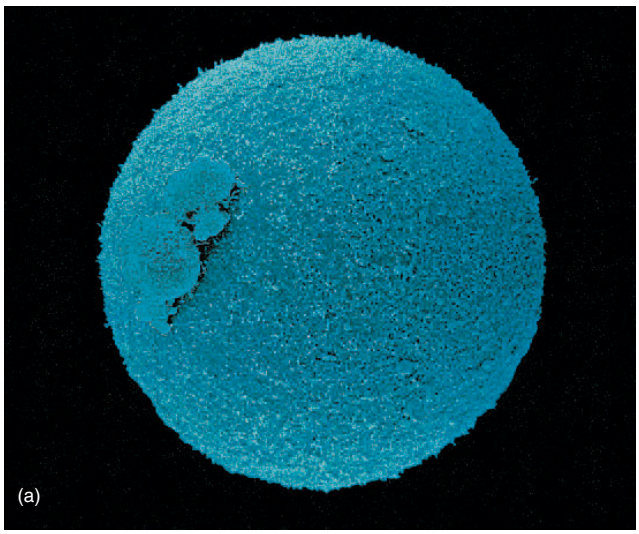
Figure 29.1 Fertilization

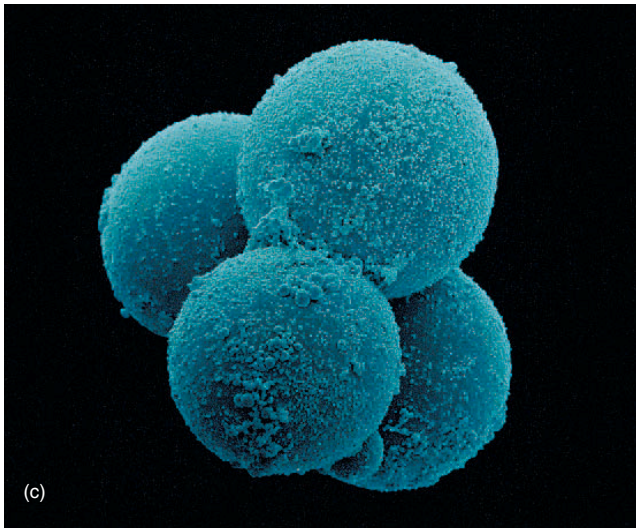
The first sperm cell through the zona pellucida attaches to the integrin α6β1 on the surface of the oocyte plasma membrane. This attachment causes depolarization of the oocyte plasma membrane within 2–3 seconds after sperm cell attachment. This depolarization, called the **fast block to polyspermy,** prevents additional sperm from attaching to the oocyte plasma membrane. Depolarization causes the intracellular release of Ca^{2+}, which, in turn, causes the exocytosis of water and other molecules from secretory vesicles, referred to as cortical granules, on the inner surface of the oocyte plasma membrane. The released fluid causes the oocyte to shrink and the zona pellucida to denature and expand away from the oocyte. As the result of denaturation of the zona pellucida, ZP3 is inactivated, and no additional sperm cells can attach. This reaction is referred to as the **slow block to polyspermy.** The fluid-filled space between the oocyte plasma membrane and the zona pellucida is called the **perivitelline space.**

Entrance of a sperm cell into the oocyte stimulates the female nucleus to undergo the second meiotic division, and the second polar body is formed. The nucleus that remains after the second meiotic division, called the **female pronucleus,** moves to the center of the oocyte, where it meets the enlarged head of the sperm cell, the **male pronucleus.** Both the male and female pronuclei are haploid, each having one-half of each chromosome pair (see chapter 3). Fusion of the pronuclei completes the process of fertilization and restores the diploid number of chromosomes. The product of fertilization is a single cell, the **zygote** (zī′gōt; figure 29.2*a*).

Early Cell Division

About 18–39 hours after fertilization, the zygote divides to form two cells. Those two cells divide to form four cells, which divide to form eight cells, and so on (figure 29.2*b–d*). The cells of this dividing embryonic mass are referred to as **pluripotent** (ploo-rip′ō-tent;





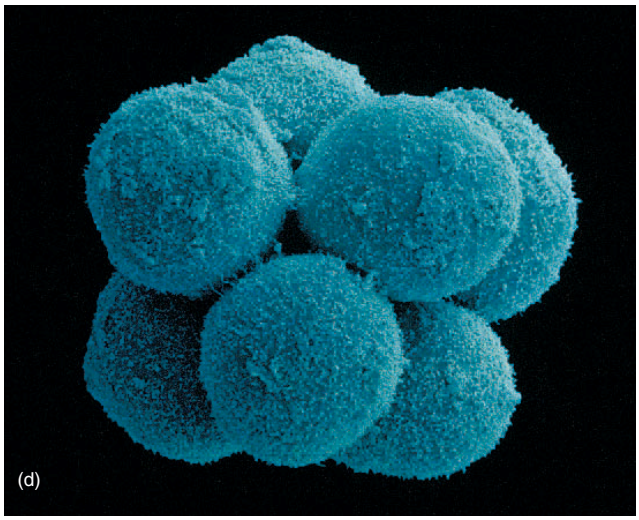


Figure 29.2 Early Stages of Human Development

(*a*) Zygote (120 μm in diameter). (*b*)–(*d*) During the early cell divisions, the zygote divides, and then the embryonic mass divides into more and more cells, but the total size of the embryonic mass remains relatively constant. (*b*) Two cells. (*c*) Four cells. (*d*) Eight cells.

multiple-powered), which means that any cell of the mass has the ability to develop into a wide range of tissues. As a result, the total number of embryonic cells can decrease, increase, or reorganize without affecting the normal development of the embryo.

Twins

In rare cases, following early cell divisions, the cells may separate and develop to form two individuals, called "identical," or **monozygotic, twins.** Identical twins have identical genetic information in their cells. Other mechanisms that occur a little later in development can also cause identical twins. Occasionally a woman may ovulate two or more secondary oocytes at the same time. Fertilization of two oocytes by different sperm cells results in "fraternal," or **dizygotic, twins.** Multiple ovulations can occur naturally or be stimulated by injection of drugs that stimulate gonadotropin release. These drugs are sometimes used to treat certain forms of infertility. This drug treatment may result in multiple births in women undergoing the treatment.

Morula and Blastocyst

Once the dividing embryonic mass is a solid ball of 12 or more cells, it is a sphere composed of numerous smaller spheres and is, therefore, called a **morula** (mōr′oo-lă, mōr′ū-lă; mulberry; figure 29.3). Three or 4 days after ovulation, the morula consists of about 32 cells. Near this time, a fluid-filled cavity called the **blastocele** (blas′tō-sēl) begins to appear approximately in the center of the cellular mass. The hollow sphere that results is called a **blastocyst** (blas′tō-sist; see figure 29.3). A single layer of cells, the **trophoblast** (trof′ō-blast, trō′fō-blast; feeding layer), surrounds most of the blastocele, but at one end of the blastocyst the cells are several layers thick. The thickened area is the **inner cell mass** and is the tissue from which the embryo develops. The trophoblast forms the placenta and the membranes (chorion and amnion) surrounding the embryo.

Stem Cell Research

Cells of the inner cell mass are referred to as **stem cells** because they theoretically have the potential to become any type of tissue in the body. Researchers are taking advantage of this pluripotent potential of stem cells to develop normal tissue lines to supplement defective tissues in people with a wide variety of diseases. Current research focuses on the right combination of growth factors that can drive stem cell lines toward a specific tissue type. For example, pancreatic islet cells, derived from stem cells, may be implanted into the pancreas of a person with diabetes to provide the needed supply of insulin.

The issue of stem cell research is very controversial, with opponents arguing that the blastocyst is a living human being and that the blastocyst has to be killed to obtain the stem cells. Their argument is that the sanctity of human life extends well into the prenatal period to include the earliest stages of human development. Proponents of stem cell research argue that the sanctity and quality of human life for those suffering from debilitating, often fatal, and currently incurable diseases is worth the price. Other proponents argue that the definition of a human being does not extend to the blastocyst. The debate will probably not end soon.

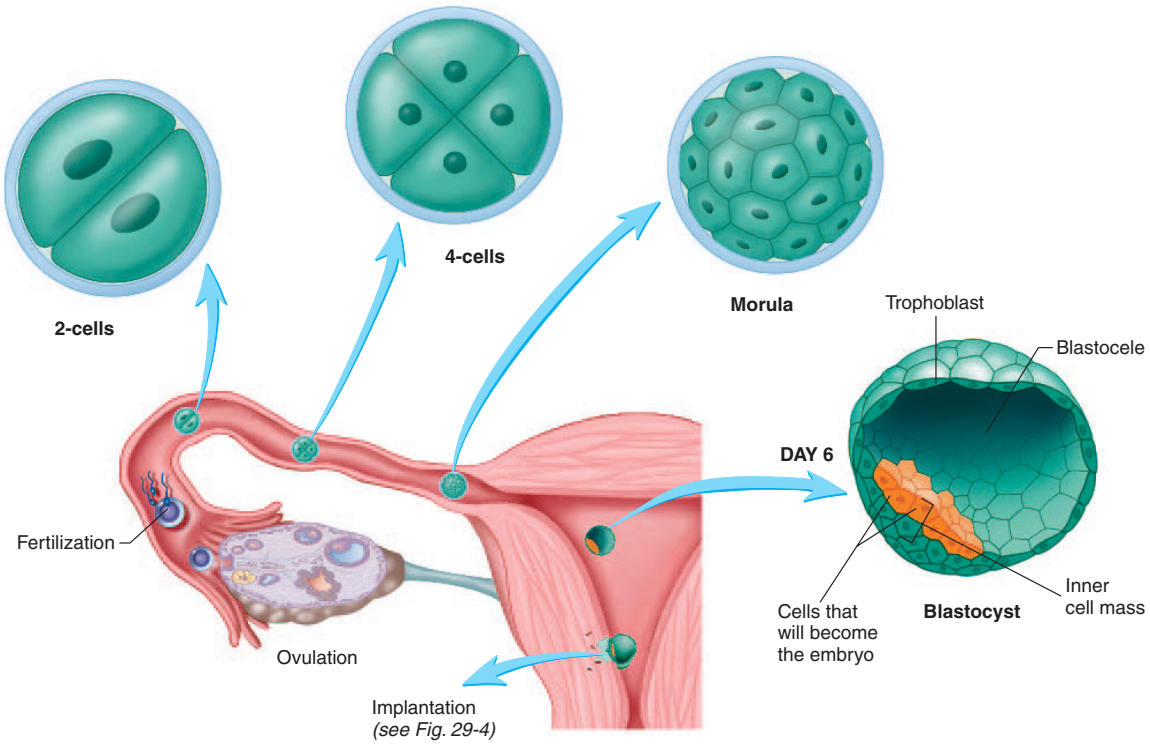


Figure 29.3 Blastocyst

Green cells are trophoblastic, and *orange* cells are embryonic.

Clinical Focus In Vitro Fertilization and Embryo Transfer

In a small number of women, normal pregnancy is not possible because of some anatomic or physiologic condition. In 87% of these cases, the uterine tubes are incapable of transporting the zygote to the uterus or of allowing sperm cells to reach the oocyte. In vitro fertilization and embryo transfer have made pregnancy possible in hundreds of such women since 1978. **In vitro fertilization (IVF)** involves removal of secondary oocytes from a woman, placing the oocytes into a petri dish, and adding sperm cells to the dish to allow fertilization and early development to occur in vitro, which means "in glass." **Embryo transfer** involves the removal of the developing embryonic cellular mass (not yet technically an embryo) from the petri dish and introduction of the mass into the uterus of a recipient female.

For IVF and embryo transfer to be accomplished, a woman is first injected with an LH-like substance, which causes more than one follicle to mature at one time. Just before the follicles rupture, the secondary oocytes are surgically removed from the ovary. The oocytes are then incubated in a dish and maintained at body temperature for 6 hours. Then sperm cells are added to the dish.

After 24–48 hours, when the zygotes have divided to form two- to eight-cell masses, several of the embryonic masses are transferred to the uterus. Several cell masses are transferred, because only a small percentage of them survives. Implantation and subsequent development then proceed in the uterus as they would for natural implantation; however, the woman is usually required to lie perfectly still for several hours after the cell masses have been introduced into the uterus to prevent possible expulsion before implantation can occur, which happens within 2–3 days after transfer. It's not fully understood why such expulsion does not occur in natural fertilization and implantation.

The implantation rate of embryo transfer is about 30%. The success rate varies with the number of embryonic masses implanted per transfer. Typically, three embryonic masses are transferred at a time. The rate of complications, such as multiple pregnancies, miscarriage, and prematurity, however, also increases with the greater numbers of embryonic masses per transfer.

About one-third of transfers of three embryonic masses end in multiple pregnancies. Of triplets born as a result of IVF, 64% require intensive care after birth, and 75% of quadruplets require intensive care, often for several weeks.

Prematurity from IVF pregnancies in the United Kingdom results in newborn mortality in 2.7% of cases, a rate three times that of natural pregnancies. As a result of the possible complications, no more than two to three embryonic masses are now transferred per IVF in the United Kingdom.

The success rate for IVF has dramatically increased through time. The success rate at the best U.S. clinics was 20% in 1982, 30% in 1995, and is now about 50%. This success rate may be approaching the natural limits, because only 50% or less of natural fertilizations result in a successful delivery.

Implantation of the Blastocyst and Development of the Placenta

Objective

- ***Describe implantation of the blastocyst and development of the placenta.***

All of the events of the early germinal phase, including the first cell division through formation of the blastocele and the inner cell mass, occur as the embryonic mass moves from the site of fertilization in the ampulla of the uterine tube to the site of implantation in the uterus. About 7 days after fertilization, the blastocyst attaches itself to the uterine wall, usually in the area of the uterine fundus, and begins the process of **implantation,** which is the burrowing of the blastocyst into the uterine wall.

As the blastocyst invades the uterine wall, two populations of trophoblast cells develop and form the embryonic portion of the **placenta** (figure 29.4), the organ of nutrient and waste product exchange between the embryo and the mother. The first is a proliferating population of individual trophoblast cells called the **cytotrophoblast** (sī-tō-trof′ō-blast). The other is a nondividing syncytium, or multinucleated cell, called the **syncytiotrophoblast** (sin-sish′ē-ō-trō′fō-blast). The cytotrophoblast remains nearer the other embryonic tissues, and the syncytiotrophoblast invades the endometrium of the uterus. The syncytiotrophoblast is nonantigenic, which means that as it invades the maternal tissue, no immune reaction is triggered.

As the syncytiotrophoblast encounters maternal blood vessels, it surrounds them and digests the vessel wall, forming pools of maternal blood within cavities called **lacunae** (lă-koo′nē; figure 29.4*c*). The lacunae are still connected to intact maternal vessels so that blood circulates from the maternal vessels through the lacunae. Cords of cytotrophoblast surround the syncytiotrophoblast and lacunae (figure 29.4*d*). Branches sprout from these cords and protrude into the lacunaelike fingers called **chorionic** (kō-rē-on′ik) **villi,** and the entire embryonic structure facing the maternal tissues is called the **chorion** (kō′rē-on). Embryonic blood vessels follow the cords into the lacunae. In the mature placenta (figure 29.5), the cytotrophoblast disappears, so that the embryonic blood supply is separated from the maternal blood supply by only the embryonic capillary wall, a basement membrane, and a thin layer of syncytiotrophoblast.

Placental Problems

If the blastocyst implants near the cervix, a condition called **placenta previa** (prē′vē-ă) occurs. In this condition, as the placenta grows, it may extend partially or completely across the internal cervical opening. As the fetus and placenta continue to grow and the uterus stretches, the region of the placenta over the cervical opening may tear, and hemorrhaging may occur. **Abruptio** (ab-rŭp′shē-ō) **placentae** is a tearing away of a normally positioned placenta from the uterine wall accompanied by hemorrhaging. Both of these conditions can result in miscarriage and can also be life-threatening to the mother.

(a) Frontal section of the uterus and uterine tube showing development 7 days after fertilization.

(b) Implantation of the blastocyst with syncytiotrophoblast beginning to invade the uterine wall (at about 8–12 days).

(c) Intermediate stage of placental formation (at about 14–20 days). As maternal blood vessels are encountered by the syncytiotrophoblast, lacunae are formed and filled with maternal blood.

(d) Cytotrophoblast cords surround the syncytiotrophoblast and lacunae, and embryonic mesoderm enters the cord (at about 1 month).

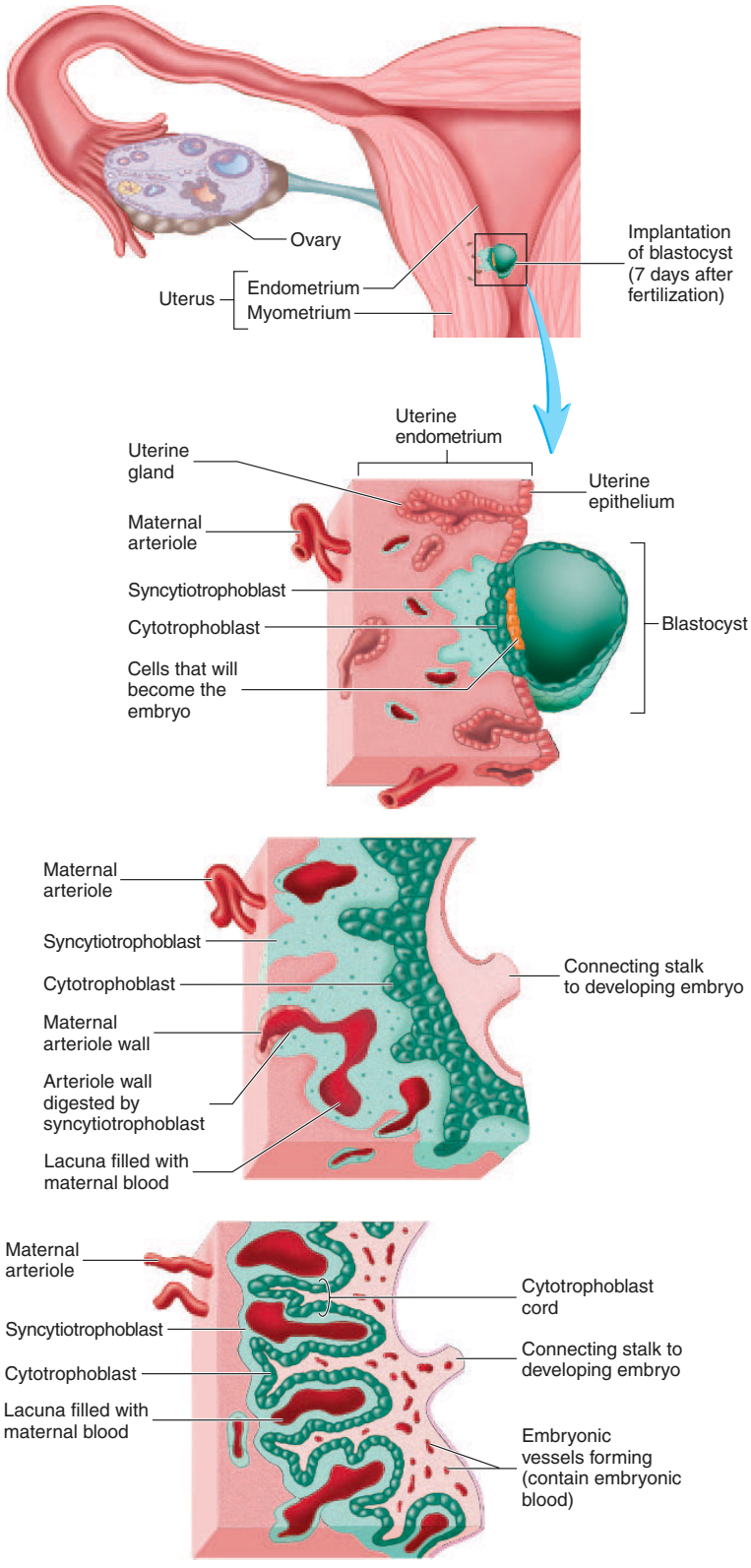


Figure 29.4 Formation of the Placenta

Implantation of the blastocyst and invasion of the trophoblast to form the placenta.

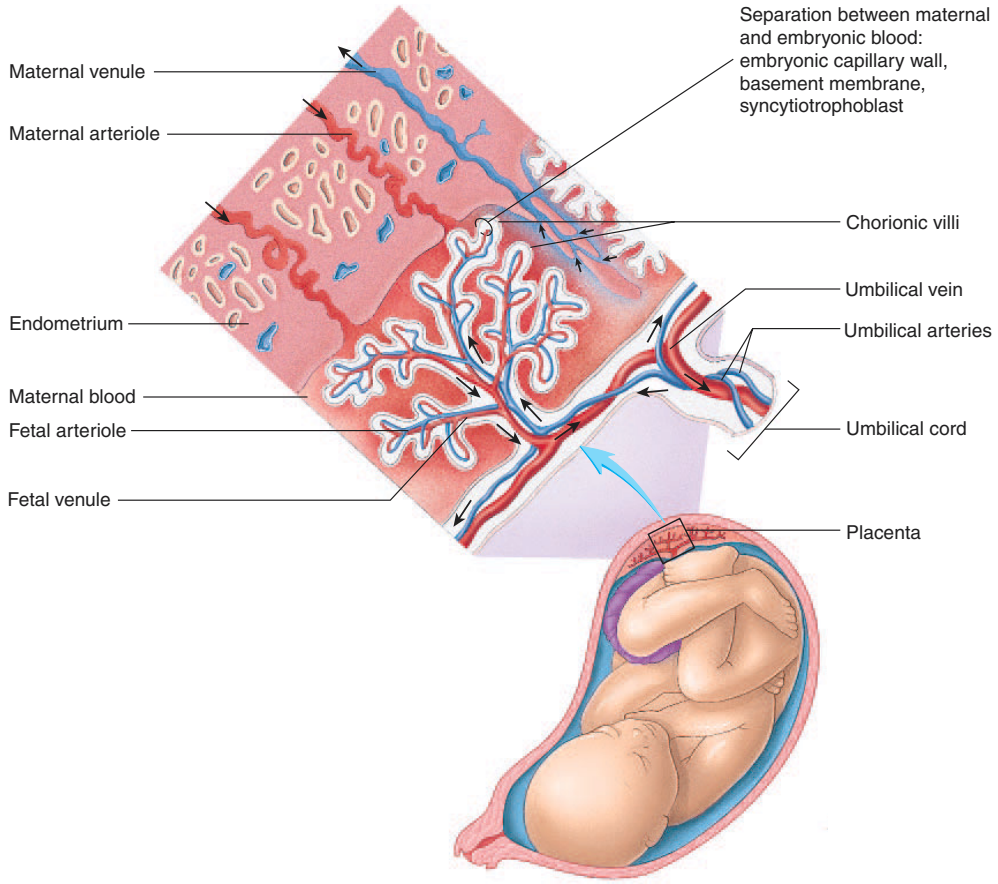


Figure 29.5 Mature Placenta and Fetus

Fetal blood vessels and maternal blood vessels are in close contact, and nutrients are exchanged between fetal and maternal blood, but fetal and maternal blood don't mix.

