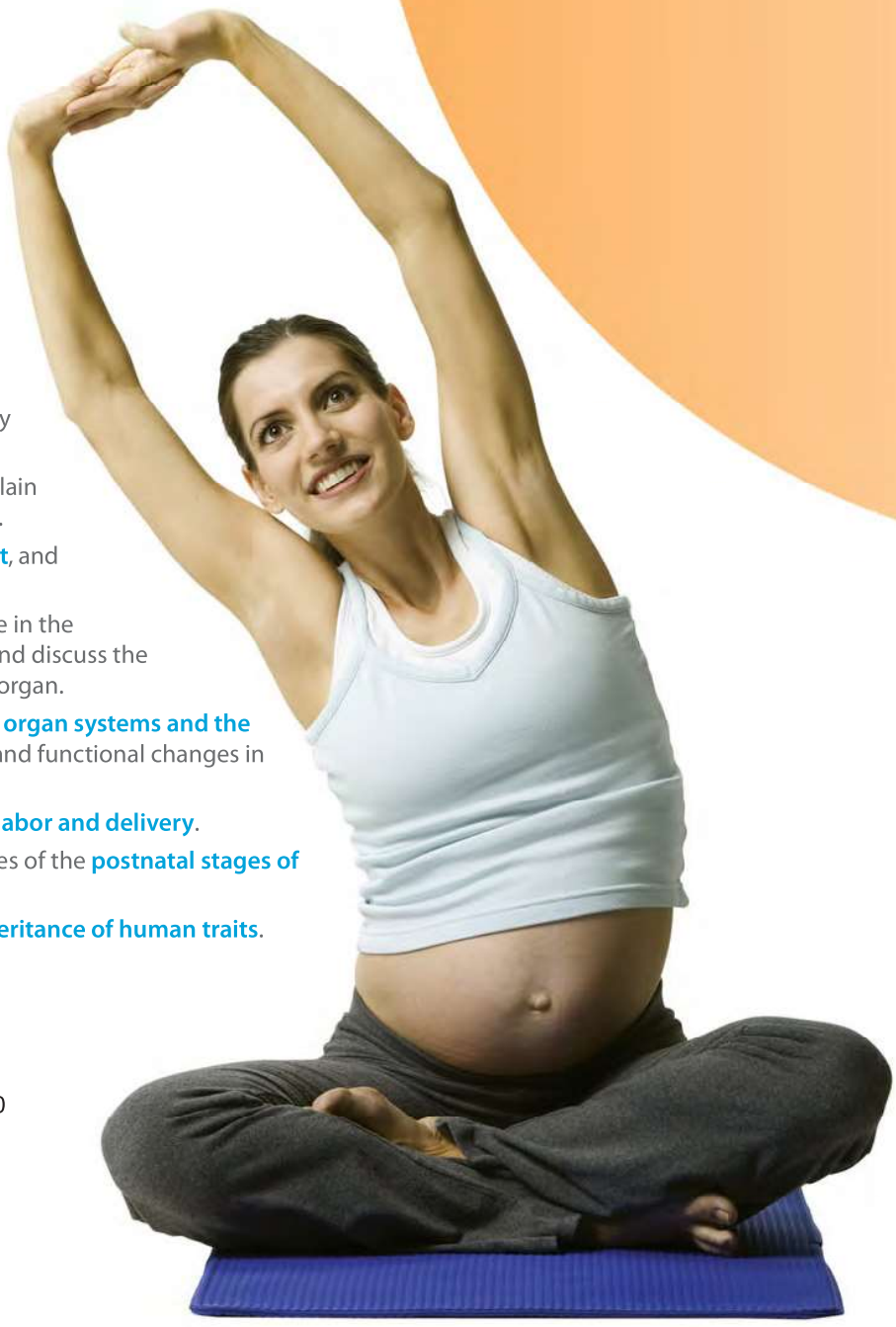
29

Development and Inheritance



Learning Outcomes

These Learning Outcomes correspond by number to this chapter's sections and indicate what you should be able to do after completing the chapter.

29-1 Explain the relationship between **differentiation and development**, and specify the various **stages of development**.

29-2 Describe the **process of fertilization**, and explain how **developmental processes** are regulated.

29-3 List the **three stages of prenatal development**, and describe the major events of each.

29-4 Explain how the **three germ layers** participate in the **formation of extraembryonic membranes**, and discuss the **importance of the placenta** as an endocrine organ.

29-5 Describe the interplay between the **maternal organ systems and the developing fetus**, and discuss the structural and functional changes in the **uterus during gestation**.

29-6 List and discuss the events that occur during **labor and delivery**.

29-7 Identify the features and physiological changes of the **postnatal stages of life**.

29-8 Relate **basic principles of genetics** to the **inheritance of human traits**.

Clinical Notes

An Introduction to Development and Inheritance

The physiological processes we have studied so far are relatively brief. Many last only a fraction of a second; others may take hours. But some important processes are measured in months, years, or decades. A human being develops in the womb for nine months, grows to maturity in 15 to 20 years, and may live the better part of a century. During that time, he or she is always changing. Birth, growth, maturation, aging, and death are all parts of a single, continuous process. That process does not end with the individual, because humans can pass at least some of their characteristics on to their offspring. Therefore, each generation gives rise to a new generation that will repeat the cycle. In this chapter, we explore how genetic programming, environmental factors, and various physiological processes affect the events following the union of male and female gametes. The explanation begins at prenatal development and continues through childhood and adolescence and into maturity and senescence (aging).