1. *List the three parts of the prenatal period. Give the length of time for each part.*
2. *Define clinical age and postovulatory age, and distinguish between the two.*
3. *Describe the events of fertilization. Where does fertilization occur?*
4. *What are the events the first week after fertilization? Define the terms zygote, morula, blastocyst, and blastocele. What is meant by the term pluripotent?*
5. *Describe the trophoblast and inner cell mass, and explain what develops from each.*
6. *Describe the implantation of the blastocyst and development of the placenta.*

Formation of the Germ Layers

Objective

- ***List the three germ layers, describe their formation, and list their adult derivatives.***

After implantation, a new cavity called the **amniotic** (am-nē-ot′ik) **cavity** forms inside the inner cell mass and is surrounded by a layer of cells called the **amnion** (am′nē-on), or **amniotic sac.** Formation of the amniotic cavity causes part of the inner cell mass nearest the blastocele to separate as a flat disk of tissue called the **embryonic disk** (figure 29.6). This embryonic disk is composed of two layers of cells: an **ectoderm** (ek′tō-derm; outside layer) adjacent to the amniotic cavity and an **endoderm** (en′dō-derm; inside layer) on the side of the disk opposite the amnion. A third cavity, the **yolk sac,** forms inside the blastocele from the endoderm. The amniotic sac, yolk sac, and intervening double-layered embryonic disk can be thought of as resembling two balloons pushed together. One balloon represents the amniotic sac, and the other represents the yolk sac. The circular double layer of balloon wall where the two balloons are pressed together represents the embryonic disk. The amniotic sac eventually enlarges to surround the developing embryo, providing it with a protective fluid environment, the "bag of waters," where the embryo forms.

About 13 or 14 days after fertilization, the embryonic disk becomes a slightly elongated oval structure. Proliferating cells of the ectoderm migrate toward the center and the caudal end of the disk, forming a thickened line called the **primitive streak.** Some ectoderm cells leave the ectoderm, migrate through the primitive streak, and emerge between the ectoderm and endoderm as a new germ layer, the **mesoderm** (mez′o-derm; middle layer; figure 29.7). These three germ layers, the ectoderm, mesoderm, and endoderm, are the beginning of the **embryo.** All tissues of the adult can be traced to them (table 29.1). A cordlike structure called the **notochord** extends from the cephalic end of the primitive streak.

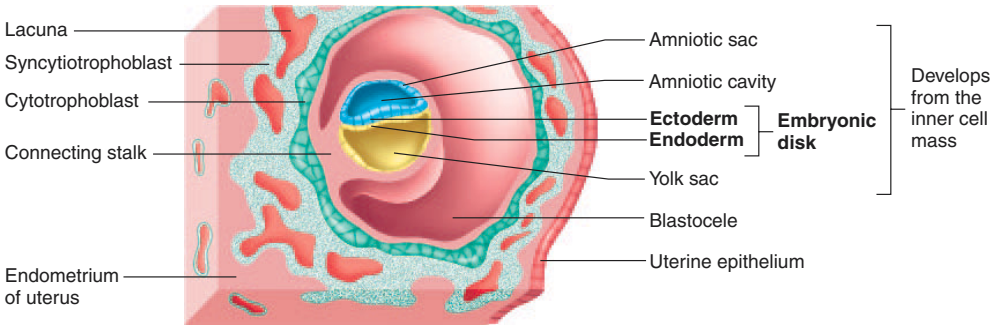


Figure 29.6 Embryonic Disk

Embryonic disk consisting of ectoderm (*blue*) and endoderm (*yellow*), with the amniotic cavity and yolk sac.

1. Cells in the surface ectoderm move toward the primitive streak and migrate through the streak (*blue arrow tails*).
2. Cells of the ectoderm that migrate through the primitive streak become mesodermal cells (*red arrows*).
3. The mesoderm (*red*) lies between the ectoderm (*blue*) and endoderm (*yellow*).

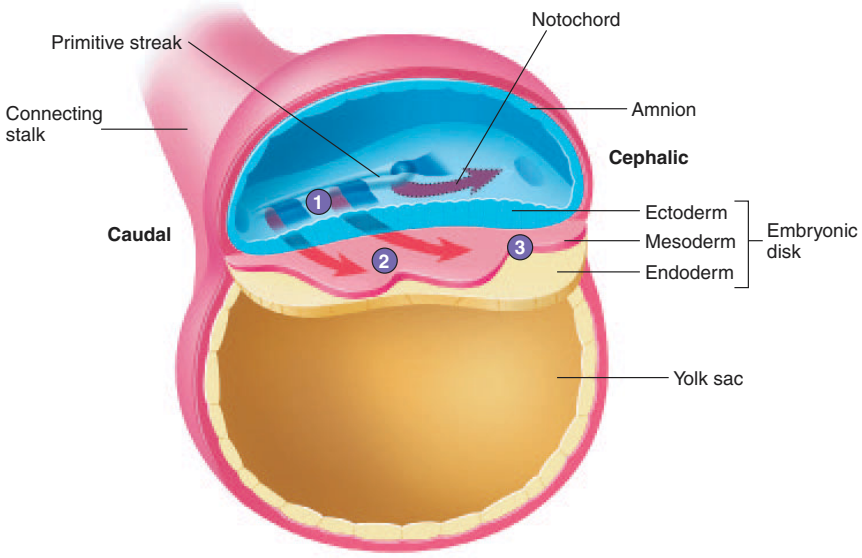


Figure 29.7 Primitive Streak

Embryonic disk with a primitive streak. The head of the embryo will develop over the notochord.

Table 29.1 Germ Layer Derivatives

Ectoderm	**Mesoderm**
Epidermis of skin	Dermis of skin
Tooth enamel	Circulatory system
Lens and cornea of eye	Parenchyma of glands
Outer ear	Muscle
Nasal cavity	Bones (except facial)
Anterior pituitary	Microglia
Neuroectoderm	
Brain and spinal cord	**Endoderm**
Somatic motor neurons	Lining of gastrointestinal tract
Preganglionic autonomic neurons	Lining of lungs
Neuroglia cells (except microglia)	Lining of hepatic, pancreatic, and other exocrine ducts
Neural crest cells	Urinary bladder
Melanocytes	Thymus
Sensory neurons	Thyroid
Postganglionic autonomic neurons	Parathyroid
Adrenal medulla	Tonsils
Facial bones	
Teeth (dentin, pulp, and cementum) and gingiva	
A few skeletal muscles in head	

P R E D I C T 1

Predict the results of two primitive streaks forming in one embryonic disk. What if the two primitive streaks are touching each other?

Neural Tube and Neural Crest Formation

Objective

- ***Describe the formation of the neural tube.***

The ectoderm near the cephalic end of the primitive streak is stimulated about 18 days after fertilization to form a thickened **neural plate.** The lateral edges of the plate begin to rise like two ocean waves coming together. These edges are called the **neural folds,** and a **neural groove** lies between them (figure 29.8). The underlying notochord stimulates the folding of the neural plate at the neural groove. The crests of the neural folds begin to meet in the midline and fuse into a **neural tube,** which is completely closed by 26 days. The neural tube becomes the brain and the spinal cord, and the cells of the neural tube are called **neuroectoderm** (see table 29.1).

As the neural folds come together and fuse, a population of cells breaks away from the neuroectoderm all along the crests of the folds. These **neural crest cells** migrate down along the side of the developing neural tube to become part of the peripheral nervous system and the adrenal medulla and migrate laterally to just below the ectoderm, where they become melanocytes of the skin. In the head, neural crest cells perform additional functions; they contribute to the skull, the dentin of teeth, a few small skeletal muscles, and general connective tissue. Because neural crest cells in the head give rise to many of the same tissues as the mesoderm in the head and trunk, the general term **mesenchyme** (mez′enkīm) is sometimes applied to cells of either neural crest or mesoderm origin.

Malformations

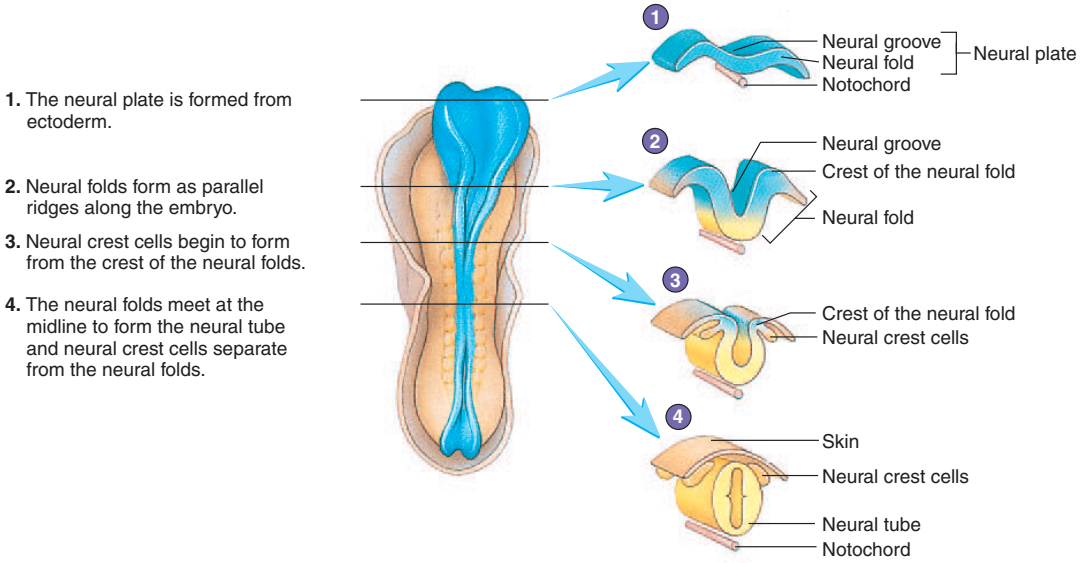
During the first 2 weeks of development, the embryo is quite resistant to outside influences that may cause malformations. Factors that adversely affect the embryo at this age are more likely to kill it. Between 2 weeks and the next 4–7 weeks (depending on the structure considered), the embryo is more sensitive to outside influences that cause malformations than at any other time.

Somite Formation

Objective

- ***Describe somite formation.***

As the neural tube develops, the mesoderm immediately adjacent to the tube forms distinct segments called **somites** (sō′mītz). In the head, the first few somites never become clearly divided but develop into indistinct segmented structures called **somitomeres.** The somites and somitomeres eventually give rise to a part of the skull, the vertebral column, and skeletal muscle. Most of the head muscles are derived from the somitomeres.



Process Figure 29.8 Formation of the Neural Tube

The neural folds come together in the midline and fuse to form a neural tube. This fusion begins in the center and moves both cranially and caudally. The embryo shown is about 21 days after fertilization. The insets to the *right* show progressive closure of the neural tube.

Formation of the Gut and Body Cavities

Objective

- ***Describe the formation of the gastrointestinal tract and the body cavities.***

At the same time its neural tube is forming, the embryo itself is becoming a tube along the upper part of the yolk sac. The **foregut** and **hindgut** develop as the cephalic and caudal ends of the yolk sac are separated from the main yolk sac. This is the beginning of the digestive tract (figure 29.9*a*). The developing digestive tract pinches off from the yolk sac as a tube but remains attached in the center to the yolk sac by a yolk stalk.

The foregut and hindgut (figure 29.9*b*) are in close relationship to the overlying ectoderm and form membranes called the oropharyngeal membrane and the cloacal membrane, respectively. The **oropharyngeal membrane** opens to form the mouth, and the **cloacal membrane** opens to form the urethra and anus. Thus, the digestive tract becomes a tube that is open to the outside at both ends.

A considerable number of **evaginations** (ē-vaj-i-nā′shŭnz; outpocketings) occur along the early digestive tract (figure 29.9*c*). They develop into structures like the anterior pituitary, the thyroid gland, the lungs, the liver, the pancreas, and the urinary bladder. At the same time, solid bars of tissue known as **branchial arches** (figures 29.9*c* and 29.10) form along the lateral sides of the head, and the sides of the foregut expand as pockets between the branchial arches. The central expanded foregut is called the **pharynx,** and the pockets along both sides of the pharynx are called **pharyngeal pouches.** Adult derivatives of the pharyngeal pouches include the auditory tubes, tonsils, thymus, and parathyroids.

At about the same time the gut is developing, a series of isolated cavities starts to form within the embryo, thus beginning development of the **celom** (sē′lom; see figure 29.9), or body cavities. The most cranial group of cavities enlarges and fuses to form the **pericardial cavity.** Shortly thereafter, the celomic cavity extends toward the caudal end of the embryo as the **pleural** and **peritoneal cavities.** Initially, all three of these cavities are continuous, but they eventually separate into three distinct adult cavities (see chapter 1).

7. Describe the formation of the gut and body cavities.

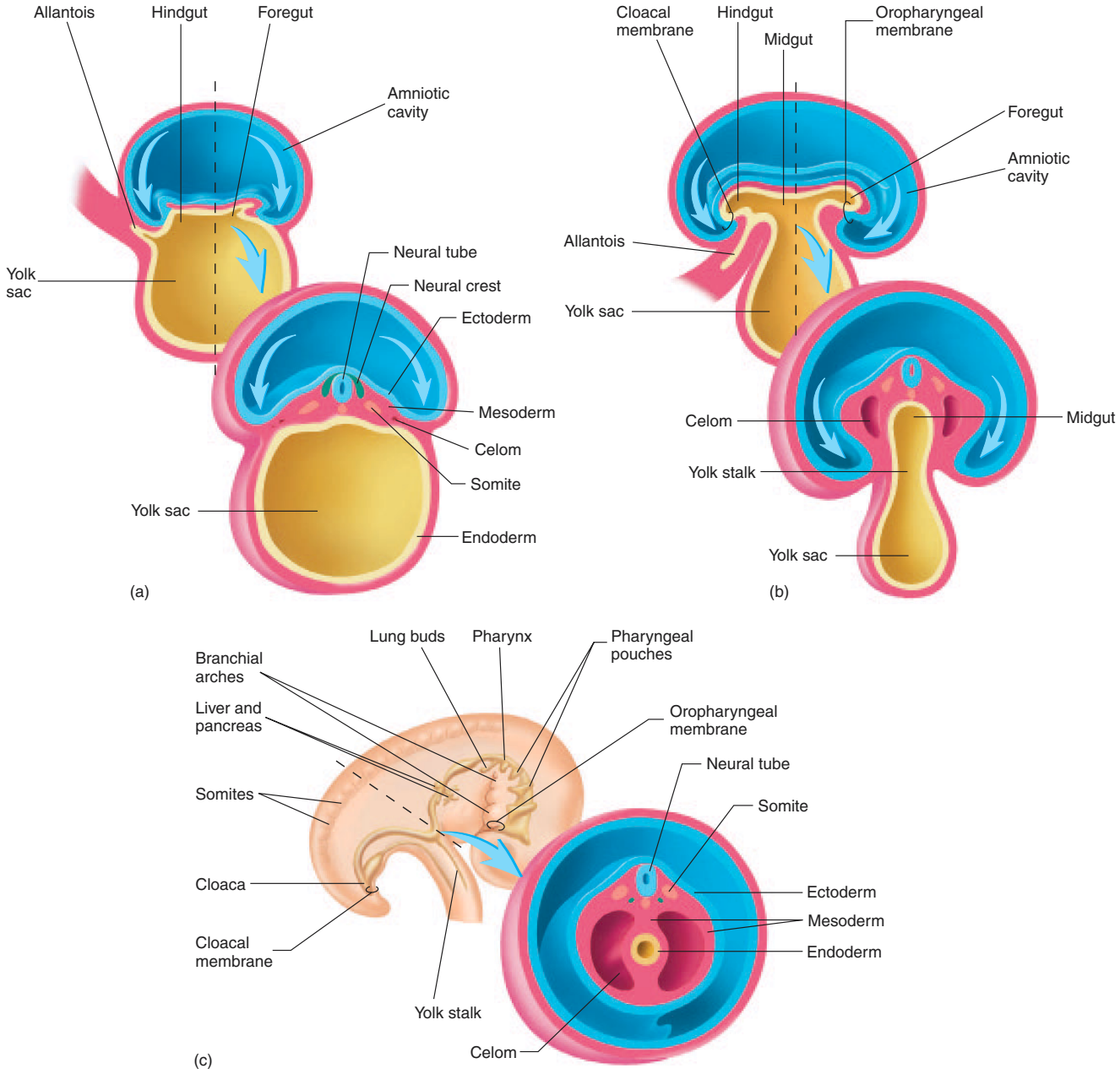


Figure 29.9 Formation of the Digestive Tract

Blue arrows show the folding of the digestive tract into a tube. *Dotted lines* show the plane of the section from which insets were taken. (*a*) 20 days after fertilization. (*b*) 25 days after fertilization. (*c*) 30 days after fertilization. Evaginations are identified along the pharynx and digestive tract in part (*c*).

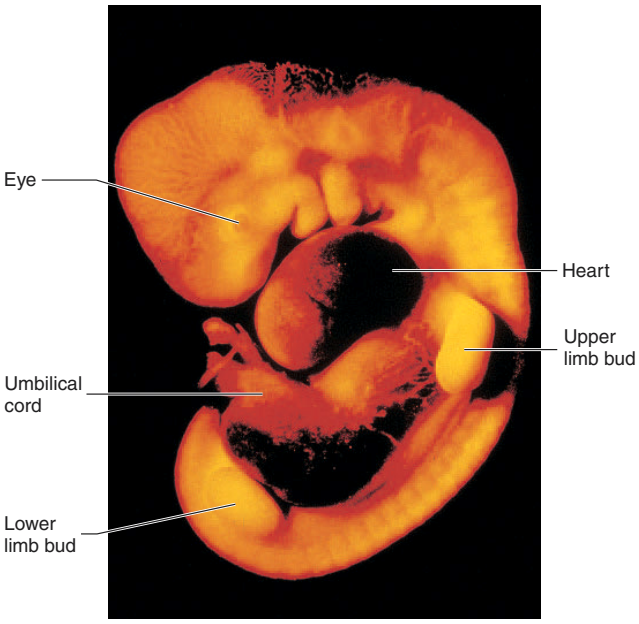


Figure 29.10 Human Embryo 35 Days After Fertilization

Limb Bud Development

Objective

- *Describe limb formation.*

Arms and legs first appear at about 28 days as limb buds (see figure 29.10). The **apical ectodermal ridge,** a specialized thickening of the ectoderm, develops on the lateral margin of each limb bud and stimulates its outgrowth. As the buds elongate, limb tissues are laid down in a proximal-to-distal sequence. For example, in the upper limb, the arm is formed before the forearm, which is formed before the hand.

8. Describe limb formation. What does a proximal-to-distal growth sequence mean?

Development of the Face

Objective

- *Describe the formation of the face and palate.*

The face develops by fusion of five embryonic structures: the **frontonasal process,** which forms the forehead, nose, and midportion of the upper jaw and lip; two **maxillary processes,** which form the lateral parts of the upper jaw and lip; and two **mandibular processes,** which form the lower jaw and lip (figure 29.11 *1*). **Nasal placodes** (plak′ōdz), which develop at the lateral margins of the frontonasal process, develop into the nose and the center of the upper jaw and lip (figure 29.11 *2*).

As the brain enlarges and the face matures, the nasal placodes approach each other in the midline. The medial edges of the placodes fuse to form the midportion of the upper jaw and lip (figure 29.11 *3* and *4*). This part of the frontal process is between the two maxillary processes, which are expanding toward the midline, and fuses with them to form the upper jaw and lip, known as the **primary palate.**

9. Describe the processes involved in the formation of the face. What clefts may result if these processes fail to fuse?

Cleft Lip

A **cleft lip** results from failure of the frontonasal and two maxillary processes to fuse (figure 29.11). Because three structures—one midline and two lateral—are involved in formation of the primary palate, cleft lips usually do not occur in the midline but to one side (or both sides) and extend from the mouth to the naris (nostril).

At about the same time that the primary palate is forming, the lateral edges of the nasal placodes fuse with the maxillary processes to close off the groove extending from the mouth to the eye (figure 29.11 *4* and *5*). On rare occasions, these structures fail to meet, resulting in a facial cleft extending from the mouth to the eye. The inferior margins of the maxillary processes fuse with the superior margins of the mandibular processes to decrease the size of the mouth. All of the previously described fusions and the growth of the brain give the face a recognizably "human" appearance by about 50 days.

The roof of the mouth, known as the **secondary palate,** begins to form as vertical shelves, which swing to a horizontal position and begin to fuse with each other at about 56 days of development. Fusion of the entire palate is not completed until about 90 days. If the secondary palate does not fuse, a midline cleft in the roof of the mouth, called a **cleft palate,** results.

10. Describe the formation of the germ layers and the role of the primitive streak. Where is the notochord found?
11. How are the neural tube and the neural crest formed? What do they become? What are mesenchyme cells?
12. What is a somite?

Development of the Organ Systems

Objective

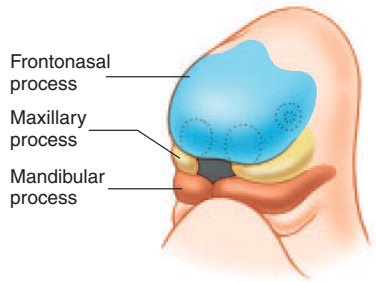
- *Briefly describe the formation of the following major organ systems: integumentary, skeletal, muscular, nervous, endocrine, circulatory, respiratory, digestive, urinary, and reproductive.*

The major organ systems appear and begin to develop during the embryonic period. The period between 14 and 60 days is, therefore, called the period of organogenesis (table 29.2).

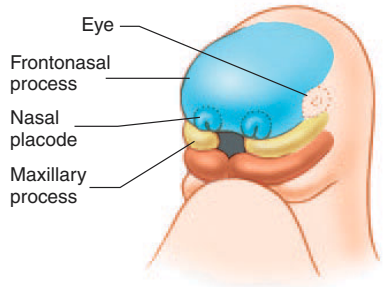
Skin

The **epidermis** of the skin is derived from ectoderm, and the **dermis** is derived from mesoderm, or from neural crest cells in the case of the face. Nails, hair, and glands develop from the epidermis (see chapter 5). Melanocytes and sensory receptors in the skin are derived from neural crest cells.