29-1 Development, marked by various stages, is a continuous process that occurs from fertilization to maturity

Time refuses to stand still; today's infant will be tomorrow's adult. The gradual modification of anatomical structures and physiological characteristics during the period from fertilization to maturity is called **development.** The changes that occur during development are truly remarkable. In a mere 9 months, all the tissues, organs, and organ systems we have studied so far take shape and begin to function. What begins as a single cell slightly larger than the period at the end of this sentence becomes an individual whose body contains trillions of cells organized into a complex array of highly specialized structures. The formation of different types of cells required in this process is called **differentiation.** Differentiation occurs through selective changes in genetic activity. As development proceeds, some genes are turned off and others are turned on. The identities of these genes vary from one type of cell to another, and the patterns change over time.

Development begins at **fertilization,** or **conception,** when the male and female gametes fuse. We can divide development into stages characterized by specific anatomical changes. **Embryological development** comprises the events during the first two months after fertilization. The study of these events is called **embryology** (em-brē-OL-ō-jē). **Fetal development** begins at the start of the ninth week and continues until birth. Embryological and fetal development are sometimes referred to collectively as **prenatal** (*natus*, birth) **development,** the primary focus of this chapter. **Postnatal development** begins at birth and continues to **maturity,** the state of full development or completed growth.

A basic understanding of human development provides important insights into anatomical structures. In addition, many of the mechanisms of development and growth are similar to those for the repair of injuries. In this chapter, we focus on major aspects of development. We consider highlights of the developmental process rather than examine the events in great detail. We also consider the regulatory mechanisms involved, and how developmental patterns can be modified—for good or harm. Few topics in the biological sciences are so fascinating, and fewer still confront investigators with so daunting an array of scientific, technological, and ethical challenges. The ongoing debate over research with embryonic stem cells and fetal tissue has brought several ethical issues into the public eye. The information presented in this final chapter should help you formulate your opinions on many difficult moral, legal, and public-policy questions.

Although all humans go through the same developmental stages, differences in their genetic makeup produce distinctive individual characteristics. The term **inheritance** refers to the transfer of genetically determined characteristics from generation to generation. The study of the mechanisms responsible for inheritance is called **genetics.** In this chapter, we will also consider basic genetics as it applies to inherited characteristics, such as sex, hair color, and various diseases.

Checkpoint

1. **Define differentiation.**
2. **What event marks the onset of development?**
3. **Define inheritance.**

See the blue Answers tab at the back of the book.

29-2 Fertilization—the fusion of a secondary oocyte and a spermatozoon—forms a zygote

Fertilization involves the fusion of two haploid gametes, each containing 23 chromosomes, producing a zygote that contains 46 chromosomes, the normal complement in a somatic cell. The functional roles and contributions of the male and female gametes are very different. The spermatozoon simply delivers the paternal chromosomes to the site of fertilization. It must travel a relatively long distance and is small, efficient, and highly streamlined. In contrast, the female gamete must provide all the cellular organelles and inclusions, nourishment, and genetic programming necessary to support development of the embryo for nearly a week after conception. The volume of this gamete is therefore much greater than that of the spermatozoon. Recall from Chapter 28 that ovulation releases a secondary oocyte suspended in

metaphase of meiosis II. At fertilization, the diameter of the secondary oocyte is more than twice the entire length of the spermatozoon (**Figure 29–1a**). The ratio of their volumes is even more striking—approximately 2000:1.

The spermatozoa deposited in the vagina are already motile, as a result of contact with secretions of the seminal glands—the first step of *capacitation*. ↩ p. 1042 (An unidentified substance secreted by the epididymis appears to prevent premature capacitation.) The spermatozoa, however, cannot accomplish fertilization until they have been exposed to conditions in the female reproductive tract. Although uterine tube peg cell secretions help with capacitation, the exact mechanism responsible for capacitation remains unknown.

Fertilization typically occurs near the junction between the ampulla and isthmus of the uterine tube, generally within a day after ovulation. By this time, a secondary oocyte has traveled only a few centimeters, but spermatozoa must cover the distance between the vagina and the ampulla of the uterine tube. A spermatozoon can propel itself at speeds of only about 34 μm per second, roughly equivalent to 12.5 cm (5 in.) per hour, so in theory it should take spermatozoa several hours to reach the upper portions of the uterine tubes. The actual passage time, however, ranges from two hours to as little as 30 minutes. Contractions of the uterine musculature and ciliary currents in the uterine tubes have been suggested as likely mechanisms for accelerating the movement of spermatozoa from the vagina to the site of fertilization.

Even with transport assistance, the passage is not easy. Of the nearly 200 million spermatozoa introduced into the vagina in a typical ejaculation, only about 10,000 enter the uterine tube, and fewer than 100 reach the isthmus. In general, a male with a sperm count below 20 million per milliliter is functionally sterile because too few spermatozoa survive to reach and fertilize an oocyte. While it is true that only one spermatozoon fertilizes an oocyte, dozens of spermatozoa are required for successful fertilization. The additional sperm are essential because one sperm does not contain enough acrosomal enzymes to disrupt the *corona radiata*, the layer of follicle cells that surrounds the oocyte.

The Oocyte at Ovulation

Ovulation occurs before the oocyte is completely mature. The secondary oocyte leaving the follicle is in metaphase of meiosis II. The cell's metabolic operations have been suspended as it awaits the stimulus for further development. If fertilization does not occur, the oocyte disintegrates without completing meiosis.

Fertilization is complicated by the fact that when the secondary oocyte leaves the ovary, it is surrounded by the corona radiata. Fertilization and the events that follow are diagrammed in **Figure 29–1b**. The cells of the corona radiata protect the secondary oocyte as it passes through the ruptured follicular wall, across the surface of the ovary, and into the infundibulum of the uterine tube. Although the physical process of fertilization requires that only a single spermatozoon contact the oocyte membrane, that spermatozoon must first penetrate the corona radiata. The acrosome of each sperm contains several enzymes, including **hyaluronidase** (hī-uh-loo-RON-i-dās). Hyaluronidase breaks down the bonds between adjacent follicle cells. Dozens of spermatozoa must release hyaluronidase before the connections between the follicle cells break down enough to allow an intact spermatozoon to reach the oocyte.

No matter how many spermatozoa slip through the gap in the corona radiata, only a single spermatozoon fertilizes and activates the oocyte (1, **Figure 29–1b**). That spermatozoon must have an intact acrosome. The first step is the binding of the spermatozoon to *sperm receptors* in the zona pellucida, a thick envelope surrounding the oocyte. This binding triggers the rupture of the acrosome. The hyaluronidase and **acrosin,** another proteolytic enzyme, then digest a path through the zona pellucida toward the surface of the oocyte. When the sperm contacts that surface, the sperm and oocyte membranes begin to fuse. This step is the trigger for *oocyte activation*, a complex process we discuss in the next section.

Oocyte Activation

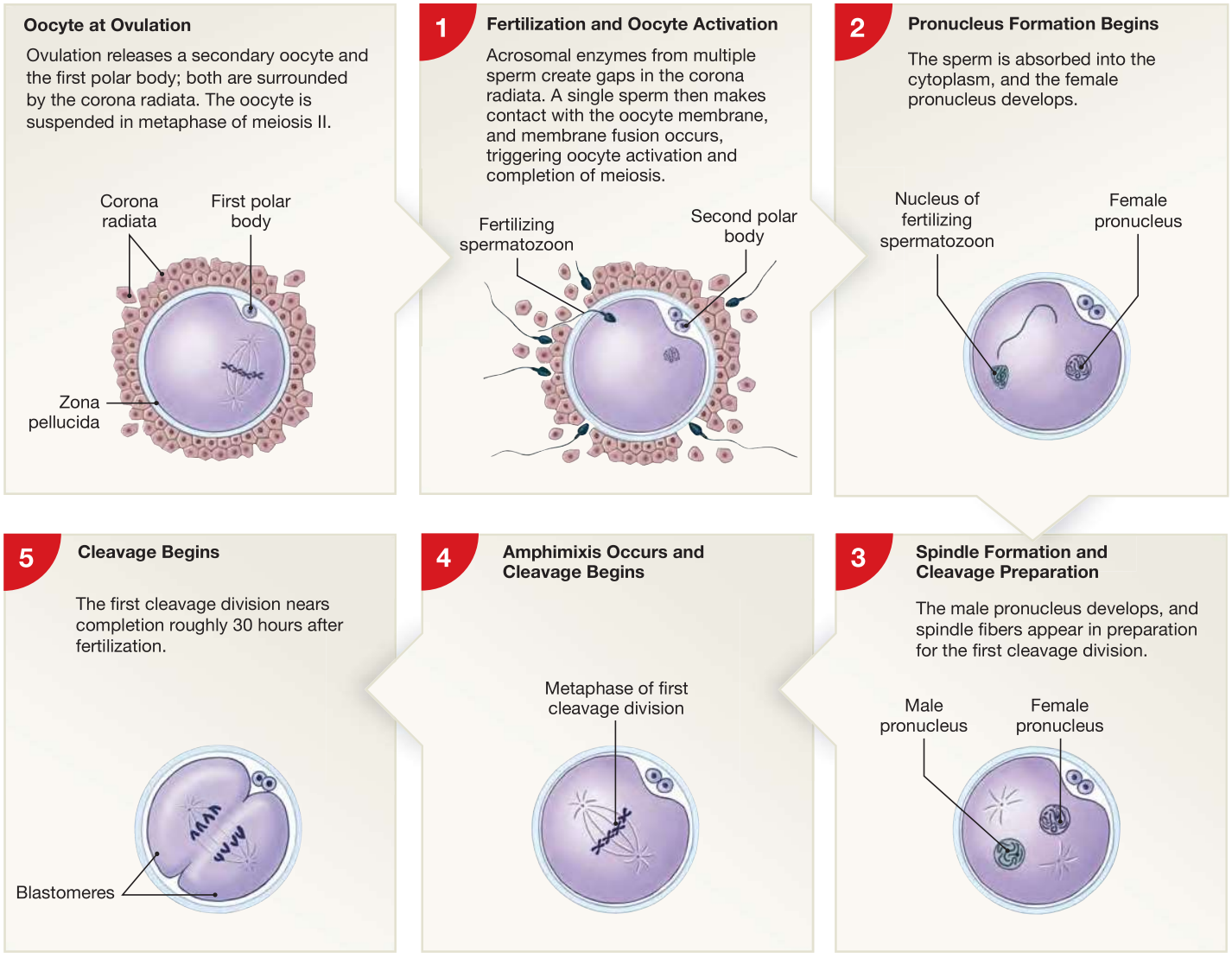
Oocyte activation involves a series of changes in the metabolic activity of the oocyte. The trigger for activation is contact and fusion of the plasma membranes of the sperm and oocyte. This process is accompanied by the depolarization of the oocyte membrane due to an increased permeability to sodium ions. The entry of sodium ions in turn causes the release of calcium ions from the smooth endoplasmic reticulum. The sudden rise in Ca^{2+} levels has important effects, including the following:

- *Exocytosis of Vesicles Located Just Interior to the Oocyte Membrane.* This process, called the *cortical reaction*, releases enzymes that both inactivate the sperm receptors and harden the zona pellucida. This combination prevents **polyspermy** (fertilization by more than one sperm), which would create a zygote that is incapable of normal development. (Prior to completion of the cortical reaction, depolarization of the oocyte membrane probably prevents fertilization by any sperm cells that penetrate the zona pellucida.)
- *Completion of Meiosis II and Formation of the Second Polar Body.* The sperm enters the oocyte and loses its plasma membrane. Meiosis II, which began in the tertiary follicle, can now be completed because fertilization occurred. The fertilized oocyte is now called an ovum.
- *Activation of Enzymes That Cause a Rapid Increase in the Cell's Metabolic Rate.* The cytoplasm contains a large number of mRNA strands that have been inactivated by special proteins. The mRNA strands are now activated, so protein synthesis accelerates rapidly. Most of the proteins synthesized are required for development to proceed.