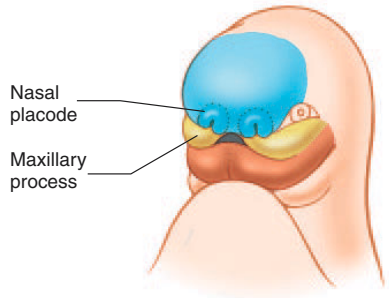
1. 28 days after fertilization
The face develops from five processes: frontonasal (*blue*), two maxillary (*yellow*), and two mandibular (*orange*; already fused).



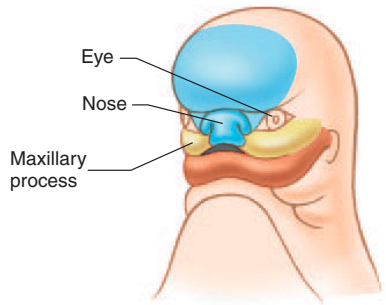
2. 33 days after fertilization
Nasal placodes appear in the frontonasal process.



3. 40 days after fertilization
Maxillary processes extend toward the midline. The nasal placodes also move toward the midline and fuse with the maxillary processes to form the jaw and lip.



4. 48 days after fertilization
Continued growth brings structures more toward the midline.



5. 14 weeks after fertilization
Colors show the contributions of each process to the adult face.

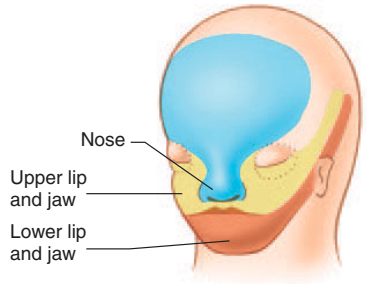


Figure 29.11 Development of the Face

Table 29.2 Development of the Organ Systems

	Age (Days Since Fertilization)					
	1–5	**6–10**	**11–15**	**16–20**	**21–25**	**26–30**
General features	Fertilization Morula Blastocyst	Blastocyst implants	Primitive streak Three germ layers	Neural plate	Neural tube closed	Limb buds and other "buds" appear
Integumentary System			Ectoderm Mesoderm			Melanocytes from neural crest
Skeletal System			Mesoderm		Neural crest (will form facial bones)	Limb buds
Muscular System			Mesoderm	Somites begin to form		Somites all present
Nervous System			Ectoderm	Neural plate	Neural tube complete Neural crest Eyes and ears begin	Lens begins to form
Endocrine System			Ectoderm Mesoderm Endoderm	Thyroid begins to develop		Parathyroids appear
Cardiovascular System			Mesoderm	Blood islands form Two heart tubes	Single-tubed heart begins to beat	Interatrial septum begins to form
Lymphatic System			Mesoderm			Thymus appears
Respiratory System			Mesoderm Endoderm		Diaphragm begins to form	Trachea forms as single bud Lung buds (primary bronchi)
Digestive System			Mesoderm Endoderm		Neural crest (will form tooth dentin) Foregut and hindgut form	Liver and pancreas appear as buds Tongue bud appears
Urinary System			Mesoderm Endoderm		Pronephros develops Allantois appears	Mesonephros appears
Reproductive System			Mesoderm Endoderm		Primordial germ cells on yolk sac	Mesonephros appears Genital tubercle forms

Age (Days Since Fertilization)					
31–35	**36–40**	**41–45**	**46–50**	**51–55**	**56–60**
Hand and foot plates on limbs	Fingers and toes appear Lips formed Embryo 15 mm	External ear forming Embryo 20 mm	Embryo 25 mm	Limbs elongate to a more adult relationship Embryo 35 mm	Face is distinctly human in appearance
Sensory receptors appear in skin		Collagen fibers clearly present in skin		Extensive sensory endings in skin	
Mesoderm condensation in areas of future bone	Cartilage in site of future humerus	Cartilage in site of future ulna and radius	Cartilage in site of hand and fingers		Ossification begins in clavicle and then in other bones
Muscle precursor cells enter limb buds			Functional muscle		Nearly all muscles appear in adult form
Nerve processes enter limb buds		External ear forming Olfactory nerve begins to form		Semicircular canals in inner ear complete	Eyelids form Cochlea in inner ear complete
Pituitary appears as evaginations from brain and mouth	Gonadal ridges form Adrenal glands forming		Pineal body appears	Thyroid gland in adult position and attachment to tongue lost	Anterior pituitary loses its connection to the mouth
Interventricular septum begins to form		Interventricular septum complete	Interatrial septum complete but still has opening until birth		
Large lymphatic vessels form in neck	Spleen appears			Adult lymph pattern form	
Secondary bronchi to lobes form	Tertiary bronchi to bronchopulmonary segments form		Tracheal cartilage begins to form		
Oropharyngeal membrane ruptures		Secondary palate begins to form Tooth buds begin to form			Secondary palate begins to fuse (fusion complete by 90 days)
Metanephros begins to develop				Mesonephros degenerates	Anal portion of cloacal membrane ruptures
	Gonadal ridges form	Primordial germ cells enter gonadal ridges	Paramesonephric ducts appear		Uterus forming Beginning of differentiation of external genitalia in male and female

Skeleton

The skeleton develops from either mesoderm or the neural crest cells through intramembranous or endochondral bone formation (see chapter 6). The bones of the face develop from neural crest cells, whereas the rest of the skull, the vertebral column, and ribs develop from somite- or somitomere-derived mesoderm. The appendicular skeleton develops from limb bud mesoderm.

Muscle

Myoblasts (mī′ō-blastz) are the early, embryonic cells that give rise to skeletal muscle fibers. Myoblasts migrate from somites or somitomeres to sites of future muscle development, where they continue to divide and begin to fuse and form multinuclear cells called **myotubes,** which enlarge to become the muscle fibers of the skeletal muscles. Shortly after myotubes form, nerves grow into the area and innervate the developing muscle fibers. After the basic form of each muscle is established, an increase in the number of muscle fibers causes continued muscle growth. The total number of muscle fibers is established before birth and remains relatively constant thereafter. Muscle enlargement after birth results from an increase in the size of individual fibers.

Nervous System

The nervous system is derived from the neural tube and neural crest cells. Neural tube closure begins in the upper cervical region and proceeds into the head and down the spinal cord. Soon after the neural tube has closed, the part of the neural tube that becomes the brain begins to expand and develops a series of pouches (see figure 13.14). The central cavity of the neural tube becomes the ventricles of the brain and the central canal of the spinal cord.

Neural Tube Defects

Anencephaly (an′en-sef′ă-lē; no brain) is a birth defect in which much of the brain fails to form. It results when the neural tube fails to close in the region of the head. A baby born with anencephaly cannot survive. **Spina bifida** (spī′nă bi′fi-dă; split spine) is a general term describing defects of the spinal cord or vertebral column (or both). Spina bifida can range from a simple defect with no clinical manifestations and with one or more vertebral spinous processes split or missing to a more severe defect that results in paralysis of the limbs or the bowels and bladder, depending on where the defect occurs.

It has now been well documented that the inclusion of **folic acid** in the diet of a woman during the early stages of her pregnancy significantly reduces the risk of neural tube defects in her developing embryo.

The neuron cell bodies of somatic motor neurons and preganglionic neurons of the autonomic nervous system, which provide axons to the peripheral nervous system, are located within the neural tube. Sensory neurons and postganglionic neurons of the autonomic nervous system are derived from neural crest cells.

Alcohol and Cigarette Smoke

A number of drugs and other chemicals are known to affect the embryo and fetus during development. The two most common are alcohol and cigarette smoke. Alcoholism or binge drinking can result in **fetal alcohol syndrome,** which includes decreased mental function. Exposure of the fetus to **cigarette smoke** throughout pregnancy can stunt the physical growth and mental development of the fetus.

Special Senses

The **olfactory bulb** and **nerve** develop as an evagination from the telencephalon (see figure 13.14). The eyes develop as evaginations from the diencephalon. Each evagination elongates to form an **optic stalk,** and a bulb called the **optic vesicle** develops at its terminal end. The optic vesicle reaches the side of the head and stimulates the overlying ectoderm to thicken into a **lens.** The sensory part of the ear appears as an ectodermal thickening or placode that invaginates and pinches off from the overlying ectoderm.

Endocrine System

An evagination from the floor of the diencephalon forms the **posterior pituitary gland.** The **anterior pituitary gland** develops from an evagination of ectoderm in the roof of the embryonic oral cavity and grows toward the floor of the brain. It eventually loses its connection with the oral cavity and becomes attached to the posterior pituitary gland (see chapter 18).

The **thyroid gland** originates as an evagination from the floor of the pharynx in the region of the developing tongue and moves into the lower neck, eventually losing its connection with the pharynx. The **parathyroid glands,** which are derived from the third and fourth pharyngeal pouches, migrate inferiorly and become associated with the thyroid gland.

The **adrenal medulla** arises from neural crest cells and consists of specialized postganglionic neurons of the sympathetic division of the autonomic nervous system (see chapter 16). The **adrenal cortex** is derived from mesoderm.

The **pancreas** originates as two evaginations from the duodenum, which come together to form a single gland (see figure 29.9*c*).

Circulatory System

The heart develops from two endothelial tubes (figure 29.12 *1*), which fuse into a single, midline heart tube (figure 29.12 *2*). Blood vessels form from blood islands on the surface of the yolk sac and inside the embryo. **Blood islands** are small masses of mesoderm that become blood vessels on the outside and blood cells on the inside. These islands expand and fuse to form the circulatory system. A series of dilations appears along the length of the primitive heart tube, and four major regions can be identified: the **sinus venosus,** the site where blood enters the heart; a single **atrium;** a single **ventricle;** and the **bulbus cordis,** where blood exits the heart (see figure 29.12 *2*).

1. **20 days after fertilization**
   At this age, the heart consists of two parallel tubes.

2. **22 days after fertilization**
   The two parallel tubes have fused to form one tube. This tube bends as it elongates (blue arrows suggest the direction of bending) within the confined space of the pericardium.

3. **31 days after fertilization**
   The interatrial septum (septum primum, *green*) and the interventricular septum grow toward the center of the heart.

4. **35 days after fertilization**
   The interventricular septum is nearly complete. A foramen opens in the septum primum (*green*) as the septum secundum begins to form (*blue*).

5. **The final embryonic condition of the interatrial septum**
   Blood from the right atrium can flow through the foramen ovale into the left atrium. After birth, as blood begins to flow in the other direction, the left side of the interatrial septum is forced against the right side, closing the foramen ovale.

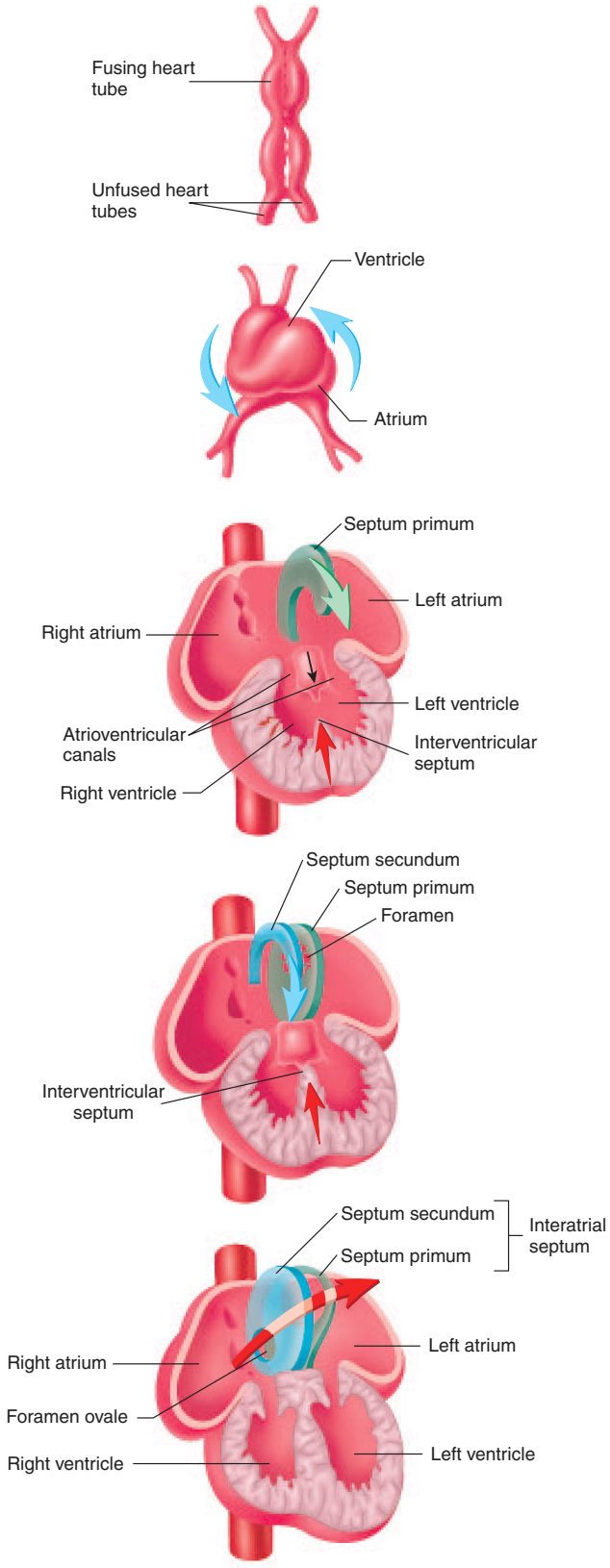


Figure 29.12 Development of the Heart

The elongating heart, confined within the pericardium, becomes bent into a loop, the apex of which is the ventricle (see figure 29.12 *2*). The major chambers of the heart, the atrium and the ventricle, expand rapidly. The right part of the sinus venosus becomes absorbed into the atrium, and the bulbus cordis is absorbed into the ventricle. The embryonic sinus venosus initiates contraction at one end of the tubular heart. Later in development, part of the sinus venosus becomes the sinoatrial node, which is the adult pacemaker.

PREDICT 2

What would happen if the sinus venosus didn't contract before other areas of the primitive heart?

An **interventricular septum** (figure 29.12 *3–5*) develops, which divides the single ventricle into two chambers. The **interatrial septum,** which separates the two atria in the adult heart, is formed from two parts: the **septum primum** (primary septum) and the **septum secundum** (secondary septum). An opening in the interatrial septum called the **foramen ovale** (ō-val′ē) connects the two atria and allows blood to flow from the right to the left atrium in the embryo and fetus.

Heart Defects

If the interventricular septum does not grow enough to completely separate the ventricles, a **ventricular septal defect (VSD)** results. If the septum secundum fails to grow far enough or if the foramen secundum becomes too large, an **atrial septal defect (ASD)** occurs, allowing blood to flow from the left atrium to the right atrium in the newborn. Both ASDs and VSDs result in abnormal heart sounds called **heart murmurs.** Blood passes through the ASD and VSD from the left to right side of the heart. The right side of the heart usually hypertrophies. The increased pressure in the pulmonary blood vessels and a decreased blood flow through the systemic blood vessels results in pulmonary edema, cyanosis (a bluish color due to deficient blood oxygenation), or heart failure.

Respiratory System

The lungs begin to develop as a single midline evagination from the foregut in the region of the future esophagus. This evagination branches to form two **lung buds** (figure 29.13 *1*). The lung buds elongate and branch, first forming the bronchi that project to the lobes of the lungs (figure 29.13 *2*) and then the bronchi that project to the bronchopulmonary segments of the lungs (figure 29.13 *3*). This branching continues (figure 29.13 *4*) until, by the end of the sixth month, about 17 generations of branching have occurred. Even after birth, some branching continues as the lungs grow larger, and in the adult about 24 generations of branches have been established.

Urinary System

The kidneys develop from mesoderm located between the somites and the lateral part of the embryo. About 21 days after fertilization, the mesoderm in the cervical region differentiates into a structure called the **pronephros** (the most forward or earliest kidney) (figure 29.14*a*), which consists of a duct and simple tubules connecting the duct to the open celomic cavity. This type of kidney is the functional adult kidney in some lower chordates, but it's probably not functional in the human embryo and soon disappears.

The **mesonephros** (middle kidney; see figure 29.14*a*) is a functional organ in the embryo. It consists of a duct, which is a caudal extension of the pronephric duct, and a number of minute tubules, which are smaller and more complex than those of the pronephros. One end of each tubule opens into the mesonephric duct, and the other end forms a glomerulus (see chapter 26).

As the mesonephros is developing, the caudal end of the hindgut begins to enlarge to form the **cloaca** (klō-ā′kă; sewer), the common junction of the digestive, urinary, and genital systems (figure 29.14*b*). A **urorectal septum** divides the cloaca into two parts: a digestive part called the **rectum** and a urogenital part called the **urethra** (figure 29.14*c*). The cloaca has two tubes associated with it: the hindgut and the **allantois** (ă-lan′tō-is; sausage), which is a blind tube extending into the umbilical cord (see figures 29.9 and 29.14). The part of the allantois nearest the cloaca enlarges to form the urinary bladder, and the remainder, which is from the bladder to the umbilicus, degenerates (figure 29.14*d*).

The mesonephric duct extends caudally as it develops and eventually joins the cloaca. At the point of junction, another tube, the **ureter,** begins to form. Its distal end enlarges and branches to form the duct system of the adult kidney, called the **metanephros** (last kidney), which takes over the function of the degenerating mesonephros.

Reproductive System

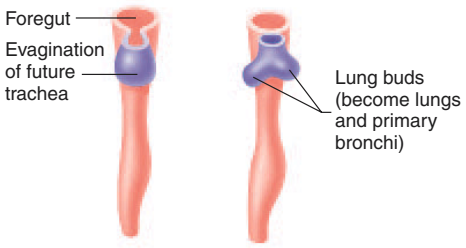
The male and female gonads appear as **gonadal ridges** along the ventral border of each mesonephros (figure 29.15*a*). **Primordial germ cells,** destined to become oocytes or sperm cells, form on the surface of the yolk sac, migrate into the embryo, and enter the gonadal ridge.

In the female, the ovaries descend from their original position high in the abdomen to a position within the pelvis. In the male, the testes descend even farther. As the testes reach the anteroinferior abdominal wall, a pair of tunnels called the **inguinal canals** form through the abdominal musculature. The testes pass through these canals, leaving the abdominal cavity and coming to lie within the **scrotum** (see figure 28.3). Descent of the testes through the canals begins about 7 months after conception, and the testes enter the scrotum about 1 month before the infant is born.

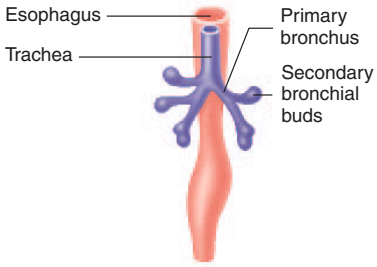
Cryptorchidism

In approximately 0.5% of male children, one or both testes fail to enter the scrotum. This condition is called undescended testes, or **cryptorchidism** (krip-tōr′ki-dizm). Because testosterone is required for the testes to descend into the scrotum, cryptorchidism is often the result of inadequate testosterone secreted by the fetal testes. If neither testis descends and the defect is not corrected, the male will be infertile because the slightly higher temperature of the body cavity, compared to that of the scrotal sac, causes the spermatogonia to degenerate. Cryptorchidism is treated with hormone therapy, or it may have to be surgically corrected.

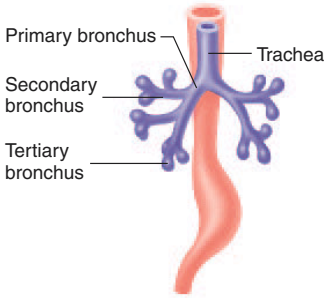
1. 28 days after fertilization
A single bud forms and divides into two buds, which will become the lungs and primary bronchi.



2. 32 days after fertilization
Primary bronchi branch to form secondary bronchi, which supply the lung lobes.



3. 35 days after fertilization
Secondary bronchi branch to form tertiary bronchi, which supply the bronchopulmonary segments.



4. 50 days after fertilization
The branching will continue to eventually form the extensive respiratory passages in the lungs.

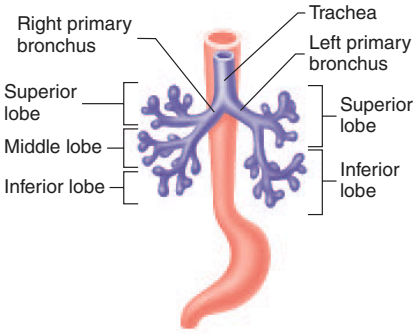
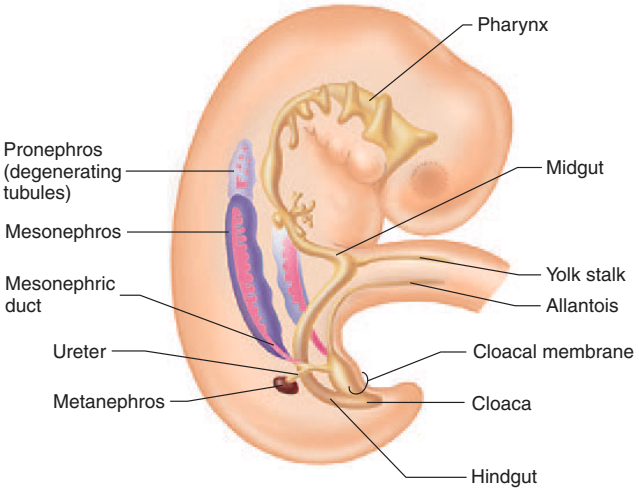
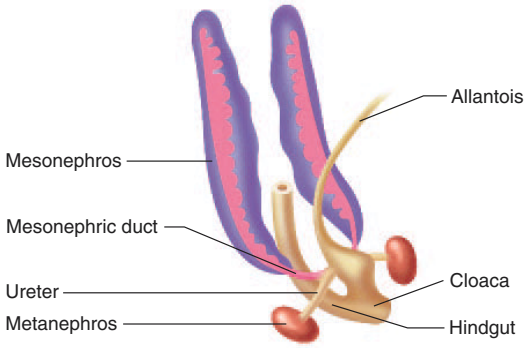


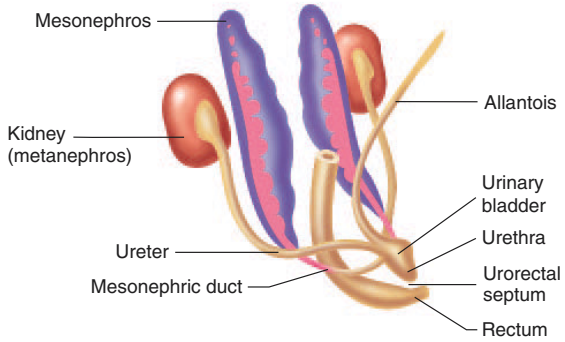
Figure 29.13 Development of the Lung



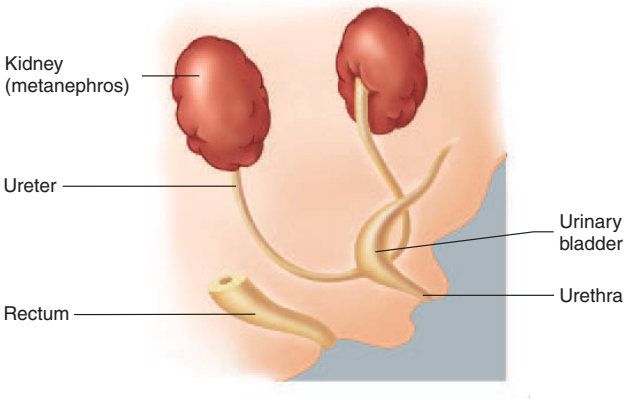
(a) The three parts of the developing kidney: pronephros, mesonephros, metanephros.