Figure 29–1 Fertilization.

a A secondary oocyte and numerous sperm at the time of fertilization. Notice the difference in size between the gametes.

After oocyte activation and the completion of meiosis, the nuclear material remaining within the ovum reorganizes as the **female pronucleus** (2, Figure 29–1b). While these changes are under way, the nucleus of the spermatozoon swells, and as it forms the **male pronucleus** the rest of the sperm cell breaks down (3). The male pronucleus then migrates toward the center of the cell, and spindle fibers form. The two pronuclei then fuse in a process called *amphimixis* (am-fi-MIK-sis) (4). The cell is now a zygote that contains the normal complement of 46 chromosomes, and fertilization is complete. This is the "moment of conception." Almost immediately the chromosomes line up along a metaphase plate, and the cell prepares to divide. This is the start of the process of *cleavage*, a series of cell divisions that produce an ever-increasing number of smaller and smaller daughter cells. The first cleavage division is completed about 30 hours after fertilization, yielding two daughter cells, each one-half the size of the original zygote (5). These cells are called *blastomeres* (BLAS-tō-mērz).



b Fertilization and the preparations for cleavage.

Tips & Tricks

Amphimixis means "both mixed together."

Checkpoint

4. **Name two sperm enzymes important to secondary oocyte penetration.**
5. **How many chromosomes are contained within a zygote?**

See the blue Answers tab at the back of the book.

29-3 Gestation consists of three stages of prenatal development: the first, second, and third trimesters

During prenatal development, a single cell ultimately forms a 3–4 kg (6.6–8.8 lb) infant, who in postnatal development will grow through adolescence and maturity toward old age and eventual death. One of the most fascinating aspects of development is its apparent order. Continuity exists at all levels and at all times. Nothing "leaps" into existence without apparent precursors. Differentiation and increasing structural complexity occur hand in hand.

Differentiation involves changes in the genetic activity of some cells but not others. A continuous exchange of information occurs between the nucleus and the cytoplasm in a cell. Activity in the nucleus varies in response to chemical messages that arrive from the surrounding cytoplasm. In turn, ongoing nuclear activity alters conditions within the cytoplasm by directing the synthesis of specific proteins. In this way, the nucleus can affect enzyme activity, cell structure, and membrane properties.

In development, differences in the cytoplasmic composition of individual cells trigger changes in genetic activity. These changes in turn lead to further alterations in the cytoplasm, and the process continues in a sequence. But if all the cells of the embryo are derived from cell divisions of a zygote, how do the cytoplasmic differences originate? What sets the process in motion? The important first step occurs before fertilization, while the oocyte is in the ovary.

Before ovulation, the growing oocyte accepts amino acids, nucleotides, and glucose, as well as more complex materials such as phospholipids, mRNA molecules, and proteins, from the surrounding granulosa cells. Because not all follicle cells manufacture and deliver the same nutrients and instructions to the oocyte, the contents of the cytoplasm are not evenly distributed. After fertilization, the zygote divides into ever-smaller cells that differ from one another in cytoplasmic composition. These differences alter the genetic activity of each cell, creating cell lines with increasingly diverse fates.

As development proceeds, some of the cells release chemical substances, including RNA molecules, polypeptides, and small proteins that affect the differentiation of other embryonic cells. This type of chemical interplay among developing cells, called *induction* (in-DUK-shun), works over very short distances, such as when two types of cells are in direct contact. It may also operate over longer distances, with the inducing chemicals functioning as hormones.

This type of regulation, which involves an integrated series of interacting steps, can control highly complex processes. The mechanism is not always error free, because the appearance of an abnormal or inappropriate inducer can throw development off course.

The time spent in prenatal development is known as **gestation** (jes-TĀ-shun). For convenience, we usually think of the gestation period as consisting of three integrated **trimesters,** each three months in duration:

1. The **first trimester** is the period of embryological and early fetal development. During this time, the rudiments of all the major organ systems appear.
2. The **second trimester** is dominated by the development of organs and organ systems, a process that nears completion by the end of the sixth month. During this time, body shape and proportions change. By the end of this trimester, the fetus looks distinctively human.
3. The **third trimester** is characterized by rapid fetal growth and deposition of adipose tissue. Early in the third trimester, most of the fetus's major organ systems become fully functional. An infant born one month or even two months prematurely has a reasonable chance of survival.

The *Atlas* accompanying this text contains "Embryology Summaries" that introduce key steps in embryological and fetal development and trace the development of specific organ systems. The text will refer to those summaries in the discussions that follow. As you proceed, reviewing the indicated material will help you understand the "big picture" as well as the specific details.

Checkpoint

6. **Define gestation.**
7. **Characterize the key features of each trimester.**

See the blue Answers tab at the back of the book.

29-4 Cleavage, implantation, placentation, and embryogenesis are critical events of the first trimester

At the moment of conception, the fertilized ovum is a single cell about 0.135 mm (0.005 in.) in diameter and weighs approximately 150 μg. By convention, pregnancies are clinically dated

from the last menstrual period (LMP), which is usually two weeks before ovulation and conception. At the end of the first trimester (12 weeks from LMP, but only 10 developmental weeks), the fetus is almost 75 mm (3 in.) long and weighs perhaps 14 g (0.5 oz).