(b) The metanephros (adult kidney) enlarges as the mesonephros degenerates.



(c) The kidney continues to grow and develop.



(d) Final duct relationships.

Figure 29.14 Development of the Kidney and Urinary Bladder

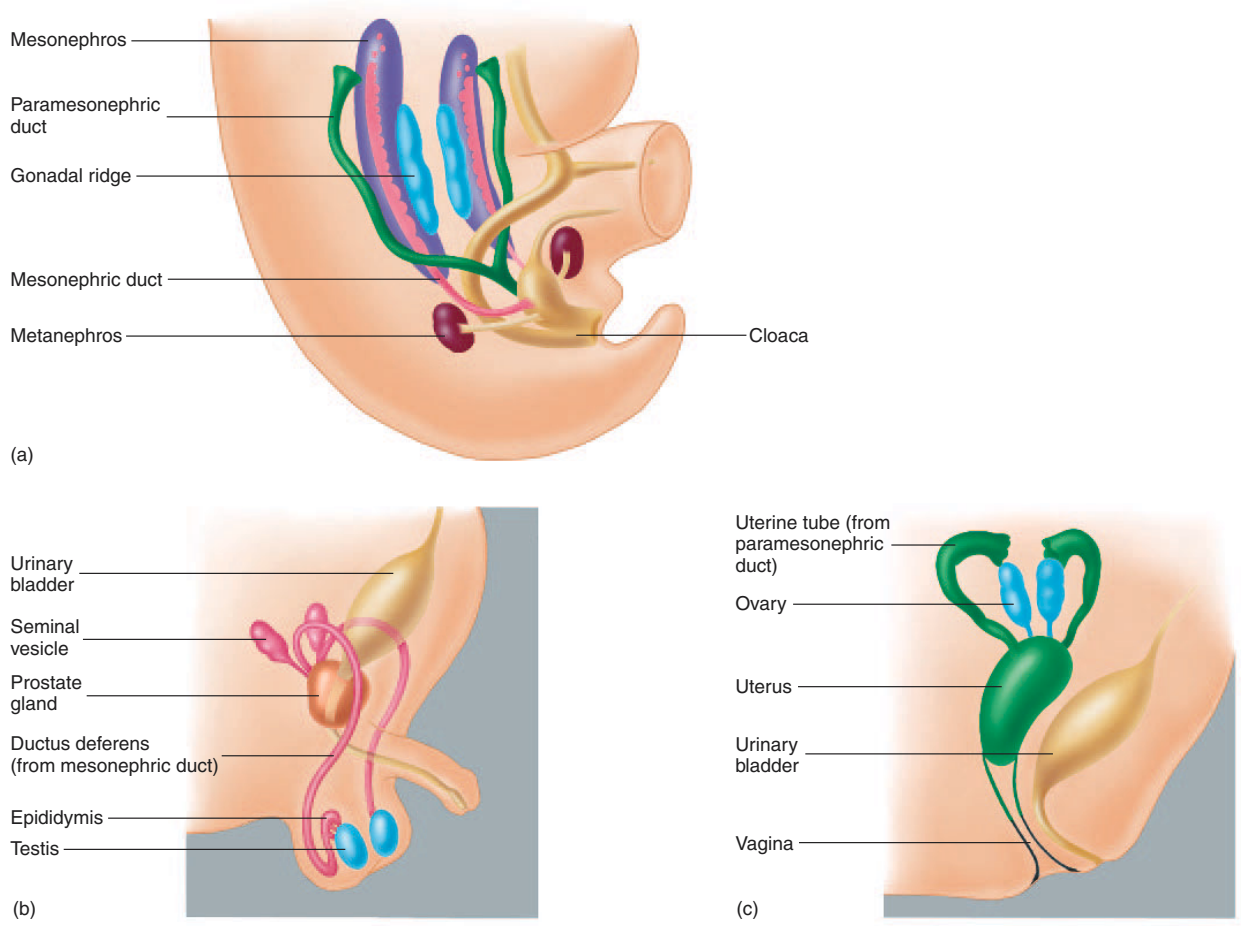


Figure 29.15 Development of the Reproductive System

(*a*) Indifferent stage. (*b*) The male, under the influence of male hormones, develops a ductus deferens from the mesonephric duct, and the paramesonephric duct degenerates. (*c*) The female, without male hormones, develops a uterus and uterine tubes from the paramesonephric duct, and the mesonephros disappears.

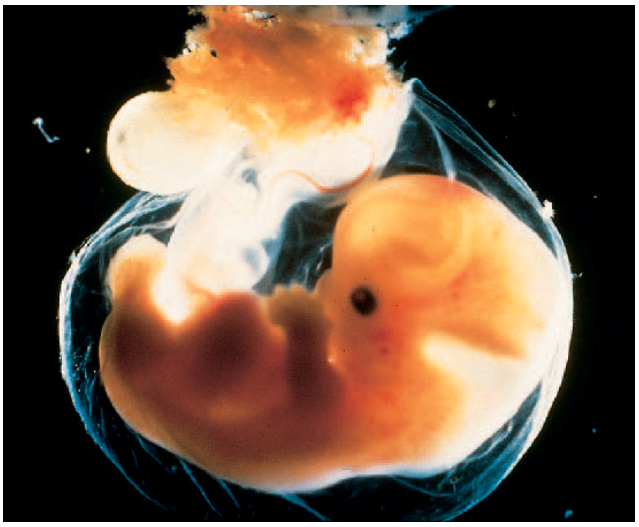
Paramesonephric ducts begin to develop just lateral to the mesonephric ducts and grow inferiorly to meet one another, where they enter the cloaca as a single, midline tube.

Testosterone, secreted by the testes, causes the mesonephric duct system to enlarge and differentiate to form the ductus deferens, the seminal vesicles, and the prostate gland (figure 29.15*b*). Müllerian-inhibiting hormone, which the testes also secrete, causes the paramesonephric ducts to degenerate. The paramesonephric ducts are also called the müllerian ducts, and they give rise to the uterine tubes, the uterus, and part of the vagina in females (figure 29.15*c*). If neither testosterone nor müllerian-inhibiting hormone is secreted, the mesonephric duct system atrophies, and the paramesonephric duct system develops to form the internal female reproductive structures.

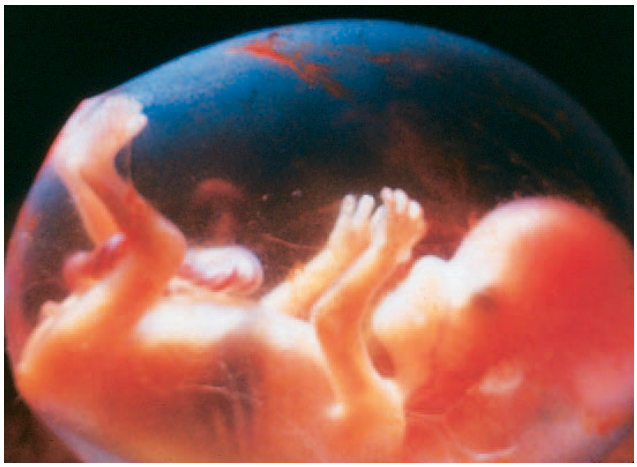
Like the other sexual organs, the external genitalia begin as the same structures in the male and female and then diverge. An enlargement called the **genital tubercle** develops in the groin of the embryo. **Urogenital folds** develop on each side of the urogenital opening, and **labioscrotal swellings** develop lateral to the folds. A **urethral groove** develops along the ventral surface of the genital tubercle.

In the male, under the influence of dihydrotestosterone, which is derived from testosterone, the genital tubercle and the urogenital folds close over the urogenital opening and the urethral groove to form the penis. If this closure does not proceed all the way to the end of the penis, a defect known as **hypospadias** (hī′pō-spā′dē-ăs) results. The testes move into the labioscrotal swellings, which become the scrotum of the male.

In the female, in the absence of testosterone, the genital tubercle becomes the clitoris. The urethral groove disappears; urogenital folds do not fuse. As a result, the urethra opens somewhat posterior to the clitoris but anterior to the vaginal opening. The unfused urogenital folds become the labia minora, and the labioscrotal folds become the labia majora.



(a)



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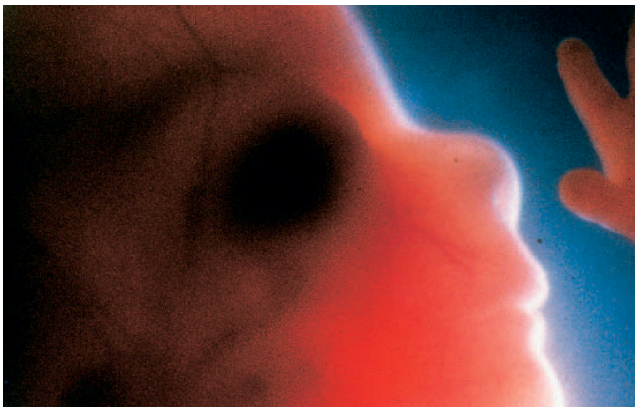


(c)

Figure 29.16 Embryos and Fetuses at Different Ages

(*a*) Fifty days after fertilization. (*b*) Three months after fertilization. (*c*) Four months after fertilization.

Growth of the Fetus

Objective

- *Describe the growth of the fetus.*

The embryo becomes a **fetus** approximately 60 days after fertilization (a 50-day-old embryo is shown in figure 29.16*a*). The major difference between the embryo and the fetus is that in the embryo most of the organ systems are developing, whereas in the fetus the organs are present. Most morphologic changes occur in the embryonic phase of development, whereas the fetal period is primarily a "growing phase."

The fetus grows from about 3 cm and 2.5 g at 60 days to 50 cm and 3300 g at term—more than a 15-fold increase in length and a 1300-fold increase in weight (figure 29.17). Although growth is certainly a major feature of the fetal period, it's not the only feature. The major organ systems still continue to develop during the fetal period.

Fine, soft hair called **lanugo** (la-noo′gō) covers the fetus, and a waxy coat of sloughed epithelial cells called **vernix caseosa** (ver′niks kā-se-ō′să) protects the fetus from the somewhat toxic nature of the amniotic fluid formed by the accumulation of waste products from the fetus.

Subcutaneous fat that accumulates in the older fetus and newborn provides a nutrient reserve, helps insulate the baby, and aids the baby in sucking by strengthening and supporting the cheeks so that negative pressure can be developed in the oral cavity.

Peak body growth occurs late in gestation, but, as placental size and blood supply limits are approached, the growth rate slows. Growth of the placenta essentially stops at about 35 weeks, thus restricting further intrauterine growth.

Fetal Surgery

Fetal surgery performed while the fetus is still in the uterus was first done in the United States in 1979 to drain excess fluid associated with hydrocephalus. These surgeries didn't usually solve the underlying neurologic problems and have been discontinued. Since 1981, in utero surgeries have successfully removed excess fluid from enlarged urinary bladders of male fetuses. The fluid buildup occurs in 1 in every 2000 male fetuses when a flap of tissue grows over the internal opening of the urethra. Without treatment, the amount of amniotic fluid is greatly reduced, and most of those babies die shortly after birth. Since 1989, more advanced surgeries have repaired diaphragmatic hernia, in which part of the abdominal organs push up through a hole in the left side of the diaphragm into the left pleural space, so that the left lung fails to develop fully. The defect occurs in 1 of every 2000 babies, and without surgery babies with this defect run a 75% risk of dying before or soon after birth. During surgery, the uterus is cut open, and the fetus is pulled far enough out of the opening so that a small incision can be made in its side. The abdominal organs are moved back into the abdomen, the hole in the diaphragm is covered with a surgical patching material called Gore-Tex, the incision in the fetus is closed, and the fetus is tucked back into the uterus. The amniotic fluid, which was removed and saved earlier in the surgery, is replaced, and the incision in the uterus and mother's skin is repaired.

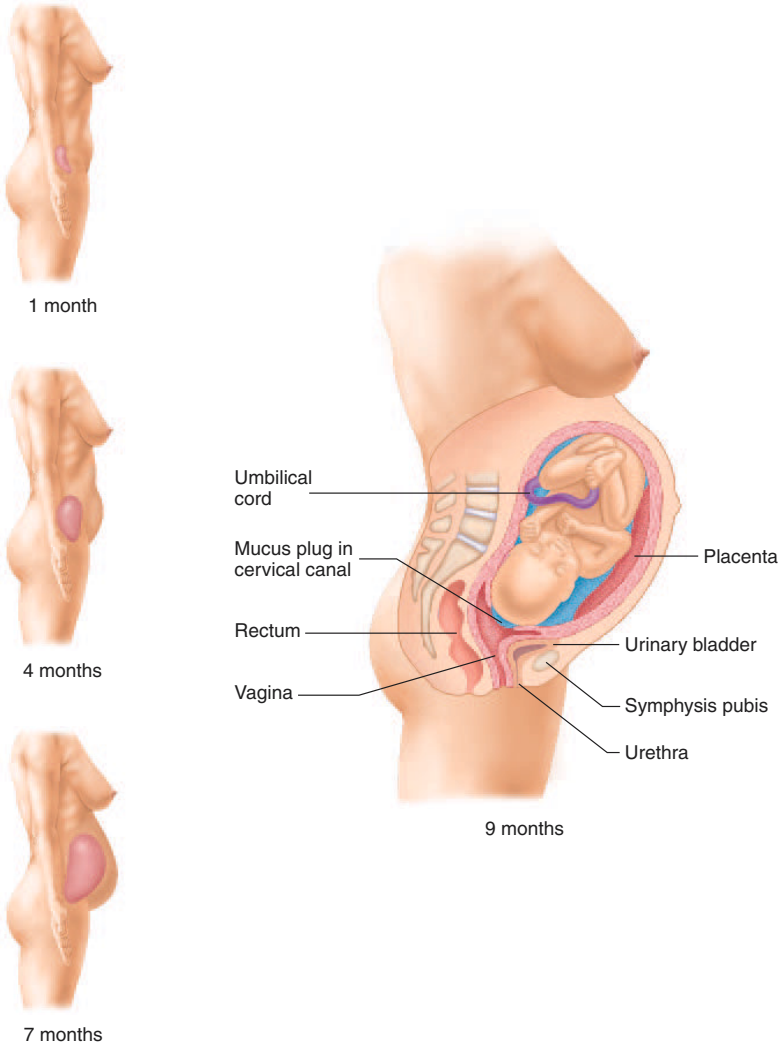


Figure 29.17 Enlargement of the Uterus During Fetal Development

At about 38 weeks of development, the fetus has progressed to the point at which it can survive outside the mother. The average weight at this point is 3250 g for a female fetus and 3300 g for a male fetus.

Exercise During Pregnancy

Healthy women with normal pregnancies are encouraged to engage in moderate exercise during pregnancy. Women who are active before becoming pregnant are able to continue most of their activities during early pregnancy. Later in pregnancy, changes in weight, balance, and joint stability can affect exercise. Exercise during pregnancy is beneficial to the woman and helps her recover more quickly after delivery.

13. *Describe the formation of these major organs: skin, bones, skeletal muscles, nervous system, eyes, and respiratory system.*
14. *Explain the formation of the following endocrine glands: anterior pituitary, posterior pituitary, thyroid, parathyroid, adrenal medulla, adrenal cortex, and pancreas.*
15. *Explain the process whereby a one-chambered heart becomes a four-chambered heart.*
16. *Describe the development of the pronephros, mesonephros, and metanephros in the development of the kidneys.*
17. *Describe the effect of hormones on the development of the male and female reproductive systems.*
18. *Compare the male and female structures formed from each of the following: genital tubercle, urogenital folds, and labioscrotal swellings.*
19. *What major events distinguish embryonic and fetal development?*

Clinical Focus Fetal Monitoring

Amniocentesis (am′nē-ō-sen-tē′sis) is the removal of amniotic fluid from the amniotic cavity (figure A). As the fetus develops, it expels molecules of various types, as well as living cells, into the amniotic fluid. These molecules and cells can be collected and analyzed. A number of normal conditions can be evaluated, and a number of metabolic disorders can be detected by analysis of the types of molecules that the fetus expels. The cells collected by amniocentesis can be grown in culture, and additional metabolic disorders can be evaluated. Chromosome analysis, called a **karyotype,** can also be performed on the cultured cells. Amniocentesis has been done as early as 10 weeks after fertilization, but the success rate at that time is quite low. It is most commonly performed at 13–14 weeks after fertilization.

Fetal tissue samples may also be obtained by **chorionic villus sampling,** in which a probe is introduced into the uterine cavity through the cervix and a small piece of chorion is removed. This technique has an advantage over amniocentesis in that it can be used earlier in development, as early as the seventh to ninth week after fertilization.

One of the molecules normally produced by the fetus and released into the amniotic fluid is **α-fetoprotein.** If the fetus has tissues exposed to the amniotic fluid that are normally covered by skin, such as nervous tissue, resulting from failure of the neural tube to close, or abdominal tissues, resulting from failure of the abdominal wall to fully form, an excessive amount of α-fetoprotein is lost into the amniotic fluid.

Some of the metabolic by-products from the fetus, such as α-fetoprotein and estriol, a weak form of estrogen produced in the placenta after 20 weeks of gestation, can enter the maternal blood. In some cases, the by-products are processed and passed to the maternal urine. The levels of these fetal products can then be measured in the mother's blood or urine.

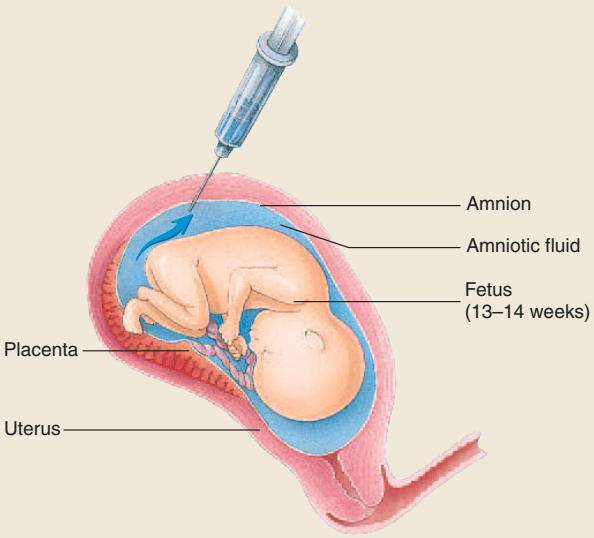


Figure A Removal of Amniotic Fluid for Amniocentesis

The fetus can be seen within the uterus by **ultrasound,** which uses sound waves that are bounced off the fetus like sonar and then analyzed and enhanced by computer; or by **fetoscopy,** in which a fiberoptic probe is introduced into the amniotic cavity. Because of the constantly increasing resolution in ultrasound and because it is noninvasive compared to fetoscopy, the latter technique is not commonly used at present. Ultrasound has not been found to pose any risk to the fetus or mother. It's accomplished by placing a transducer on the abdominal wall (transabdominal) or by inserting the transducer into the woman's vagina (transvaginal). The latter technique produces much higher resolution because fewer layers of tissue exist between the transducer and the uterine cavity. Transvaginal ultrasound can be used to identify the yolk sac of a developing embryo as early as 17 days after fertilization, and the embryo can be visualized by 25 days. Transabdominal ultrasound allows for fetal monitoring by 6–8 weeks after fertilization.

Fetal heart rate can be detected with an ultrasound stethoscope by the tenth week after fertilization and with a conventional stethoscope by 20 weeks. The normal fetal heart rate is 140 bpm (normal range is 110–160).

Parturition

Objectives

- *Describe the three stages of labor.*
- *Explain the hormonal and nervous system factors responsible for parturition.*

Parturition (par-toor-ish′ŭn) refers to the process by which a baby is born. Physicians usually calculate the gestation period, or length of the pregnancy, as 280 days (40 weeks or 10 lunar months) from the last menstrual period (LMP) to the date of delivery of the infant.

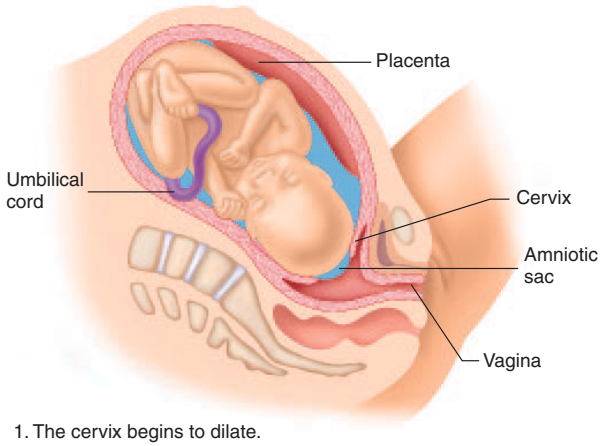
P R E D I C T 3

How many days (postovulatory age) does it take an infant to develop from fertilization to parturition?

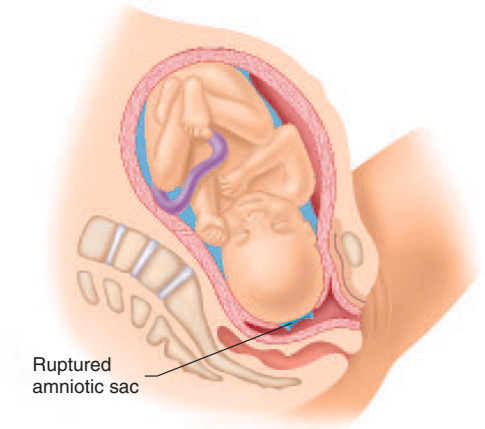
Prematurity

Occasionally, the fetus is delivered before it has sufficiently matured. It is then considered to be **premature.** Prematurity is one of the most significant problems in pediatrics, the branch of medical science dealing with children, because of all the associated complications. The most significant of these complications is **respiratory distress syndrome,** which occurs because very young premature infants cannot produce **surfactant,** a mixture of phospholipids and protein that lines the inner surface of the lungs and allows the lungs to expand as we breathe. Each year, 65,000 premature infants suffer from respiratory distress syndrome in the United States. Until recently, 10% of those infants died. Now, surfactant substitutes are being developed, and glucocorticoid administration can stimulate surfactant production. These therapies have cut the death rate in half, and more effective replacements are being investigated.