Many important and complex developmental events occur during the first trimester. Here we will focus on four general processes: cleavage, implantation, placentation, and embryogenesis:

1. **Cleavage** (KLĒV-ij) is a sequence of cell divisions that begins immediately after fertilization (**Figure 29–1b**). During cleavage, the zygote becomes a **pre-embryo,** which develops into a multicellular complex known as a *blastocyst*. Cleavage ends when the blastocyst first contacts the uterine wall. Cleavage and blastocyst formation are introduced in the *Atlas*. ATLAS: Embryology Summary 1: The Formation of Tissues
2. **Implantation** begins with the attachment of the blastocyst to the endometrium of the uterus and continues as the blastocyst invades maternal tissues. Important events during implantation set the stage for the formation of vital embryonic structures.
3. **Placentation** (plas-en-TĀ-shun) occurs as blood vessels form around the periphery of the blastocyst, and as the **placenta** develops. The placenta is a complex organ that permits exchange between maternal and embryonic blood. It supports the fetus from its formation early in the first trimester until it stops functioning and is ejected from the uterus just after birth. From that point on, the newborn is physically independent of the mother.
4. **Embryogenesis** (em-brē-ō-JEN-e-sis) is the formation of a viable embryo. This process establishes the foundations for all major organ systems.

These processes are both complex and vital to the survival of the embryo. Perhaps because the events in the first trimester are so complex, it is the most dangerous period in prenatal life. Only about 40 percent of conceptions produce embryos that survive the first trimester. For that reason, pregnant women are warned to take great care to avoid drugs and other disruptive stresses during the first trimester, in the hope of preventing an error in the delicate processes that are under way.

Cleavage and Blastocyst Formation

Cleavage is a series of cell divisions that subdivides the cytoplasm of the zygote (**Figures 29–1b** and **29–2**). The first cleavage produces a pre-embryo consisting of two identical cells. As noted earlier, the identical cells produced by cleavage

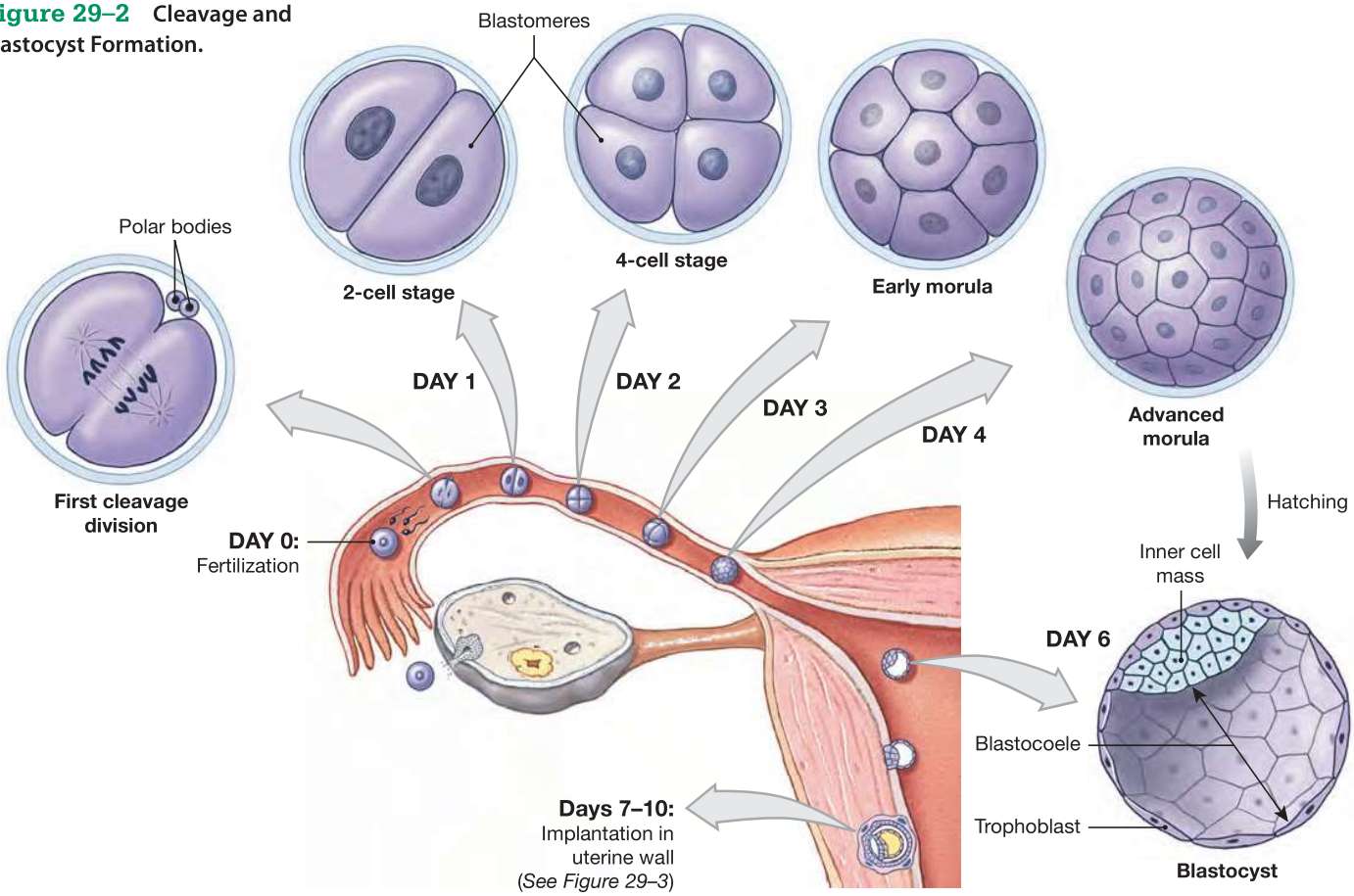


Figure 29–2 Cleavage and Blastocyst Formation.

divisions are called **blastomeres.** After the first division is completed roughly 30 hours after fertilization, subsequent divisions occur at intervals of 10–12 hours. During the initial divisions, all the blastomeres divide simultaneously. As the number of blastomeres increases, the timing becomes less predictable.