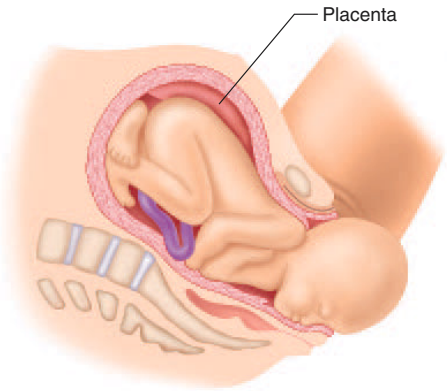
Near the end of pregnancy, the uterus becomes progressively more irritable and usually exhibits occasional contractions that become stronger and more frequent until parturition is initiated. The cervix gradually dilates, and strong uterine contractions help expel the fetus from the uterus through the vagina (figure 29.18). Before



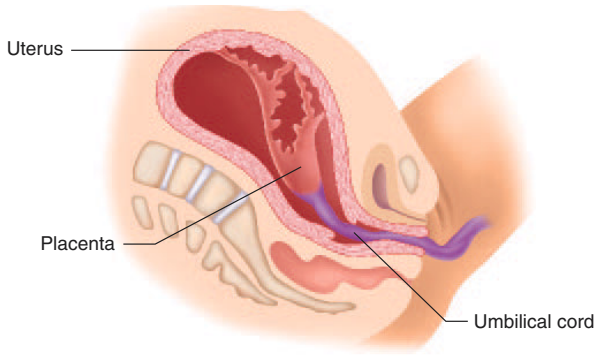
1. The cervix begins to dilate.



2. Further dilation of the cervix and rupture of the amniotic sac occur.



3. The fetus is expelled from the uterus.



4. The placenta is then expelled.

Process Figure 29.18 Parturition

expulsion of the fetus from the uterus, the amniotic sac ruptures, and amniotic fluid flows through the vagina to the exterior of the woman's body.

Labor is the period during which the contractions occur that result in expulsion of the fetus from the uterus. It occurs as three stages.

1. *First stage.* The first stage begins with the onset of regular uterine contractions and extends until the cervix dilates to a diameter about the size of the fetus's head. This stage of labor commonly lasts from 8–24 hours, but it may be as short as a few minutes in some women who have had more than one child. Normally (95% of the time), the head of the fetus is in an inferior position within the woman's pelvis during labor. The head acts as a wedge, forcing the cervix and vagina to open as the uterine contractions push against the fetus.

The Perineum in Pregnancy

The **central tendon of the perineum** (see figure 10.19) is very important in supporting the uterus and vagina. Tearing or stretching of the tendon during childbirth may weaken the inferior support of these organs, and prolapse of the uterus may occur. **Prolapse** is a "sinking" of the uterus so that the uterine cervix moves down into the vagina (first degree), moves down near the vaginal orifice (second degree), or may protrude through the vaginal orifice (third degree). During childbirth, an **episiotomy,** a cut through the perineal central tendon, prevents tearing of the perineum. The cut relieves the pressure and heals better than would a tear; however, there appears to be evidence that many episiotomies may be unnecessary.

2. *Second stage.* The second stage of labor lasts from the time of maximum cervical dilation until the baby exits the vagina. This stage may last from a minute to up to an hour. During this stage, contractions of the abdominal muscles assist the uterine contractions. The contractions generate enough pressure to compress blood vessels in the placenta so that blood flow to the fetus is stopped. During periods of relaxation, blood flow to the placenta resumes.

Oxytocin

Occasionally, drugs like oxytocin are administered to women during labor to increase the force of the uterine contractions. Caution must be exercised in the use of this drug, however, so that tetaniclike contractions, which would drastically reduce the blood flow through the placenta, do not occur.

3. *Third stage.* The third stage of labor involves the expulsion of the placenta from the uterus. Contractions of the uterus cause the placenta to tear away from the wall of the uterus. Some bleeding occurs because of the intimate contact between the placenta and the uterus; however, bleeding normally is restricted because uterine smooth muscle contractions compress the blood vessels to the placenta.

Blood levels of estrogen and progesterone fall dramatically after parturition. Once the placenta has been dislodged from the uterus, the source of these hormones is gone. In addition, during the 4 or 5 weeks after parturition, the uterus becomes much smaller, but it remains somewhat larger than it was before pregnancy. The cells of the uterus become smaller, and many of them degenerate. A vaginal discharge composed of small amounts of blood and degenerating endometrium persists for 1 week or more after parturition.

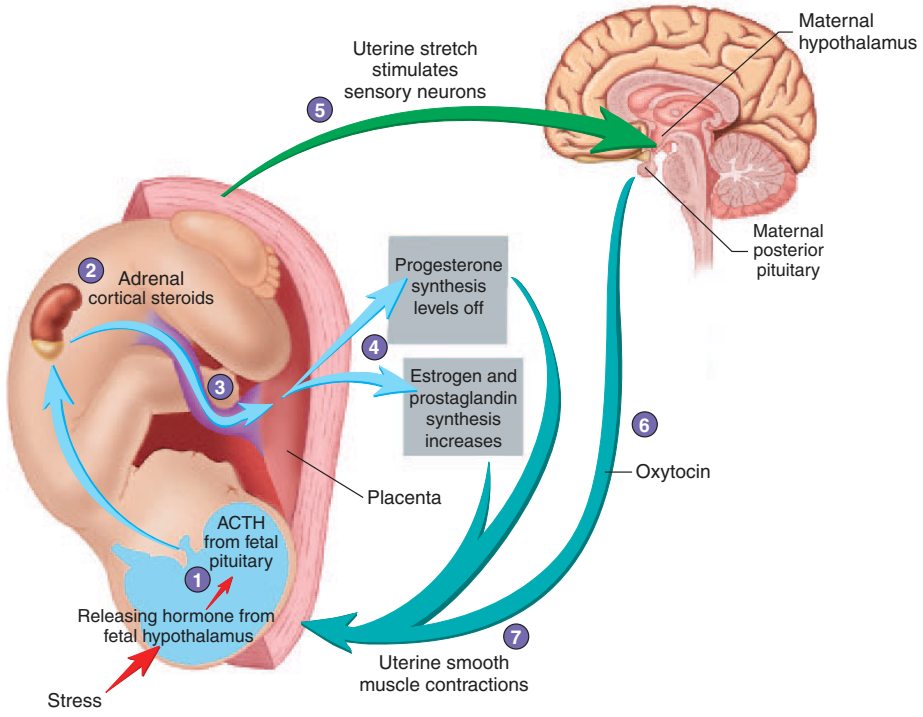
The precise signal that triggers parturition is unknown, but many of the factors that support it have been identified (figure 29.19). Before parturition, the progesterone concentration in the maternal circulation is at its highest level. Progesterone has an inhibitory effect on uterine smooth muscle cells. Near the end of pregnancy, however, estrogen levels rapidly increase in the maternal circulation, and the excitatory influence of estrogens on uterine smooth muscle cells overcomes the inhibitory influence of progesterone.

The adrenal glands of the fetus are greatly enlarged before parturition. The stress of the confined space of the uterus and the limited oxygen supply resulting from a more rapid increase in the size of the fetus than in the size of the placenta increase the rate of adrenocorticotropic hormone (ACTH) secretion by the fetus's anterior pituitary gland. ACTH causes the fetal adrenal cortex to produce glucocorticoids, which travel to the placenta, where they decrease the rate of progesterone secretion and increase the rate of estrogen synthesis. In addition, prostaglandin synthesis is initiated. Prostaglandins strongly stimulate uterine contractions.

During parturition, stretch of the uterine cervix initiates nervous reflexes that cause oxytocin to be released from the woman's posterior pituitary gland. Oxytocin stimulates uterine contractions, which move the fetus farther into the cervix, causing further stretch.

Thus, a positive-feedback mechanism is established in which stretch stimulates oxytocin release and oxytocin causes further stretch. This positive-feedback system stops after delivery, when the cervix is no longer stretched.

1. The fetal hypothalamus secretes a releasing hormone that stimulates adrenocorticotropic hormone (ACTH) secretion from the pituitary. The fetal pituitary secretes ACTH in greater amounts near parturition.
2. ACTH causes the fetal adrenal gland to secrete greater quantities of adrenal cortical steroids.
3. Adrenal cortical steroids travel in the umbilical blood to the placenta.
4. In the placenta the adrenal cortical steroids cause progesterone synthesis to level off and estrogen and prostaglandin synthesis to increase, making the uterus more irritable.
5. The stretching of the uterus produces action potentials that are transmitted to the brain through ascending pathways.
6. Action potentials stimulate the secretion of oxytocin from the posterior pituitary.
7. Oxytocin causes the uterine smooth muscle to contract.



Process Figure 29.19 Factors That Influence the Process of Parturition

Although the precise control of parturition in humans is unknown, these changes appear to play a role.

Progesterone inhibits oxytocin release; thus, decreased progesterone levels in the maternal circulation can support the increased secretion rate of oxytocin. In addition, estrogens make the uterus more sensitive to oxytocin stimulation by increasing the synthesis of receptor sites for oxytocin. Some evidence suggests that oxytocin also stimulates prostaglandin synthesis in the uterus. All these events support the development of strong uterine contractions.

20. List the stages of labor, and indicate when each stage begins and its approximate length of time.

21. Describe the hormonal changes that take place before and during delivery. How is stretch of the cervix involved in delivery?

P R E D I C T 4

A woman is having an extremely prolonged labor. From her anatomy and physiology course, she remembers the role of calcium in muscle contraction and asks the doctor to give her a calcium injection to speed the delivery. Explain why the doctor would or would not do as she requests.

The Newborn

Objectives

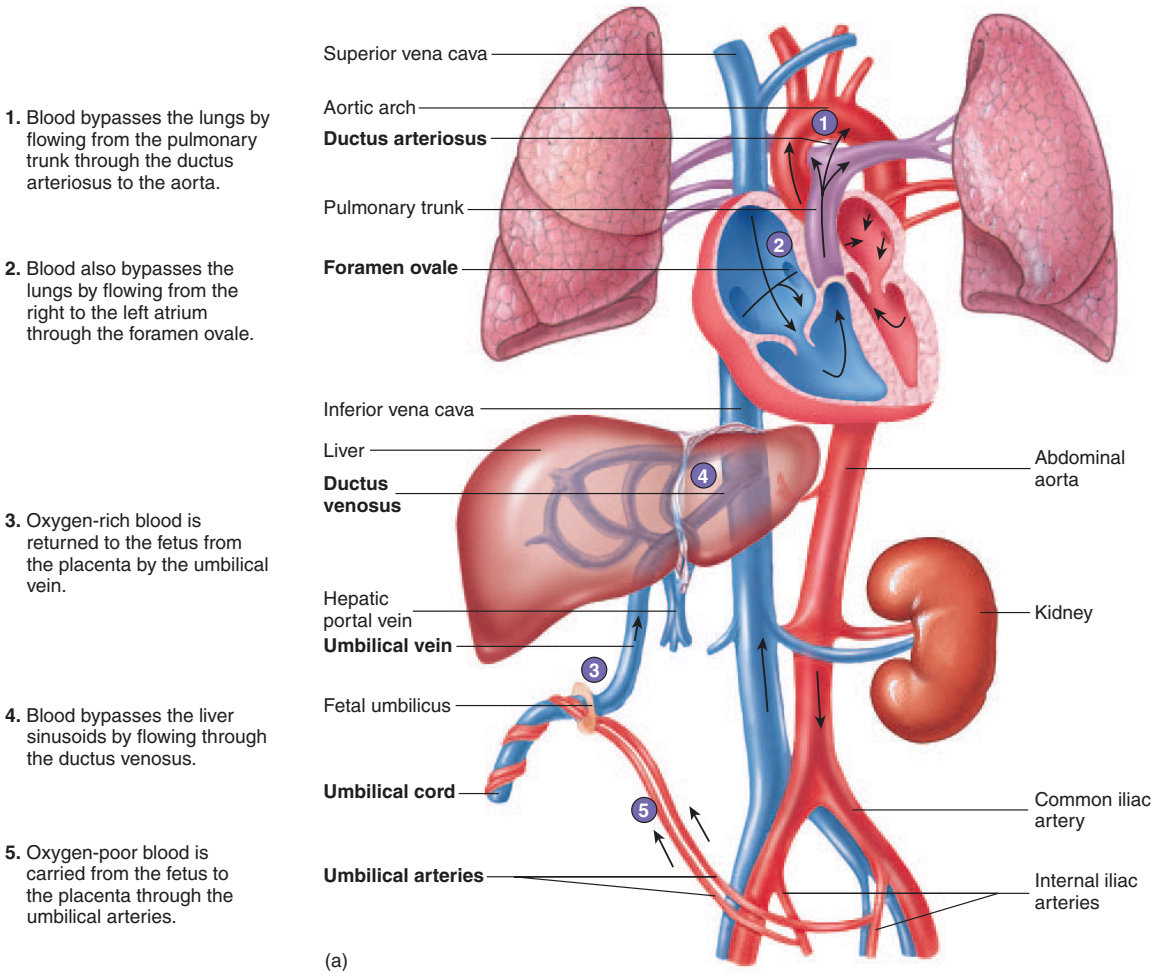
- *Discuss respiratory, circulatory, digestive, and other major changes that occur at the time of birth.*
- *Discuss the meaning of each letter in the word Apgar.*

The newborn baby, or **neonate,** experiences several dramatic changes at the time of birth. The major and earliest changes in the infant are separation from the maternal circulation and transfer from a fluid to a gaseous environment. The large, forced gasps of air that occur when the infant cries at the time of delivery help inflate the lungs.

Respiratory and Circulatory Changes

The initial inflation of the lungs causes important changes in the circulatory system (figure 29.20). Expansion of the lungs reduces the resistance to blood flow through the lungs, resulting in increased blood flow through the pulmonary arteries. Consequently, more blood flows from the right atrium to the right ventricle and into the pulmonary arteries, and less blood flows from the right atrium through the foramen ovale to the left atrium. In addition, an increased volume of blood returns from the lungs through the pulmonary veins to the left atrium, which increases the pressure in the left atrium. The increased left atrial pressure and decreased right atrial pressure, resulting from decreased pulmonary resistance, forces blood against the septum primum, causing the foramen ovale to close. This action functionally completes the separation of the heart into two pumps: the right side of the heart and the left side of the heart. The closed foramen ovale becomes the **fossa ovalis.**

The **ductus arteriosus,** which connects the pulmonary trunk to the aorta and allows blood to flow from the pulmonary trunk to the systemic circulation, closes off within 1 or 2 days after birth. This closure occurs because of the sphincterlike constriction of the artery and is probably stimulated by local changes in blood pressure and blood oxygen content. Once closed, the ductus arteriosus is replaced by connective tissue and is known as the **ligamentum arteriosum.**



Process Figure 29.20 Circulatory Changes at Birth

(*a*) Circulatory conditions in the fetus.

Patent Ductus Arteriosus

If the ductus arteriosus does not close completely, it's said to be **patent.** This is a serious birth defect, resulting in marked elevation in pulmonary blood pressure because blood flows from the left ventricle to the aorta, through the ductus arteriosus to the pulmonary arteries. If not corrected, it can lead to irreversible degenerative changes in the heart and lungs.

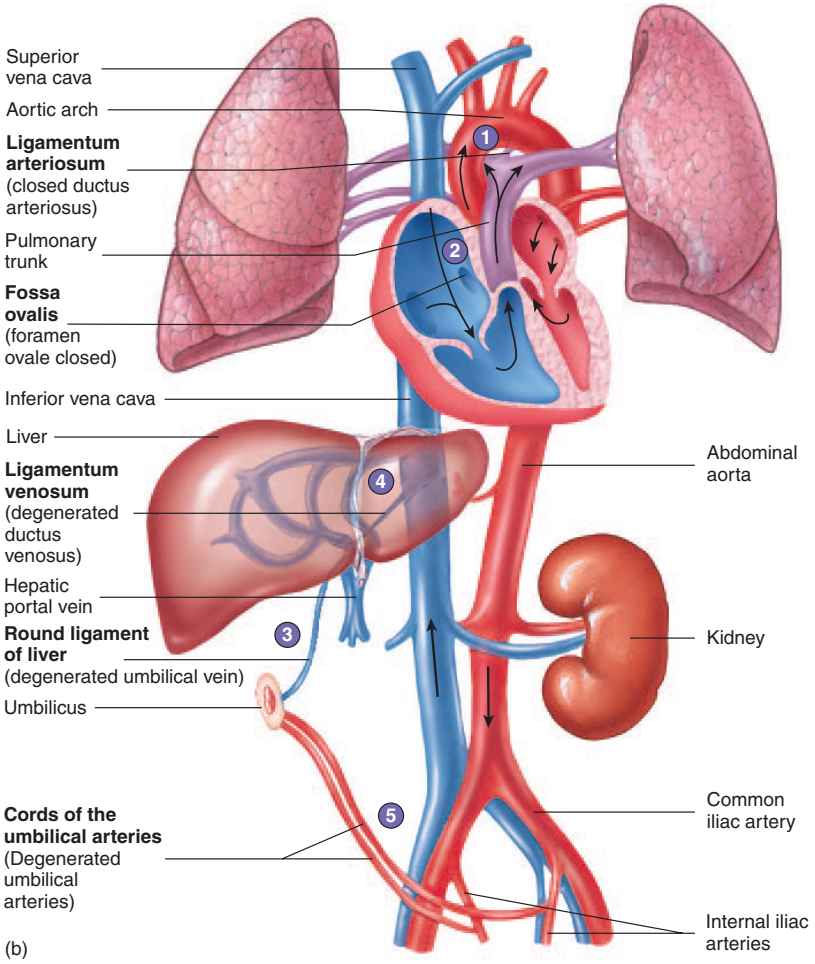
The fetal blood supply passes to the placenta through umbilical arteries from the internal iliac arteries and returns through an umbilical vein. The blood passes through the liver via the ductus venosus, which joins the inferior vena cava. When the umbilical cord is tied and cut, no more blood flows through the umbilical vein and arteries, and they degenerate. The remnant of the umbilical vein becomes the **ligamentum teres,** or **round ligament,** of the liver, and the ductus venosus becomes the **ligamentum venosum.**

Digestive Changes

When a baby is born, it's suddenly separated from its source of nutrients provided by the maternal circulation. Because of this separation and the shock of birth and new life, the neonate usually loses 5%–10% of its total body weight during the first few days of life. Although the digestive system of the fetus becomes somewhat functional late in development, it is still very immature compared to that of the adult and can digest only a limited number of food types.

Late in gestation, the fetus swallows amniotic fluid from time to time. Shortly after birth, this swallowed fluid plus cells sloughed from the mucosal lining, mucus produced by intestinal mucous glands, and bile from the liver pass from the digestive tract as a greenish anal discharge called **meconium** (mē-kō′nē-ŭm).

The pH of the stomach at birth is nearly neutral because of the presence of swallowed alkaline amniotic fluid. Within the first 8 hours of life, a striking increase in gastric acid secretion occurs, causing the stomach pH to decrease. Maximum acidity is reached at 4–10 days, and the pH gradually increases for the next 10–30 days.



Process Figure 29.20 *(continued)*

(*b*) Circulatory changes that occur at birth.

The neonatal liver is also functionally immature. It lacks adequate amounts of the enzyme required in the production of bilirubin. This enzyme system usually develops within 2 weeks after birth in a healthy neonate, but because this enzyme system is not fully developed at birth, some full-term babies may temporarily develop jaundice. Jaundice often occurs in premature babies.

The newborn digestive system is capable of digesting lactose (milk sugar) from the time of birth. The pancreatic secretions are sufficiently mature for a milk diet, but the digestive system only gradually develops the ability to digest more solid foods over the first year or two; therefore, new foods should be introduced gradually during the first 2 years. It's also advised that only one new food be introduced at a time into the infant's diet so that, if an allergic reaction occurs, the cause is more easily determined.

Amylase secretion by the salivary glands and the pancreas remains low until after the first year. Lactase activity in the small intestine is high at birth but declines during infancy, although the levels still exceed those in adults. Lactase activity is lost in many adults (see chapter 24).

Apgar Scores

The newborn baby may be evaluated soon after birth to assess its physiologic condition. This assessment is referred to as the **Apgar score.** Apgar, which was named for Virginia Apgar, the physician who developed it, also stands for **a**ppearance, **p**ulse, **g**rimace, **a**ctivity, and **r**espiratory effort. Each of these characteristics is rated on a scale of 0–2: 2 denotes normal function, 1 denotes reduced function, and 0 denotes seriously impaired function. The total Apgar score is the sum of the scores from the five characteristics, ranging, therefore, from 0–10 (table 29.3). A total Apgar score of 8–10 at 1–5 minutes after birth is considered normal. Other scoring systems to estimate normal growth and development, including general external appearance and neurologic development, may also be applied to the neonate.

22. *What changes take place in the newborn's circulatory system shortly after birth? What do each of the following become: foramen ovale, ductus arteriosus, umbilical vein, and ductus venosus?*
23. *What changes take place in the newborn's digestive system shortly after birth?*
24. *Define the term meconium. Why does jaundice often develop after birth?*
25. *What is the Apgar score?*

Lactation

Objective

- *Explain the hormonal and nervous system factors responsible for lactation.*

Lactation is the production of milk by the mother's breasts (mammary glands; figure 29.21). It normally occurs in females after parturition and may continue for 2 or 3 years, provided suckling occurs often and regularly.

During pregnancy, the high concentration and continuous presence of estrogens and progesterone cause expansion of the duct system and secretory units of the breasts. The ducts grow and branch repeatedly to form an extensive network. Additional adipose tissue is deposited also; thus, the size of the breasts increases substantially throughout pregnancy. Estrogen is primarily responsible for breast growth during pregnancy, but normal development of the breast doesn't occur without the presence of several other hormones. Progesterone causes development of the breasts' secretory alveoli, which enlarge but don't secrete milk during pregnancy. The other hormones include growth hormone, prolactin, thyroid hormones, glucocorticoids, and insulin. The placenta secretes a growth hormonelike substance (human somatotropin) and a prolactinlike substance (human placental lactogen), and these substances also help support the development of the breasts.