After three days of cleavage, the pre-embryo is a solid ball of cells resembling a mulberry. This stage is called the **morula** (MOR-ū-luh; *morula*, mulberry). The morula typically reaches the uterus on day 4. Over the next two days, the blastomeres form a **blastocyst,** a hollow ball with an inner cavity known as the **blastocoele** (BLAS-tō-sēl). The blastomeres are now no longer identical in size and shape. The outer layer of cells, which separates the outside world from the blastocoele, is called the **trophoblast** (TRŌ-fō-blast). As the word *trophoblast* implies (*trophos*, food + *blast*, precursor), cells in this layer provide nutrients to the developing embryo. A second group of cells, the **inner cell mass,** lies clustered at one end of the blastocyst. These cells are exposed to the blastocoele but are insulated from contact with the outside environment by the trophoblast. In time, the inner cell mass will form the embryo.

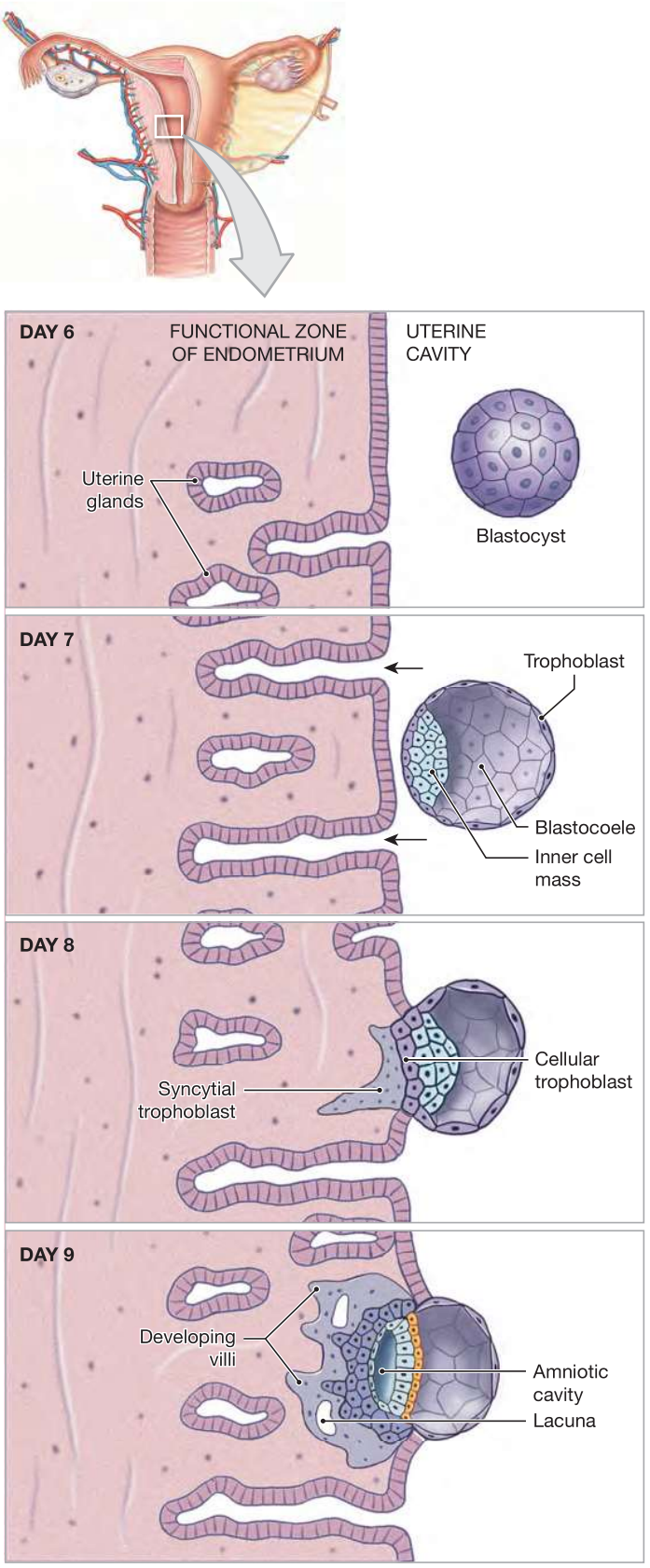
Implantation

During blastocyst formation, enzymes released by the trophoblast erode an opening in the zona pellucida, which is then shed in a process known as *hatching* (**Figure 29–2**). The blastocyst is now freely exposed to the fluid contents of the uterine cavity. The uterine glands of the uterus secrete this glycogen-rich fluid. Throughout the previous few days, the pre-embryo and early blastocyst had been absorbing fluid and nutrients from its surroundings; the process now accelerates, and the blastocyst enlarges. When fully formed, the blastocyst contacts the endometrium, and implantation occurs (**Figures 29–2** and **29–3**).

Implantation begins as the surface of the blastocyst closest to the inner cell mass touches and adheres to the uterine lining (see day 7 in **Figure 29–3**). At the point of contact, the trophoblast cells divide rapidly, making the trophoblast several layers thick. The cells closest to the interior of the blastocyst remain intact, forming a layer of **cellular trophoblast,** or *cytotrophoblast*. Near the endometrial wall, the plasma membranes separating the trophoblast cells disappear, creating a layer of cytoplasm containing multiple nuclei (day 8). This outer layer is called the **syncytial** (sin-SISH-ul) **trophoblast,** or *syncytiotrophoblast*.