Prolactin, which is produced by the anterior pituitary gland, is the hormone responsible for milk production. Before parturition, high levels of estrogen stimulate an increase in prolactin production. Milk production is inhibited during pregnancy, however, because high levels of estrogen and progesterone inhibit the effect of prolactin on the mammary gland. After parturition, estrogen, progesterone, and prolactin

Table 29.3 Examples of Apgar Rating Scales

	0	1	2
Appearance (skin color)	White or blue	Limbs blue, body pink	Pink
Pulse (rate)	No pulse	100 bpm	>100 bpm
Grimace (reflexive grimace initiated by stimulating the plantar surface of the foot)	No response	Facial grimaces, slight body movement	Facial grimaces, extensive body movement
Activity (muscle tone)	No movement, muscles flaccid	Limbs partially flexed, little movement, poor muscle tone	Active movement, good muscle tone
Respiratory effort (amount of respiratory activity)	No respiration	Slow, irregular respiration	Good, regular respiration, strong cry

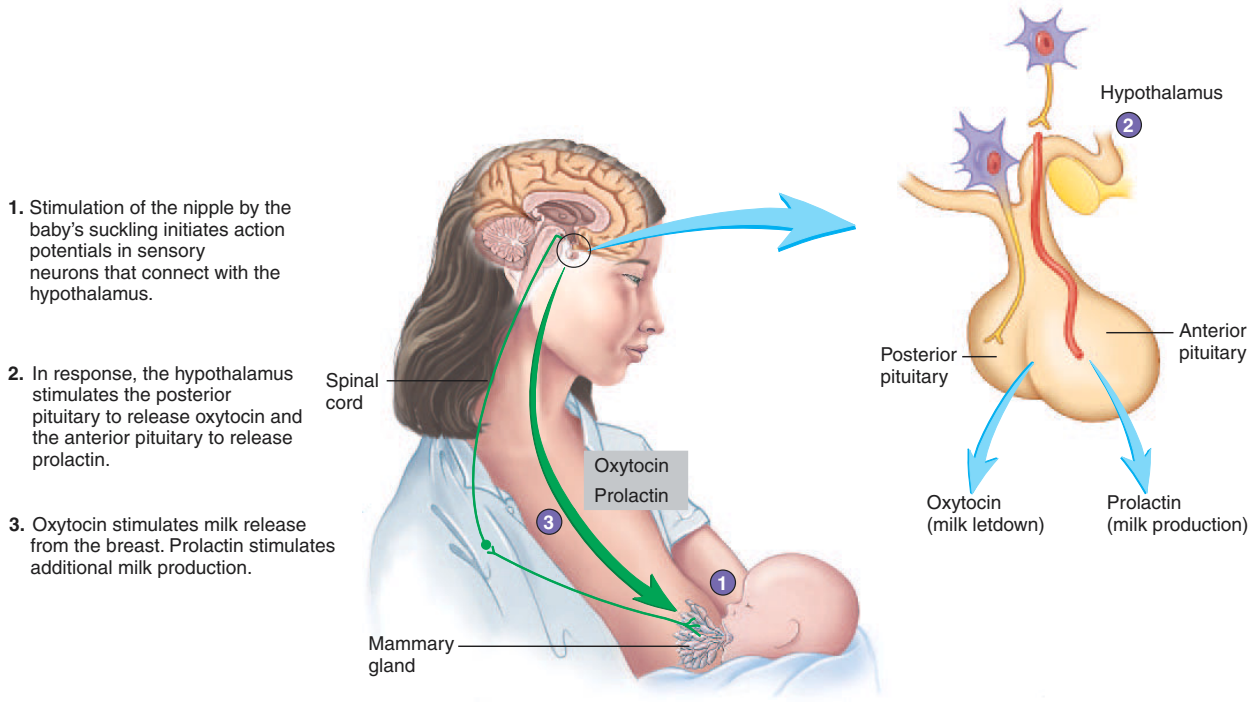


Figure 29.21 Hormonal Control of Lactation

levels decrease, and, with lower estrogen and progesterone levels, prolactin stimulates milk production. Despite a decrease in the basal levels of prolactin, a reflex response produces surges of prolactin release. During suckling, mechanical stimulation of the breasts initiates nerve impulses that reach the hypothalamus, causing the secretion of **prolactin-releasing factor (PRF)** and inhibiting the release of **prolactin-inhibiting factor (PIF).** Consequently, prolactin levels temporarily increase and stimulate milk production.

For the first few days after birth, the mammary glands secrete **colostrum** (kō-los′trŭm), which contains little fat and less lactose than milk. Eventually, more nutritious milk is produced. Colostrum and milk not only provide nutrition, but they also contain antibodies (see chapter 22) that help protect the nursing baby from infections.

HIV and the Newborn

The human immunodeficiency virus (HIV) can be transmitted from a mother to her child in utero, during parturition, or during breast-feeding. HIV has been isolated from human breast milk and colostrum.

In a study of 212 mothers in Africa who were seronegative (no HIV antibodies found in the serum) at the time of delivery, 16 seroconverted (developed HIV antibodies) during the time that they were breast-feeding. Nine of the nursing babies also seroconverted. At least four of the babies were confirmed to be seronegative at the time of birth.

Repeated stimulation of prolactin release makes nursing (breast-feeding) possible for several years. If nursing stops, however, within a few days the ability to produce prolactin ceases, and milk production stops.

Because it takes time to produce milk, an increase in prolactin results in the production of milk to be used in the next nursing period. At the time of nursing, stored milk is released as a result of a reflex response. Mechanical stimulation of the breasts produces nerve impulses that cause the release of oxytocin from the posterior pituitary, which stimulates cells surrounding the alveoli to contract. Milk is then released from the breasts, a process that is called **milk letdown.** In addition, higher brain centers can stimulate oxytocin release, and such things as hearing an infant cry can result in milk letdown.

26. What hormones are involved in preparing the breast for lactation? Describe the events involved in milk production and milk letdown. What is colostrum?

P R E D I C T 5

While nursing her baby, a woman notices that she develops "uterine cramps." Explain what is happening.

First Year After Birth

Objective

- *List the major changes that occur from birth until 1 year of age.*

Many changes occur in the life of the newborn from birth until 1 year of age. The time of these changes may vary considerably from child to child, and the dates given are only rough estimates. The brain is still developing, and much of what the neonate can do depends on how much brain development has occurred. It's estimated that the total adult number of neurons is present in the CNS at birth, but subsequent growth and maturation of the brain involve the addition of new neuroglial cells, some of which form new myelin sheaths, and the addition of new connections between neurons, which may continue throughout life.

By 6 weeks, the infant usually can hold up its head when placed in a prone position and begins to smile in response to people or objects. At 3 months of age, the infant's limbs move apparently aimlessly. The infant has enough control of the arms and hands, however, that voluntary thumb sucking can occur. The infant can follow a moving person with its eyes. At 4 months, the infant begins to raise itself by its arms. It can begin to grasp objects placed in its hand, coo and gurgle, roll from its back to its side, listen quietly when hearing a person's voice or music, hold its head erect, and play with its hands. At 5 months, the infant can usually laugh, reach for objects, turn its head to follow an object, lift its head and shoulders, sit with support, and roll over. At 8 months, the infant recognizes familiar people, sits up without support, and reaches for specific objects. At 12 months, the infant may pull itself to a standing position and may be able to walk without support. It can pick up objects in its hands and examine them carefully. It can understand much of what is said to it and may say several words of its own.

27. List the major changes that occur during the first year of life. What do most of these activities depend upon?

Life Stages

Objective

- *List the stages of life and describe the major events associated with each stage.*

The prenatal and neonatal periods of life previously described are only a small part of the total life span. The life stages from fertilization to death are as follows: (1) the germinal period: fertilization to 14 days; (2) embryo: 14–56 days after fertilization; (3) fetus: 56 days after fertilization to birth; (4) neonate: birth to 1 month after birth; (5) infant: 1 month to 1 or 2 years (the end of infancy is sometimes set at the time that the child begins to walk); (6) child: 1 or 2 years to puberty; (7) adolescent: puberty (age 11–14) to 20 years; and (8) adult: age 20 to death. Adulthood is sometimes divided into three periods: young adult, age 20–40; middle age, age 40–65; and older adult, age 65 to death (figure 29.22).

Figure 29.22 Active Older Adults

A conspicuous feature of the population of older adults is the range of variability. In some adults over 70 years, many systems are beginning to fail. Others can look forward to at least 10 more years of healthy living.

During childhood, the individual develops considerably. Many of the emotional characteristics that a person possesses throughout life are formed during early childhood.

Major physical and physiologic changes occur during adolescence that also affect the emotions and behavior of the individual. Other emotional changes occur as the adolescent attempts to fit into an adult world. Puberty usually occurs somewhat earlier in females (at about 11–13 years) than in males (at about 12–14 years). A period of rapid growth usually accompanies the onset of puberty. This rapid growth period is followed by a period of slower growth. Full adult stature is usually achieved by age 17 or 18 in females and 19 or 20 years in males.

28. Define the different life stages, starting with the germinal stage and ending with the adult.

Aging

Objective

- *Describe the major changes associated with aging and death.*

Development of a new human being begins at fertilization, as does the process of aging. Cells proliferate at an extremely rapid rate during early development and then the process begins to slow as various cells become committed to specific functions within the body.

Many cells of the body, such as liver and skin cells, continue to proliferate throughout life, replacing dead or damaged tissue. Many other cells, however, such as the neurons in the central nervous system, cease to proliferate once they have reached a certain number, and dead cells are not replaced. After the number of neurons reaches a peak, at about the time of birth, their numbers begin to decline. Neuronal loss is most rapid early in life and later decreases to a slower, steadier rate.

A natural, but as yet unexplained, decline occurs in mitochondrial DNA function with age. If this decline reaches a threshold, which apparently differs from tissue to tissue, the normal function of the mitochondrion is lost, and the tissue or organ may exhibit disease symptoms. In a small number of people, this mitochondrial degeneration occurs very early in life, resulting in premature aging.

The physical plasticity (i.e., the state of being soft and pliable) of young embryonic tissues results largely from the presence of large amounts of hyaluronate and relatively small amounts of collagen; furthermore, the collagen and other related proteins that are present are not highly cross-linked; thus, the tissues are very flexible and elastic. Many of these proteins produced during development are permanent components of the individual, however, and, as the individual ages, more and more cross-links form between these protein molecules, thereby rendering the tissues more rigid and less elastic.

The tissues with the highest content of collagen and other related proteins are those most severely affected by the collagen cross-linking and tissue rigidity associated with aging. The lens of the eye is one of the first structures to exhibit pathologic changes as a result of this increased rigidity. Vision of close objects becomes more difficult with advancing age until most middle-aged people require reading glasses (see chapter 15). Loss of elasticity also affects other tissues, including the joints, blood vessels, kidneys, lungs, and heart, and greatly reduces the functional ability of these organs.

Like nervous tissue, mature muscle cells don't normally proliferate after terminal differentiation occurs before birth. As a result, the total number of skeletal and cardiac muscle fibers declines with age. The strength of skeletal muscle reaches a peak between 20 and 30 years of life and declines steadily thereafter. Furthermore, like the collagen of connective tissue, the macromolecules of muscle undergo biochemical changes during aging and render the muscle tissue less functional. A good exercise program, however, can slow or even reverse this process.

The decline in muscular function also contributes to a decline in cardiac function with advancing age. The heart loses elastic recoil ability and muscular contractility. As a result, total cardiac output declines, and less oxygen and fewer nutrients reach cells, such as neurons in the brain and cartilage cells in the joints, thereby contributing to the decline in these tissues. Reduced cardiac function also may result in decreased blood flow to the kidneys, thus contributing to decreases in their filtration ability. Degeneration of the connective tissues as a result of collagen cross-linking and other factors also decreases the filtration efficiency of the glomerular basement membrane.

Atherosclerosis (ath′er-ō-skler-ō′sis) is the deposit and subsequent hardening of a soft, gruel-like material in lesions of the intima of large- and medium-sized arteries. These deposits then become fibrotic and calcified, resulting in **arteriosclerosis** (ar-tēr′ē-ō-skler-ō′sis; hardening of the arteries). Arteriosclerosis interferes with normal blood flow and can result in a **thrombus,** which is a clot or plaque formed inside a vessel. A piece of the plaque, called an **embolus** (em′bō-lŭs) can break loose, float through the circulation, and lodge in smaller arteries to cause myocardial infarctions or strokes. Atherosclerosis occurs to some extent in all middle-aged and older people and even may occur in certain young people. People with high blood cholesterol, however, appear to be at increased risk for developing atherosclerosis. In addition to dietary influences, this condition seems to have a heritable component, and blood tests are available to screen people for high blood cholesterol levels.

Many other organs, such as the liver, pancreas, stomach, and colon, undergo degenerative changes with age. The ingestion of harmful agents may accelerate such changes. Examples include the degenerative changes induced in the lungs, aside from lung cancer, by cigarette smoke and sclerotic changes in the liver as a result of alcohol consumption.

In addition to the previously described changes associated with aging, cellular wear and tear, or cytologic aging, is another factor that contributes to aging. Progressive damage from many sources like radiation and toxic substances may result in irreversible cellular insults and may be one of the major factors leading to aging. It has been speculated that ingestion of the antioxidant vitamins C and E in combination may help slow this part of aging by stimulating cell repair. Vitamin C also stimulates collagen production and may slow the loss of tissue plasticity associated with aging collagen.

According to the **free radical theory of aging,** free radicals, which are atoms or molecules with an unpaired electron, can react with and alter the structure of molecules that are critical for normal cell function. Alteration of these molecules can result in cell dysfunction, cancer, or other types of cellular damage. Free radicals are produced as a normal part of metabolism and are introduced into the body from the environment through the air we breathe and the food we eat. The damage caused by free radicals may accumulate with age. Antioxidants, such as beta carotene (provitamin A), vitamin C, and vitamin E, can donate electrons to free radicals, without themselves becoming harmful. Thus antioxidants may prevent the damage caused by the free radicals and may ward off age-related disorders, ranging from wrinkles to cancer. Experiments designed to test this hypothesis, however, have not consistently produced positive results.

As a result of poor diet, many people over age 50 do not get the minimum daily allotment of several vitamins and minerals. Feeling "bad" is not necessarily a part of aging but is mostly a result of poor nutrition and lack of exercise. Moderate exercise and avoiding overeating can prolong life. Moderate exercise can reduce the risk of heart attack by as much as 20%. It can also reduce the risk of stroke, high blood pressure, and some forms of cancer. Exercise can also increase a person's ability to reason and remember. Walking 30 minutes a day is recommended.

One characteristic of aging is an overall decrease in ATP production. This decrease is associated with a decline in oxidative phosphorylation, which has been shown in many cases to be associated with **mitochondrial DNA mutations.** Such mutations are also often associated with Alzheimer's disease. There are also genes in nuclear DNA associated with Alzheimer's.

Immune system changes may also be a major factor contributing to aging. The aging immune system loses its ability to respond to outside antigens but becomes more sensitive to the body's own antigens. These autoimmune changes add to the degeneration of the tissues already described and may be responsible for such things as arthritic joint disorders, chronic glomerular nephritis, and hyperthyroidism. In addition, T lymphocytes tend to lose their functional capacity with aging and cannot destroy abnormal cells as efficiently. This change may be one reason that certain types of cancer occur more readily in older people.

Genetic traits may also cause many of the changes associated with aging. As a general rule, animals with a very high metabolic rate have a shorter life span than those with a lower metabolic rate. In humans, a very small number of exceptional people have a slightly reduced normal body temperature, suggesting a lower metabolic rate. These same people often have an unusually long life span. This tendency appears to run in families and probably has some genetic basis. Studies of the general population suggest that if your parents and grandparents have lived long, so will you.

Another piece of evidence suggesting that a strong genetic component to aging exists comes from a disorder called **progeria** (prō-jēr′ē-ă; premature aging). This apparent genetic trait causes the degenerative changes of aging to occur shortly after the first year of life, and the child may look like a very old person by age 7.

One of the greatest disadvantages of aging is the increasing lack of ability to adjust to stress. Older people have a far more precarious homeostatic balance than younger people, and eventually some stress is encountered that is so great that the body's ability to recover is surpassed, and death results.

29. *How does the loss of cells that are not replaced affect the aging process? Give examples.*
30. *How does loss of tissue plasticity affect the aging process? Give examples.*
31. *Explain the free radical theory of aging.*
32. *How does aging affect the immune system?*
33. *What role does genetics play in aging?*

Death

Objective

- *Describe the characteristics of death.*

Death is usually not attributed to old age. Some other problem, such as heart failure, renal failure, or stroke, is usually listed as the cause of death.

Death was once defined as the loss of heartbeat and respiration. In recent years, however, more precise definitions of death have been developed because both the heart and the lungs can be kept working artificially, and the heart can even be replaced by an artificial device. Modern definitions of death are based on the permanent cessation of life functions and the cessation of integrated tissue and organ function. The most widely accepted indication of death in humans is **brain death,** which is defined as irreparable brain damage manifested clinically by the absence of response to stimulation, the absence of spontaneous respiration and heart beat, and an isoelectric ("flat") electroencephalogram for at least 30 minutes, in the absence of known CNS poisoning or hypothermia.

34. *Define death.*

Genetics

Objectives

- *Define the term genetics, and explain how chromosomes are related to genes. Define the term gene, and explain how genes control cell functions.*
- *Explain the major inheritance patterns.*
- *Give examples of different genetic disorders. Explain the processes involved in genetic counseling.*

Genetics is the study of heredity, that is, those characteristics inherited by children from their parents. Although the environment can influence gene expression, people's physical characteristics and abilities are largely determined by their genetic makeup. Many of a person's abilities, susceptibility to disease, and even life span are influenced by heredity. Because many of the diseases caused by microorganisms now are preventable or treatable, diseases that have a genetic basis are receiving more attention.

Chromosomes

Deoxyribonucleic (dē-oks′ē-rī′bō-noo-klē′ic) **acid (DNA)** is the hereditary material of cells and is responsible for controlling cell activities. DNA molecules and their associated proteins become visible as densely stained bodies, called **chromosomes** (krō′mō-sōmz; colored bodies), during cell division (see figure 2.26). Somatic cells contain 23 pairs of chromosomes, or 46 total chromosomes, and gametes contain 23 chromosomes. **Somatic** (sō-mat′ik) **cells** are all the cells of the body except for the **gametes** (gam′ētz), or sex cells. Examples of somatic cells are epithelial cells, muscle cells, neurons, fibroblasts, lymphocytes, and macrophages. In the male, the gametes are sperm cells, and in the female, the gametes are oocytes (see chapter 28).

A **karyotype** (kar′ē-ō-tīp), or display of the chromosomes in a somatic cell, can be produced by photographing the chromosomes through a microscope, cutting the pictures of the chromosomes out of the photograph, and arranging the chromosomes in pairs (figure 29.23). The 23 pairs of chromosomes are divided into two groups: 22 pairs of **autosomal** (aw-tō-sō′măl) **chromosomes,** all the chromosomes but the sex chromosomes, and one pair of **sex chromosomes,** which determines the sex of the individual. For convenience, the autosomes are numbered in pairs from 1 through 22, and sex chromosomes are denoted as **X** or **Y chromosomes.** A normal female has two X chromosomes (XX) in each somatic cell, whereas a normal male has one X and one Y chromosome (XY) in each somatic cell.

Figure 29.23 Human Karyotype

The 23 pairs of chromosomes in humans consist of 22 pairs of autosomal chromosomes (numbered 1–22) and 1 pair of sex chromosomes. This karyotype is of a male and has an X and a Y sex chromosome. A female karyotype would have two X chromosomes.

Sex Chromosome Abnormalities

A wide range of sex chromosome abnormalities exist. The presence of a Y chromosome makes a person male, and the absence of a Y chromosome makes a person female, regardless of the number of X chromosomes. Individuals with XO (Turner's syndrome), XX, XXX, or XXXX karyotypes are, therefore, females, and individuals with XY, XXY, XXXY, or XYY karyotypes are males. A YO condition is lethal, because the genes on the X chromosome are necessary for survival. Secondary sexual characteristics are usually underdeveloped in both the XXX female and the XXY male (called Klinefelter's syndrome), and additional X chromosomes (XXXX or XXXY) are often associated with some degree of mental retardation.

Gametes are derived from somatic cells by **meiosis** (mī-ō′sis). In this process, the somatic cells divide twice, and the chromosomes from the somatic cells are distributed to the gametes. Meiosis is called a reduction division because the number of chromosomes in the gametes is half the number in the somatic cells. When a sperm cell and an oocyte fuse during fertilization, each contributes one-half of the chromosomes necessary to produce new somatic cells; therefore, half of an individual's genetic makeup comes from the father and half from the mother.

During meiosis, the chromosomes are distributed in such a way that each gamete receives only one chromosome from each **homologous** (hŏ-mol′ō-gŭs) pair of chromosomes. Homologous chromosomes contain the same complement of genetic information. The inheritance of sex illustrates, in part, how chromosomes are distributed during gamete formation and fertilization. During meiosis and gamete formation, the pair of sex chromosomes separates so that each oocyte receives one of a homologous pair of X chromosomes, whereas each sperm cell receives either an X chromosome or a Y chromosome (figure 29.24). When a sperm cell fertilizes an oocyte to form a single cell, the sex of the individual is determined randomly. If a sperm cell with a Y chromosome fertilizes the oocyte, a male results, but if a sperm cell with an X chromosome fertilizes the oocyte, a female results. Estimating the probability of any given zygote being male or female is much like flipping a coin. When all the possible combinations of sperm cells with oocytes are considered, about half the individuals should be female and the other half should be male.

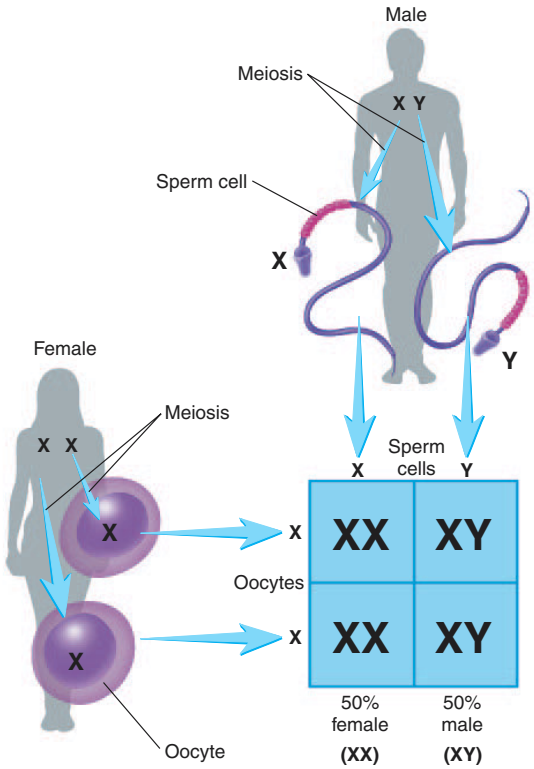


Figure 29.24 Inheritance of Sex

The female produces oocytes containing one X chromosome, whereas the male produces sperm cells with either an X or a Y chromosome. There are four possible combinations of an oocyte with a sperm cell, half of which produce females and half of which produce males.