The syncytial trophoblast erodes a path through the uterine epithelium by secreting hyaluronidase. This enzyme dissolves the proteoglycans between adjacent epithelial cells, just as hyaluronidase released by spermatozoa dissolved the connections between cells of the corona radiata. At first, the erosion creates a gap in the uterine lining, but migration and divisions of maternal epithelial cells soon repair the surface. By day 10

Figure 29–3 Stages in Implantation.



the repairs are complete, and the blastocyst has lost contact with the uterine cavity. Further development occurs entirely within the functional zone of the endometrium.

In most cases, implantation occurs in the fundus or in the body of the uterus. In an **ectopic pregnancy,** implantation occurs somewhere other than within the uterus, such as in one of the uterine tubes. Approximately 0.6 percent of pregnancies are ectopic pregnancies, which do not produce a viable embryo and can be life-threatening to the mother.

As implantation proceeds, the syncytial trophoblast continues to enlarge and spread into the surrounding endometrium (see day 9, **Figure 29–3**). The erosion of uterine glands releases nutrients that are absorbed by the syncytial trophoblast and distributed by diffusion through the underlying cellular trophoblast to the inner cell mass. These nutrients provide the energy needed to support the early stages of embryo formation. Trophoblastic extensions grow around endometrial capillaries. As the capillary walls are destroyed, maternal blood begins to percolate through trophoblastic channels known as **lacunae.** Fingerlike **villi** extend away from the trophoblast into the surrounding endometrium, gradually increasing in size and complexity until about day 21. As the syncytial trophoblast spreads, it begins breaking down larger endometrial veins and arteries, and blood flow through the lacunae accelerates.

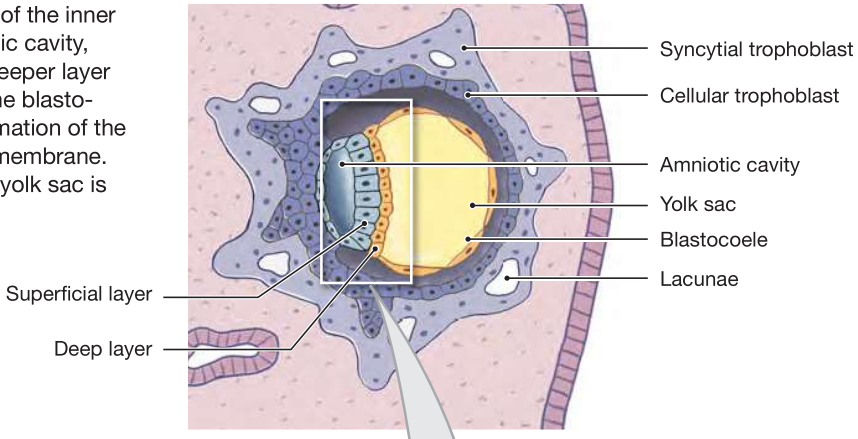
Formation of the Amniotic Cavity

The inner cell mass has little apparent organization early in the blastocyst stage. Yet by the time of implantation, the inner cell mass has separated from the trophoblast. The separation gradually increases, creating a fluid-filled chamber called the **amniotic** (am-nē-OT-ik) **cavity** (see day 9 in **Figure 29–3**; details from days 10–12 are shown in **Figure 29–4**). The trophoblast will later be

Figure 29–4 The Inner Cell Mass and Gastrulation.

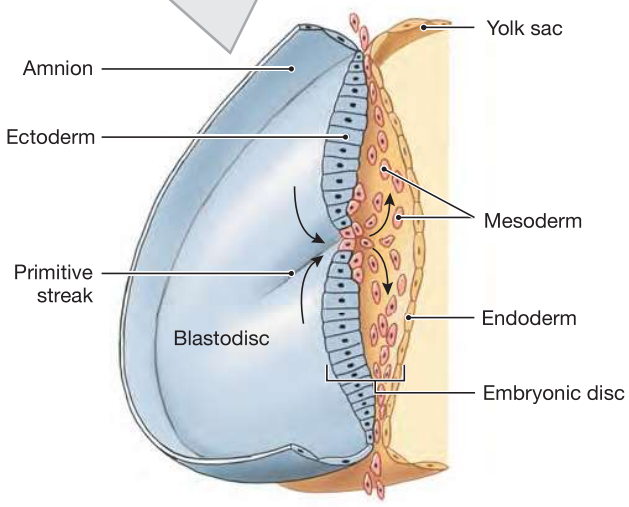
Day 10: Yolk Sac Formation

While cells from the superficial layer of the inner cell mass migrate around the amniotic cavity, forming the amnion, cells from the deeper layer migrate around the outer edges of the blastocoele. This is the first step in the formation of the yolk sac, a second extraembryonic membrane. For roughly the next two weeks, the yolk sac is the primary nutrient source for the inner cell mass; it absorbs and distributes nutrients released into the blastocoele by the trophoblast.



Day 12: Gastrulation

By day 12, superficial cells of the blastodisc have begun to migrate toward a central line known as the **primitive streak**. At the primitive streak, the migrating cells leave the surface and move between the two existing layers. This movement creates three distinct embryonic layers: (1) the **ectoderm**, consisting of superficial cells that did not migrate into the interior of the blastodisc; (2) the **endoderm**, consisting of the cells that face the yolk sac; and (3) the **mesoderm**, consisting of the poorly organized layer of migrating cells between the ectoderm and the endoderm. Collectively, these three embryonic layers are called **germ layers**, and the migration process is called gastrulation. Gastrulation produces an oval, three-layered sheet known as the **embryonic disc.** This disc will form the body of the embryo, whereas all other cells of the blastocyst will be part of the extraembryonic membranes.