Genes

The functional unit of heredity is the gene. Each **gene** is a certain portion of a DNA molecule but not necessarily a continuous stretch of DNA (see figure 3.41). Each chromosome contains thousands of genes, and each gene occupies a specific **locus** on a chromosome. Both chromosomes of a given pair contain similar but not necessarily identical genes. The genes occupying the same locus on homologous chromosomes are called **alleles** (ă-lēlz′). If the two allelic genes are identical, the person is **homozygous** (hŏ-mŏ-zī′gŭs) for the trait specified by that gene locus. If the two alleles are slightly different, the person is **heterozygous** (het′er-ō-zī′gŭs) for the trait.

Two major types of genes exist: structural and regulatory. **Structural genes** are those DNA sequences that serve as a template for mRNA and code for specific amino acid sequences in proteins like enzymes, hormones, or structural proteins like collagen. **Regulatory genes** are segments of DNA involved in controlling which structural genes are transcribed in a given tissue. By determining the structure of proteins and which proteins are produced by which cells, genes are responsible for the characteristics of cells and, therefore, the characteristics of the entire organism. All the genes in one homologous set of 23 chromosomes in one individual, taken together, is called the **genome** (jē′nōm, jē′nom). The two combined genomes of a person are responsible for all of that person's genetic traits.

Phenylketonuria

Situations in which the alteration of a single gene results in a genetic disorder dramatically illustrate the importance of genes. For example, in **phenylketonuria** (fen′il-kē′tō-noo′rē-ă; **PKU**), the gene responsible for producing an enzyme that converts the amino acid phenylalanine to the amino acid tyrosine is defective. Phenylalanine, therefore, accumulates in the blood and is eventually converted to harmful substances that can cause mental retardation.

Through the processes of meiosis, gamete formation, and fertilization, essentially a random distribution of genes is received from each parent, a process called **independent assortment** of the genes. Several factors, however, influence this random distribution. For example, all of the genes on a given chromosome are **linked,** that is, they tend to be inherited as a set rather than as individual genes, because chromosomes, not individual genes, segregate during meiosis. Sets of linked genes can be broken up, however. When tetrads are formed during meiosis (see chapter 3), homologous chromosomes may exchange genetic information by **crossing-over** (see figure 3.47).

Furthermore, segregation errors may occur during meiosis. As the chromosomes separate during meiosis, the two members of a homologous pair may become "sticky" and not segregate as they normally do. As a result, one of the daughter cells receives both chromosome pairs and the other daughter cell receives none. This event is called **nondisjunction.** When the gametes are fertilized, the resulting zygote has either 47 chromosomes or 45 chromosomes rather than the normal 46, a condition called **aneuploidy** (an′ū-ploy-dē). This condition is usually lethal and is one reason for a high rate of early embryo loss. Some types of aneuploidy are not lethal, however. The sex chromosome abnormalities described in the section dealing with chromosomes are examples. Another example is **Down's syndrome,** or **trisomy 21,** a type of aneuploidy in which three chromosomes 21 are present.

Dominant and Recessive Genes

Most human genetic traits that we are aware of are recognized because defective alleles for those traits exist in the population. For example, on chromosome 11, a gene is present that produces an enzyme necessary for the synthesis of melanin, the pigment responsible for skin, hair, and eye color (see chapter 5). The normal allele for the melanin gene produces a normal, functional enzyme. Another, abnormal allele, however, produces a defective enzyme not capable of catalyzing one of the normal steps in melanin synthesis. If a given person inherits two defective alleles at that melanin-producing enzyme locus, a homozygous condition, the person is unable to produce melanin and, therefore, lacks normal pigment in the skin, hair, and eyes. This condition is referred to as **albinism.** Instead of the normal coloring, the color of a person with albinism consists of shades of pink, blue, and yellow. The pink and blue colors result from blood seen through the skin (see chapter 5), and the yellow color is from the natural accumulation of ingested yellow plant pigments in the skin.

For many genetic traits, the effects of one allele for that trait can mask the effect of another allele for that same trait. For example, a person who is heterozygous for the melanin-producing enzyme gene on chromosome 11 has a normal gene for melanin production on one chromosome 11 and the defective gene for melanin production at the same locus on the other chromosome 11. In the case of this melanin-producing enzyme, one copy of the gene and its resulting enzymes are enough to make normal melanin. As a result, the person who is heterozygous produces melanin and appears normal. In this case, the allele that produces the normal enzyme and is responsible for normal appearance is said to be **dominant,** whereas the allele producing the abnormal enzyme is **recessive.** The lost function of the defective enzyme is masked by the dominant, normal allele. Thus, normal pigmentation is a dominant trait and albinism is a recessive trait. By convention, dominant traits are indicated by uppercase letters, and recessive traits are indicated by lowercase letters. In this example, the letter *A* designates the dominant normal, pigmented condition and the letter *a* the recessive albino condition. It's important to note that not all dominant traits are the normal condition and that not all recessive traits are abnormal. Many examples exist in which the dominant trait is abnormal.

The possible combinations of dominant and recessive alleles for normal melanin production versus albinism are *AA* (homozygous dominant), *Aa* (heterozygous), and *aa* (homozygous recessive). The actual set of alleles that a person has for a given trait is called the **genotype** (jēn′ō-tīp). The person's appearance is called the **phenotype** (fē′nō-tīp). A person with the genotype *AA* or *Aa* has the phenotype of normal pigmentation, whereas a person with the genotype *aa* has the phenotype of albinism. Note that the recessive trait is expressed when it is not masked by the dominant trait.

PREDICT 6

Polydactyly (pol-ē-dak′ti-lē) is a condition in which a person has extra fingers or toes. Given that polydactyly is a dominant trait, list all the possible genotypes and phenotypes for polydactyly. Use the letters *D* and *d* for the genotypes.

The inheritance of dominant and recessive traits can be determined if the genotypes of the parents are known. For example, if an albino person (*aa*) mates with a heterozygous normal person (*Aa*), the probability is that half of the children will be albino (*aa*), and half will be normal heterozygous carriers (*Aa*). If two carriers (*Aa*) mate, the probability is that one in four will be homozygous dominant (*AA*), one in four will be homozygous recessive (*aa*), and one in two will be heterozygous (*Aa*). Such a probability can be easily determined by the use of a table called a **Punnett square** (figure 29.25). **Carriers** are heterozygous persons with an abnormal recessive gene but with a normal phenotype because they also have a normal dominant allele for that gene.

35. *What is the number and type of chromosomes in the karyotype of a human somatic cell? How do the chromosomes of a male and female differ from each other?*
36. *How do the chromosomes in somatic cells and gametes differ from each other?*
37. *What is a gene, and how are genes responsible for the structure and function of cells? Define structural genes and regulatory genes.*
38. *What is the cause of the genetic disorder called Down's syndrome?*
39. *Define the terms homozygous dominant, heterozygous, and homozygous recessive.*
40. *What is the difference between genotype and phenotype?*

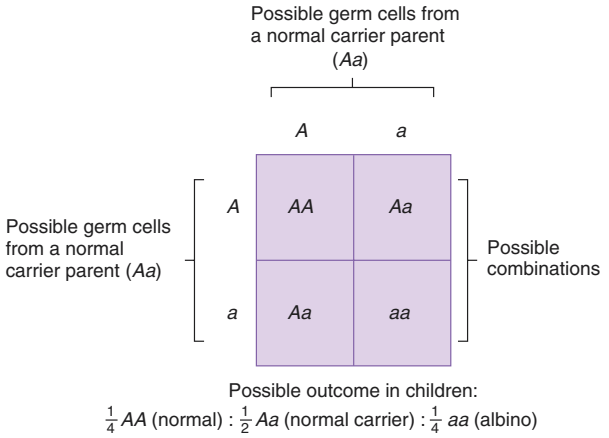


Figure 29.25 Inheritance of a Recessive Trait: Albinism

A represents the normal pigmented condition, and *a* represents the recessive unpigmented condition. The figure shows a Punnett square of a mating between two normal carriers.

PREDICT 7

If a carrier for albinism mates with a homozygous normal person, what is the likelihood that any of their children will be albinos? Explain.

Sex-Linked Traits

Traits affected by genes on the sex chromosomes are called **sex-linked traits.** Most sex-linked traits are **X-linked,** that is, they are on the X chromosome, whereas, only a few **Y-linked** traits exist, largely because the Y chromosome is very small. An example of an X-linked trait is **hemophilia A** (classic hemophilia) in which the ability to produce one of the clotting factors is not present (see chapter 19). Consequently, clotting is impaired and persistent bleeding occurs either spontaneously or as a result of an injury. Hemophilia A is a recessive trait located on the X chromosome. The possible genotypes and phenotypes are, therefore, X^HX^H (normal homozygous female), X^HX^h (normal heterozygous female), X^hX^h (hemophiliac homozygous female), X^HY (normal male), and X^hY (hemophiliac male). Note that a female must have both recessive genes to exhibit hemophilia, whereas a male, because he has only one X chromosome, has hemophilia if he has only one of the recessive genes. An example of the inheritance of hemophilia is illustrated in figure 29.26. If a woman who is a carrier for hemophilia mates with a man who does not have hemophilia, none of their daughters but half of their sons will have hemophilia.

Other Types of Gene Expression

The expression of a dominant over a recessive gene is the simplest manner in which genes determine a person's phenotype. Many other ways exist in which genes influence the expression of a trait. In some cases, the dominant gene doesn't completely mask the

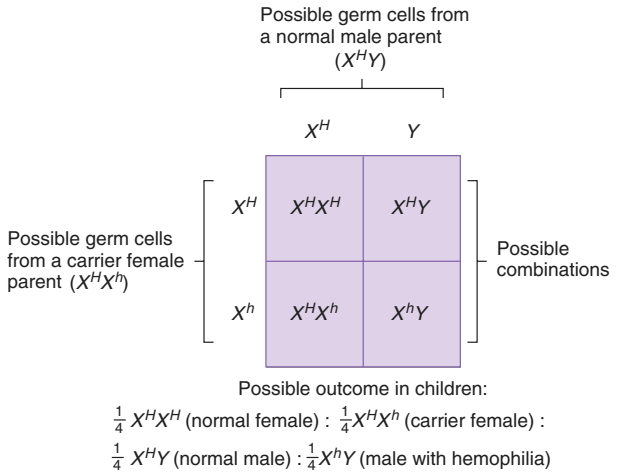


Figure 29.26 Inheritance of an X-Linked Trait: Hemophilia

X^H represents the normal X chromosome condition with all clotting factors, and X^h represents the X chromosome lacking a gene for one clotting factor. The figure shows a Punnett square of a mating between a normal male and a normal carrier female.

effects of the recessive gene, a phenomenon called **incomplete dominance.** An example of incomplete dominance is **sickle-cell disease,** in which a gene responsible for producing hemoglobin in red blood cells is abnormal. Consequently, the hemoglobin produced by the gene is abnormal. The result is red blood cells that are stretched into an elongated sickle shape. These red blood cells tend to stick in capillaries, thereby blocking blood flow to tissues. In addition, the sickle-shaped cells tend to rupture more easily than normal red blood cells. The normal allele (*S*) for producing normal hemoglobin is dominant over the sickle cell allele (*s*) responsible for producing the abnormal hemoglobin. A person with genotype *SS* has normal hemoglobin. A person with sickle-cell disease has genotype *ss* and has abnormal hemoglobin. A person who is heterozygous has the genotype *Ss,* has half normal hemoglobin and half abnormal hemoglobin, and usually has only a few sickle-shaped red blood cells. This condition is called **sickle-cell trait.** Usually, a person with sickle-cell trait exhibits no adverse symptoms. For this set of alleles, expressing incomplete dominance, however, each genotype presents a unique, recognizable phenotype.

In another type of gene expression, called **codominance,** two alleles can combine to produce an effect without either of them being dominant or recessive. For example, a person with type AB blood has A antigens and B antigens on the surface of the red blood cells (see chapter 19). The antigens result from a gene that causes the production of the A antigen and a different gene that causes the production of the B antigen. In this case, A and B are neither dominant nor recessive in relation to each other.

Polygenic traits are determined by the expression of multiple genes on different chromosomes. Examples are a person's height, intelligence, eye color, and skin color. Polygenic traits typically are characterized by having a great amount of variability. For example, many different shades of eye color and skin color exist (figure 29.27). Because of the many genes involved, it's difficult to predict how a polygenic trait will be passed from one generation to the next. Notice, however, that even though a complex combination of genes determines skin color, one single defective gene can eliminate skin color completely, resulting in albinism, which is inherited as a simple dominant trait.

Genetic Disorders

Abnormalities in a person's genetic makeup, that is, in his or her DNA, cause **genetic disorders.** They may involve a single gene or an entire chromosome, as in the case of aneuploidy (table 29.4). Genetic disorders are often confused with **congenital disorders.** Congenital means "present at birth" and a congenital disorder is commonly referred to as a birth defect, but all congenital disorders are not necessarily genetic. Approximately 15% of all congenital disorders have a known genetic cause, and approximately 70% of all birth defects are of unknown cause. The remaining 15% are the result of environmental causes or a combination of environmental and genetic causes. In the case of environmental causes, the birth defect results from damage to the fetus during development. Agents that cause birth defects are called **teratogens** (ter′ă-tō-jenz). For example, fetal alcohol syndrome results when a pregnant woman drinks alcohol, which crosses the placenta and damages the fetus. The baby is born with a smaller-than-normal head and mental retardation and may exhibit other birth defects.

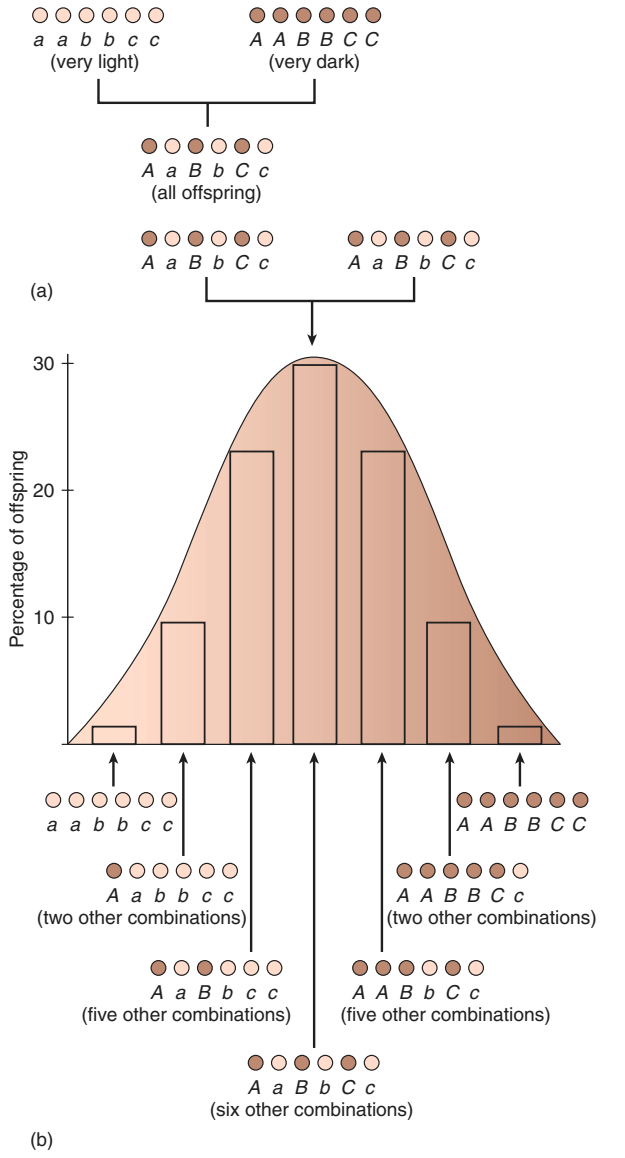


Figure 29.27 Inheritance of a Polygenic Trait: Skin Color

In this example, three genes for skin color are shown. The dominant alleles *(A, B, C),* each of which contributes one "unit of dark color" to the offspring (indicated by a *dark dot*), are incompletely dominant over the recessive alleles *(a, b, c),* each of which contributes one "unit of light color" to the offspring (indicated by a *light dot*). (*a*) A mating between a very light-skinned person *(aabbcc)* and a very dark-skinned person *(AABBCC)* is shown. All the offspring are of intermediate color. (*b*) A mating between two people of intermediate skin color *(AaBbCc)*. The possible offspring skin color falls within a normal distribution in which a very low percentage (less than 2%) are either very light or very dark, and most of the offspring are of intermediate color.

Table 29.4 Genetic Disorders

Disorder	Description
Dominant Traits	
Achondroplasia	Dwarfism characterized by shortening of the upper and lower limbs
Huntington's chorea	Severe degeneration of the basal nuclei and frontal cerebral cortex; characterized by purposeless movements and mental deterioration; onset is usually between 40 and 50 years of age
Hypercholesterolemia	Elevated blood cholesterol levels that contribute to atherosclerosis and cardiovascular disease
Marfan's syndrome	Abnormal connective tissue results in increased height, elongated digits, and weakness in the aortic wall
Neurofibromatosis	Small pigmented lesions (café-au-lait spots) in the skin and disfiguring tumors (noncancerous) caused by proliferation of Schwann cells along nerves
Osteogenesis imperfecta	Abnormal phosphate metabolism results in brittle bones that repeatedly break
Recessive Traits	
Albinism	Lack of the enzyme necessary to produce the pigment melanin; characterized by lack of skin, hair, and eye coloration
Cystic fibrosis	Impaired transport of chloride ions across plasma membranes; results in excessive production of thick mucus that blocks the respiratory and gastrointestinal tract; the most common fatal genetic disorder
Phenylketonuria	Lack of the enzyme necessary to convert the amino acid phenylalanine to the amino acid tyrosine; an accumulation of phenylalanine leads to mental retardation
Severe combined immune deficiency	Inability to form the white blood cells (B cells, T cells, and phagocytes) necessary for an immune system response
Sickle-cell disease	Inability to produce normal hemoglobin; results in abnormally shaped red blood cells that clog capillaries or rupture
Tay-Sachs disease	Lack of the enzyme necessary to break down certain fatty substances; an accumulation of fatty substances impairs action potential propagation, resulting in deterioration of mental and physical functions and death by 3–4 years of age
Thalassemia	Decreased rate of hemoglobin synthesis; results in anemia, enlargement of the spleen, increased cell numbers in red bone marrow, and congestive heart failure
Sex-Linked Traits	
Hemophilia	Most commonly, a recessive gene causes a failure to produce blood clotting factors; resulting in prolonged bleeding
Red-green color blindness	Most commonly, a recessive gene causes a deficiency in functional green-sensitive cones; inability to distinguish between red and green colors
Chromosomal Disorders	
Down's syndrome	Caused by having three chromosomes 21; results in mental retardation, short stature, and poor muscle tone
Duchenne's muscular dystrophy	Caused by deletion or alteration of part of the X chromosome; results in progressive weakness and wasting of muscles
Klinefelter's syndrome	Caused by two or more X chromosomes in a male (XXY); results in small testes, sterility, and development of femalelike breasts
Turner's syndrome	Caused by having only one X chromosome; results in immature uterus, lack of ovaries, and short stature

One cause of genetic disorders is a **mutation,** a change in a gene that usually involves a change in the number or kinds of nucleotides composing the DNA (see chapter 2). Mutations are known to occur by chance (randomly without known cause) or may be caused by chemicals, radiation, or viruses. Agents that cause mutations are called **mutagens** (mūʹtă-jenz). In most cases, a specific cause of a mutation cannot be determined. Once a mutation has occurred, however, the abnormal trait can be passed from one generation to the next.

Cancer is a result of uncontrolled cell divisions. **Oncogenes** (ongʹkō-jēnz) are genes associated with cancer. Many oncogenes are actually control genes involved in regulating cell proliferation and differentiation in the embryo and fetus. A change in an oncogene or in the regulation of an oncogene can result in uncontrolled cell proliferation and the development of cancerous tumors. The normal control of oncogenes involves other genes, called **tumor suppressor genes.** Cancer may occur when a mutation activates an oncogene or inactivates a tumer supressor gene. An accumulation of several mutations is necessary for cancer to occur. It's believed that certain chemicals called **carcinogens** (kar-sinʹō-jenz, karʹsi-nō-jenz) can induce such mutations and, thereby, initiate the development of cancer. For example, chemicals in cigarette smoke are known to cause lung cancer. Thus, even though everyone has oncogenes, an outside agent may be necessary for a cancer to begin.

A change in somatic cells that results in cancer is not usually inheritable; nonetheless, a genetic basis may exist that allows cancer development, especially under the right environmental conditions. In this sense, the inheritance of cancer and other abnormalities has been described as **genetic susceptibility,** or **genetic predisposition.** For example, if a woman's close relatives, such as her mother or sister, have breast cancer, she has a greater-than-average risk of developing breast cancer. Similar genetic susceptibilities have been found for diabetes mellitus, schizophrenia, and other disorders.

Clinical Focus The Human Genome Project

The human genome is all of the genes found in one homologous set of human chromosomes. It's estimated that humans have 20,500–30,000 genes. A **genomic map** is a description of the DNA nucleotide sequences of the genes and their locations on the chromosomes (figure B). Celera, a private corporation working on the **Human Genome Project,** announced on February 12, 2001, that it had completed sequencing the entire genome.

Armed with a knowledge of the human genome and what effects the genome has on a person's physical, mental, and behavioral abilities, medicine and society will be transformed in many ways. Medicine, for example, will shift emphasis from the curative to the preventative. The potential disorders or diseases a person is likely to develop can be prevented or their severity lessened. When prevention is not possible, knowledge of the enzymes or other molecules involved in a disorder may result in new drugs and techniques that can compensate for the genetic disorder. Knowledge of the genes involved in a disorder may result in **gene therapy,** or **genetic engineering,** that repairs or replaces defective genes, resulting in cures of genetic disorders.

Despite the great promise of benefits from the Human Genome Project, the knowledge that will be produced has raised a number of ethical and legal questions for society. Should a person's genomic information be public knowledge? Should persons with a genome that predisposes them to cancer or behavioral disorders be barred from certain types of employment or be refused medical insurance because they are a high risk? Can a person demand to know a prospective mate's genome? Should parents know the genome of their fetus and be allowed to make decisions regarding abortion based on this knowledge? Should the same genetic-engineering techniques that provide alteration of the genome to cure genetic disorders be used to create genomes that are deemed to be superior? Such questions raise the specter of genetic discrimination.

Treatment of genetic disorders usually involves treatment of symptoms but doesn't result in a cure because the treatment doesn't change the basic genetic material. For example, treating the problems associated with mucus buildup in cystic fibrosis does not cure the disorder. Currently, research is underway to actually alter a person's genetic makeup. Ultimately, it may be possible to insert a normal gene into cells to replace an abnormal or missing gene. Then, if the normal gene functions, the disorder will be cured.

Genetic Counseling

Genetic counseling includes predicting the possible results of matings involving carriers of harmful genes and talking to parents or prospective parents about the possible outcomes and treatments of a genetic disorder. With this knowledge, prospective parents can make informed decisions about having children.

A first step in genetic counseling is to attempt to determine the genotype of the individuals involved. For example, a couple may suspect that they are carriers for a genetic disorder. A family tree, or **pedigree,** provides historical information about family members (figure 29.28). Sometimes, by knowing the phenotypes of relatives, it's possible to determine a person's genotype. Direct means of obtaining genetic information are also available. A karyotype can be taken from white blood cells or the epithelial cells lining the inside of the cheek. Alternatively, the amount of a given substance, such as an enzyme, produced by a carrier can be tested. Sometimes a carrier produces slightly more or less of a given substance because they are heterozygous and have only one dominant gene for the normal or abnormal trait. For example, carriers for cystic fibrosis produce more salt in their sweat than is normal.

Sometimes, it's suspected that a fetus may have a genetic abnormality. Fetal cells can be tested by amniocentesis, which takes cells floating in the amniotic fluid (see figure A on p. 1084), or chorionic villus sampling, which takes cells from the fetal side of the placenta.

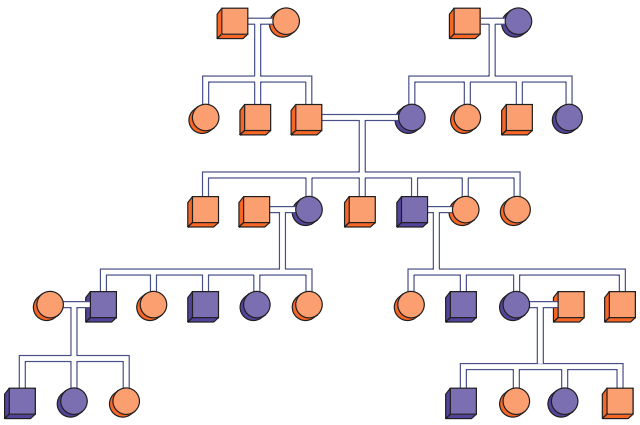
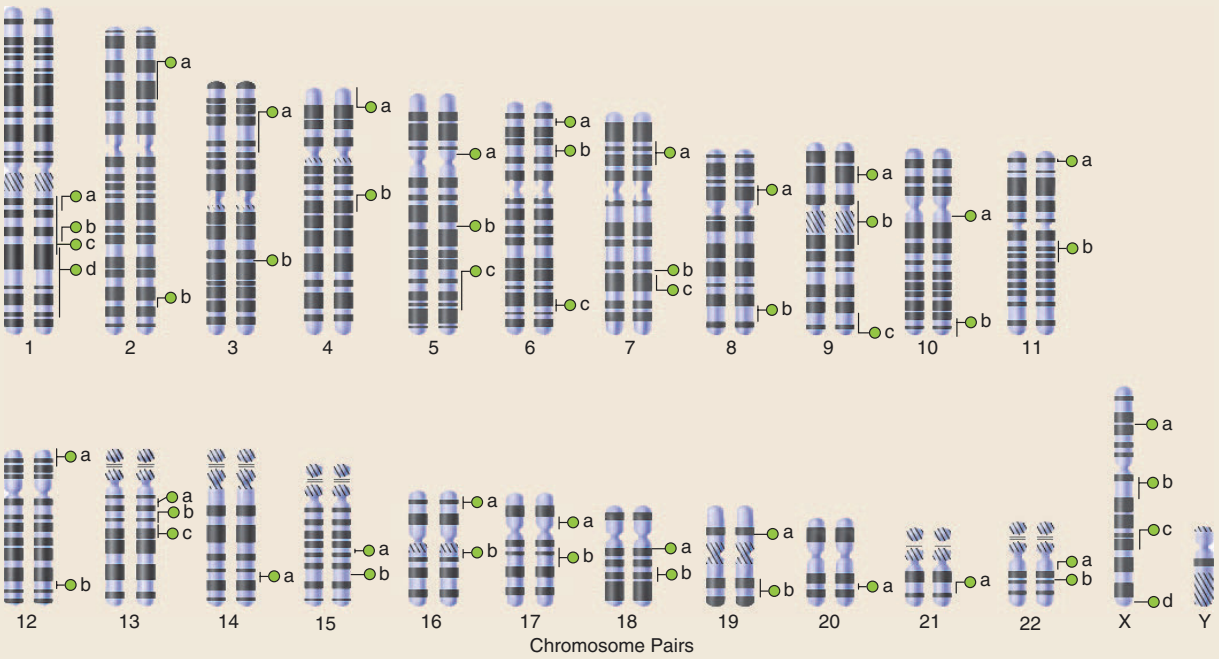


Figure 29.28 Pedigree of a Simple Dominant Trait

Males are indicated by *squares,* females by *circles.* Affected people are indicated by the *purple* symbols, unaffected people are indicated by the *orange* symbols. The *horizontal line* between symbols represents a mating. The symbols connected to the mating line by vertical and horizontal lines represent the children resulting from the mating in order of birth from *left* to *right.* Matings not related to the pedigree are not shown.

- ***41. Explain how sex-linked traits are inherited. Give an example.***
- ***42. How does sickle-cell disease, type AB blood, and a person's height result from the expression of genes?***
- ***43. What is a mutation?***
- ***44. Define and give examples of teratogens, mutagens, and carcinogens. What is an oncogene?***
- ***45. What is genetic susceptibility?***
- ***46. How are pedigrees, karyotypes, chemical tests, amniocentesis, and chorionic villus sampling used in genetic counseling?***



1. a. Gaucher's disease
   b. Prostate cancer
   c. Glaucoma
   d. Alzheimer's disease*
2. a. Familial colon cancer*
   b. Waardenburg syndrome
3. a. Lung cancer
   b. Retinitis pigmentosa*
4. a. Huntington's chorea
   b. Parkinson disease
5. a. Cockayne syndrome
   b. Familial polyposis of the colon
   c. Asthma
6. a. Spinocerebellar ataxia
   b. Diabetes*
   c. Epilepsy*
7. a. Diabetes*
   b. Cystic fibrosis
   c. Obesity*
8. a. Werner syndrome
   b. Burkitt lymphoma
9. a. Malignant melanoma
   b. Friedreich ataxia
   c. Tuberous sclerosis
10. a. Multiple endocrine neoplasia, type 2
    b. Gyrate atrophy
11. a. Sickle-cell disease
    b. Multiple endocrine neoplasia
12. a. Zellweger syndrome
    b. Phenylketonuria (PKU)
13. a. Breast cancer*
    b. Retinoblastoma
    c. Wilson disease
14. a. Alzheimer's disease*
15. a. Marfan syndrome
    b. Tay-Sachs disease
16. a. Polycystic kidney disease
    b. Crohn disease*
17. a. Peroneal muscular atrophy
    b. Breast cancer*
18. a. Amyloidosis
    b. Pancreatic cancer*
19. a. Familial hypercholesterolemia
    b. Myotonic dystrophy
20. a. Severe combined immunodeficiency
21. a. Amyotrophic lateral sclerosis*
22. a. DiGeorge syndrome
    b. Neurofibromatosis, type 2

X a. Duchenne's muscular dystrophy
  b. Menkes syndrome
  c. X-linked severe combined immunodeficiency
  d. Factor VIII deficiency (hemophilia A)

*Gene responsible for only some cases.

Figure B The Human Genomic Map

Representative genetic defects mapped to date. The *green circles* indicate the location of the genes listed for each chromosome.

S U M M A R Y

Prenatal development is an important part of an individual's life.

Prenatal Development (p. 1062)

1. Prenatal development is divided into the germinal, embryonic, and fetal periods.
2. Postovulatory age is 14 days less than clinical age.
3. Fertilization, the union of the oocyte and sperm, results in a zygote.
4. The product of fertilization undergoes divisions until it becomes a mass, called a morula, and then a hollow ball of cells, called a blastocyst.
5. The cells of the morula are pluripotent (capable of making any cell of the body).
6. The blastocyst implants into the uterus about 7 days after fertilization. The placenta is derived from the trophoblast of the blastocyst.
7. All tissues of the body are derived from three primary germ layers: ectoderm, mesoderm, and endoderm.
8. The nervous system develops from a neural tube that forms in the ectodermal surface of the embryo and from neural crest cells derived from the developing neural tube.
9. Segments called somites that develop along the neural tube give rise to the musculature, vertebral column, and ribs.
10. The gastrointestinal tract develops as the developing embryo closes off part of the yolk sac.
11. The celom develops from small cavities that fuse within the embryo.
12. The limbs develop from proximal to distal as outgrowths called limb buds.
13. The face develops from the fusion of five major tissue processes.

Development of the Organ Systems

1. The skin develops from ectoderm (epithelium), mesoderm and neural crest (dermis), and the neural crest (melanocytes).
2. The skeletal system develops from mesoderm or neural crest cells.
3. Muscle develops from myoblasts, which migrate from somites.
4. The brain and spinal cord develop from the neural tube, and the peripheral nervous system develops from the neural tube and the neural crest cells.
5. The special senses develop mainly as neural tube or neural crest cell derivatives.
6. Many endocrine organs develop mainly as outpocketings of the brain or digestive tract.
7. The heart develops as two tubes fuse into a single tube that bends and develops septa to form four chambers.
8. The peripheral circulation develops from mesoderm as blood islands become hollow and fuse to form a network.
9. The lungs form as evaginations of the digestive tract. These evaginations undergo repeated branching.
10. The urinary system develops in three stages—pronephros, mesonephros, and metanephros—from the head to the tail of the embryo. The ducts join the allantois, part of which becomes the urinary bladder.
11. The reproductive system develops in conjunction with the urinary system. The presence or absence of certain hormones are very important to sexual development.

Growth of the Fetus

1. The embryo becomes a fetus at 60 days.
2. The fetal period is from day 60 to birth. It is a time of rapid growth.

Parturition (p. 1085)

1. The total length of gestation is 280 days (clinical age).
2. Uterine contractions force the baby out of the uterus during labor.
3. Increased estrogen levels and decreased progesterone levels help initiate parturition.
4. Fetal glucocorticoids act on the placenta to decrease progesterone synthesis and to increase estrogen and prostaglandin synthesis.
5. Stretching of the uterus and decreased progesterone levels stimulate oxytocin secretion, which stimulates uterine contraction.

The Newborn (p. 1088)

Respiratory and Circulatory Changes

1. The foramen ovale closes, separating the two atria.
2. The ductus arteriosus closes, and blood no longer flows between the pulmonary trunk and the aorta.
3. The umbilical vein and arteries degenerate.

Digestive Changes

1. Meconium is a mixture of cells from the digestive tract, amniotic fluid, bile, and mucus excreted by the newborn.
2. The stomach begins to secrete acid.
3. The liver does not form adult bilirubin for the first 2 weeks.
4. Lactose can be digested, but other foods must be gradually introduced.

Apgar Scores

1. Apgar represents appearance, pulse, grimace, activity, and respiratory effort.
2. Apgar and other methods are used to assess the physiologic condition of the newborn.

Lactation (p. 1090)

1. Estrogen, progesterone, and other hormones stimulate the growth of the breasts during pregnancy.
2. Suckling stimulates prolactin and oxytocin synthesis. Prolactin stimulates milk production, and oxytocin stimulates milk letdown.

First Year After Birth (p. 1092)

1. The number of neuron connections and glial cells increases.
2. Motor skills gradually develop, especially head, eye, and hand movements.

Life Stages (p. 1092)

The life stages include the following: germinal, embryo, fetus, neonate, infant, child, adolescent, and adult.

Aging (p. 1092)

1. Loss of cells that are not replaced contributes to aging.
   - A loss of neurons occurs.
   - Loss of muscle cells can affect skeletal and cardiac muscle function.
2. Loss of tissue plasticity results from cross-link formation between collagen molecules. The lens of the eye loses the ability to accommodate. Other organs, such as the joints, kidneys, lungs, and heart, also have reduced efficiency with advancing age.
3. The immune system loses the ability to act against foreign antigens and may attack self-antigens.
4. Many aging changes are probably genetic.

Death (p. 1094)

Death is the loss of brain functions.

Genetics (p. 1094)

Chromosomes

1. Humans have 46 chromosomes in 23 pairs; 22 pairs of autosomes and 1 pair of sex chromosomes.
2. Males have the sex chromosomes XY and females XX.
3. During gamete formation, the chromosomes of each pair of chromosomes separate; therefore, half of a person's genetic makeup comes from the father and half from the mother.

Genes

1. A gene is a portion of a DNA molecule. Genes determine the proteins in a cell.
2. Genes are paired (located on the paired chromosomes).
3. Dominant genes mask the effects of recessive genes.
4. Sex-linked traits result from genes on the sex chromosomes.
5. In incomplete dominance, the heterozygote expresses a trait that is intermediate between the two homozygous traits.
6. In codominance, neither gene is dominant or recessive, but both are fully expressed.
7. Polygenic traits result from the expression of multiple genes.

Genetic Disorders

1. A mutation is a change in the number or kinds of nucleotides in DNA.
2. Some genetic disorders result from an abnormal distribution of chromosomes during gamete formation.
3. Oncogenes are genes associated with cancer.
4. Genetic predisposition makes it more likely a person will develop a disorder.

Genetic Counseling

1. A pedigree (family history) can be used to determine the risk of having children with a genetic disorder.
2. Specific chemical testing or examination of a person's karyotype can be used to determine a person's genotype.

REVIEW AND COMPREHENSION

1. The major development of organs takes place in the
   a. organ period.
   b. fetal period.
   c. germinal period.
   d. embryonic period.
2. Given these structures:
   1. blastocyst
   2. morula
   3. zygote

   Choose the arrangement that lists the structures in the order in which they are formed during development.
   a. 1,2,3
   b. 1,3,2
   c. 2,3,1
   d. 3,1,2
   e. 3,2,1
3. The embryo develops from the
   a. inner cell mass.
   b. trophoblast.
   c. blastocele.
   d. yolk sac.
4. The placenta
   a. develops from the trophoblast.
   b. allows maternal blood to mix with embryonic blood.
   c. invades the lacunae of the embryo.
   d. all of the above.
5. The embryonic disk
   a. forms between the amniotic cavity and the yolk sac.
   b. contains the primitive streak.
   c. becomes a three-layered structure.
   d. all of the above.
6. The brain develops from
   a. ectoderm.
   b. endoderm.
   c. mesoderm.
7. Most of the skeletal system develops from
   a. ectoderm.
   b. endoderm.
   c. mesoderm.
8. Given these structures:
   1. neural crest
   2. neural plate
   3. neural tube

   Choose the arrangement that lists the structure in the order in which they form during development.
   a. 1,2,3
   b. 1,3,2
   c. 2,1,3
   d. 2,3,1
   e. 3,2,1
9. The somites give rise to the
   a. circulatory system.
   b. skeletal muscle.
   c. skin.
   d. kidneys.
   e. brain.
10. The pericardial cavity forms from
    a. evagination of the early gastrointestinal tract.
    b. the neural tube.
    c. the celom.
    d. the branchial arches.
    e. pharyngeal pouches.
11. The parts of the limbs develop
    a. in a proximal-to-distal sequence.
    b. in a distal-to-proximal sequence.
    c. at approximately the same time.
    d. before the primitive streak is formed.
12. Concerning development of the face,
    a. the face develops by the fusion of five embryonic structures.
    b. the maxillary processes normally meet at the midline to form the lip.
    c. the primary palate forms the roof of the mouth.
    d. cleft palates normally occur to one side of the midline.
13. Concerning the development of the heart,
    a. the heart develops from a single tube.
    b. the sinus venosus becomes the SA node.
    c. the foramen ovale lets blood flow from the right atrium to the left atrium.
    d. the bulbis cordis is absorbed into the ventricle.
    e. all of the above.

14. Given these structures:
    1. mesonephros
    2. metanephros
    3. pronephros

    Choose the arrangement that lists the structures in the order in which they form during development.
    a. 1,2,3
    b. 1,3,2
    c. 2,3,1
    d. 3,1,2
    e. 3,2,1
15. A study of the early embryo indicates that the penis of the male develops from the same embryonic structure as which of these female structures?
    a. labia majora
    b. uterus
    c. clitoris
    d. vagina
    e. urinary bladder
16. Which hormone causes differentiation of sex organs in the developing male fetus?
    a. FSH and LH
    b. LH and testosterone
    c. testosterone and dihydrotestosterone
    d. estrogen and progesterone
    e. GnRH and FSH
17. Onset of labor may be a result of
    a. increased estrogen secretion by the placenta.
    b. increased glucocorticoid secretion by the fetus.
    c. increased secretion of oxytocin.
    d. stretch of the uterus.
    e. all of the above.
18. Following birth,
    a. the ductus arteriosus closes.
    b. the pH of the stomach increases.
    c. the fossa ovalis becomes the foramen ovale.
    d. blood flow through the pulmonary arteries decreases.
    e. all of the above.
19. The hormone involved in milk production is
    a. oxytocin.
    b. prolactin.
    c. estrogen.
    d. progesterone.
    e. ACTH.
20. Which of these most appropriately predicts the consequences of removing the sensory neurons from the areola of a lactating rat (or human).
    a. Blood levels of oxytocin decrease.
    b. Blood levels of prolactin decrease.
    c. Milk production and letdown decreases.
    d. All of the above.
21. Which of these life stages is correctly matched with the time that the stage occurs?
    a. neonate—birth to 1 month after birth
    b. infant—1 month to 6 months
    c. child—6 months to 5 years
    d. puberty—10–12 years
    e. middle age—20–40 years
22. Which of these occurs as we get older?
    a. Neurons replicate to replace lost neurons.
    b. Skeletal muscle cells replicate to replace lost muscle cells.
    c. Cross-links between collagen molecules increases.
    d. The immune system become less sensitive to the body's own antigens.
    e. Free radicals help to prevent cancer.
23. A gene is
    a. the functional unit of heredity.
    b. a certain portion of a DNA molecule.
    c. a part of a chromosome.
    d. all of the above.
24. Which of these does *not* contribute to genetic differences between gametes?
    a. crossing-over
    b. independent assortment
    c. linkage
    d. nondisjunction
25. Which of these terms is correctly matched with its definition?
    a. autosome—an X or Y chromosome
    b. phenotype—the genetic makeup of an individual
    c. allele—genes occupying the same locus on homologous chromosomes
    d. heterozygous—having two identical genes for a trait
    e. recessive—a trait expressed when the genes are heterozygous
26. Which of these genotypes is heterozygous?
    a. *DD*
    b. *Dd*
    c. *dd*
    d. both a and c
27. The ABO blood group is an example of
    a. dominant versus recessive alleles.
    b. incomplete dominance.
    c. codominance.
    d. a polygenic trait.
    e. sex-linked inheritance.
28. Assume that a trait is determined by an X-linked dominant gene. If the mother exhibits the trait, but the father does not, then their
    a. sons are more likely than their daughters to exhibit the trait.
    b. daughters are more likely than their sons to exhibit the trait.
    c. sons and daughters are equally likely to exhibit the trait.
29. Which of these could result in a congenital disorder?
    a. a parent has the same disorder
    b. a teratogen
    c. a mutagen
    d. all of the above

Answers in Appendix F

CRITICAL THINKING

1. A woman is told by her physician that she is pregnant and that she is 44 days past her LMP. Approximately how many days has the embryo been developing, and what developmental events are occurring?
2. A high fever can prevent neural tube closure. If a woman has a high fever approximately 35–45 days after her LMP, what kinds of birth defects may be seen in the developing embryo?
3. If the apical ectodermal ridge is damaged during embryonic development when the limb bud is about one-half grown, what kinds of birth defects might be expected? Describe the anatomy of the affected structure.
4. What are the results of exposing a female embryo to high levels of testosterone while she is developing?
5. Three minutes after birth, a newborn has an Apgar score of 5 as follows: A, 0; P, 1; G, 1; A, 1; and R, 2. What are some of the possible causes for this low score? What might be done for this neonate?
6. When a woman nurses, it's possible for milk letdown to occur in the breast that is not being suckled. Explain how this response happens.
7. Dimpled cheeks are inherited as a dominant trait. Is it possible for two parents, each of whom has dimpled cheeks, to have a child without dimpled cheeks? Explain.
8. The ability to roll the tongue to form a "tube" results from a dominant gene. Suppose that a woman and her son can both roll their tongues, but her husband cannot. Is it possible to determine if the husband is the father of her son?
9. A woman who does not have hemophilia mates with a man who has the disorder. Determine the genotype of both parents if half of their children have hemophilia.

Answers in Appendix G

ANSWERS TO PREDICT QUESTIONS

1. Two primitive streaks on one embryonic disk result in the development of two embryos. If the two primitive streaks are touching or are very close to each other, the embryos may be joined. This condition is called conjoined (Siamese) twins.
2. Because the early embryonic heart is a simple tube, blood must be forced through the heart in almost a peristaltic fashion, and the contraction begins in the sinus venosus. If the sinus venosus didn't contract first, blood could flow in the opposite direction.
3. Postovulatory age is defined as 14 days less than clinical age, which is 280 days to parturition. Parturition is therefore 266 days after ovulation (280 days minus 14 days).
4. Elevation of calcium levels might cause the uterine muscles to contract tetanically. This tetanic contraction could compress blood vessels and cut the blood supply to the fetus. Hypercalcemia can also result in arrythmias and muscle weakness (see chapter 27). The doctor would therefore not administer calcium to the woman in labor but may give oxytocin, which strengthens contractions but is less likely to produce tetany.
5. Nursing stimulates the release of oxytocin from the mother's posterior pituitary gland, which is responsible for milk letdown. Oxytocin can also cause uterine contractions and cramps.
6. Genotype *DD* (homozygous dominant) would have the polydactyly phenotype, genotype *Dd* (heterozygous) would have the polydactyly phenotype, and genotype *dd* (homozygous recessive) would have the normal phenotype.
7. None. One in two will be homozygous normal and one in two will be normal heterozygous carriers.

	A	*a*
A	*AA*	*Aa*
A	*AA*	*Aa*