Clinical Note

Gestational Trophoblastic Neoplasia The trophoblast undergoes repeated nuclear divisions, shows extensive and rapid growth, has a very high demand for energy, invades and spreads through adjacent tissues, and fails to activate the maternal immune system—in short, the trophoblast has many of the characteristics of cancer cells. In about 0.1 percent of pregnancies, something goes wrong with the regulatory mechanisms, and instead of developing normally, the syncytial trophoblast behaves like a tumor. This condition is called *gestational trophoblastic neoplasia*. The least dangerous form, a *hydatidiform* (hī-da-TID-i-form) *mole*, is not malignant. However, about 20 percent of gestational trophoblastic neoplasias metastasize to other tissues, with potentially fatal results. Consequently, prompt surgical removal of the mass is essential, and the surgery is sometimes followed by chemotherapy.

separated from the amniotic cavity by layers of cells that originate at the inner cell mass and line the amniotic cavity. These layers form the *amnion*, a membrane we will examine later in the chapter. When the amniotic cavity first appears, the cells of the inner cell mass are organized into an oval sheet that is two layers thick: a superficial layer that faces the amniotic cavity, and a deeper layer that is exposed to the fluid contents of the blastocoele.

Gastrulation and Germ Layer Formation

By day 12, a third layer of cells begins to form between the superficial and deep layers of cells of the inner cell mass through **gastrulation** (gas-troo-LĀ-shun) (day 12, **Figure 29–4**). Together, the three layers of cells are called *germ layers*. **Table 29–1** contains a comprehensive listing of the contributions each germ layer makes to form the body systems described in earlier chapters. The formation of the mesoderm between the ectoderm and endoderm, and the developmental fates of the three germ layers are also summarized in the *Atlas*. ATLAS: Embryology Summary 4: The Development of Organ Systems

Table 29–1 The Fates of the Germ Layers

ECTODERMAL CONTRIBUTIONS
Integumentary system: epidermis, hair follicles and hairs, nails, and glands communicating with the skin (sweat glands, mammary glands, and sebaceous glands)
Skeletal system: pharyngeal cartilages and their derivatives in adults (portion of sphenoid, the auditory ossicles, the styloid processes of the temporal bones, the cornu and superior rim of the hyoid bone)*
Nervous system: all neural tissue, including brain and spinal cord
Endocrine system: pituitary gland and adrenal medullae
Respiratory system: mucous epithelium of nasal passageways
Digestive system: mucous epithelium of mouth and anus, salivary glands
MESODERMAL CONTRIBUTIONS
Integumentary system: dermis and hypodermis
Skeletal system: all components except some pharyngeal derivatives
Muscular system: all components
Endocrine system: adrenal cortex, endocrine tissues of heart, kidneys, and gonads
Cardiovascular system: all components
Lymphatic system: all components
Urinary system: the kidneys, including the nephrons and the initial portions of the collecting system
Reproductive system: the gonads and the adjacent portions of the duct systems
Miscellaneous: the lining of the body cavities (pleural, pericardial, and peritoneal) and the connective tissues that support all organ systems
ENDODERMAL CONTRIBUTIONS
Endocrine system: thymus, thyroid gland, and pancreas
Respiratory system: respiratory epithelium (except nasal passageways) and associated mucous glands
Digestive system: mucous epithelium (except mouth and anus), exocrine glands (except salivary glands), liver, and pancreas
Urinary system: urinary bladder and distal portions of the duct system
Reproductive system: distal portions of the duct system, stem cells that produce gametes

*The neural crest is derived from ectoderm and contributes to the formation of the skull and the skeletal derivatives of the embryonic pharyngeal arches.

Formation of the Extraembryonic Membranes

Germ layers also form four **extraembryonic membranes:** (1) the *yolk sac* (endoderm and mesoderm), (2) the *amnion* (ectoderm and mesoderm), (3) the *allantois* (endoderm and mesoderm), and (4) the *chorion* (mesoderm and trophoblast). Although these membranes support embryological and fetal development, few traces of their existence remain in adult systems. **Figure 29–5** shows representative stages in the development of the extraembryonic membranes.

The Yolk Sac. The **yolk sac** begins as a layer of cells spread out around the outer edges of the blastocoele to form a complete pouch. This pouch is already visible 10 days after fertilization (**Figure 29–4**). As gastrulation proceeds, mesodermal cells migrate around the pouch and complete the formation of the yolk sac (week 2, **Figure 29–5**). Blood vessels soon appear within the mesoderm, and the yolk sac becomes an important site of blood cell formation.

The Amnion. The ectodermal layer enlarges, and ectodermal cells spread over the inner surface of the amniotic cavity. Mesodermal cells soon follow, creating a second, outer layer (see week 2, **Figure 29–5**). This combination of mesoderm and ectoderm is the **amnion** (AM-nē-on). As development proceeds, the amnion and the amniotic cavity continue to enlarge. The amniotic cavity contains **amniotic fluid,** which surrounds and cushions the developing embryo or fetus (see week 3 through week 10, **Figure 29–5**).

The Allantois. The third extraembryonic membrane begins as an outpocketing of the endoderm near the base of the yolk sac (see week 3, **Figure 29–5**). The free endodermal tip then grows toward the wall of the blastocyst, surrounded by a mass of mesodermal cells. This sac of endoderm and mesoderm is the **allantois** (a-LAN-tō-is), the base of which later gives rise to the urinary bladder. The formation of the allantois and its relationship to the urinary bladder is illustrated in the *Atlas*. ATLAS: Embryology Summary 20: The Development of the Urinary System

The Chorion. The mesoderm associated with the allantois spreads around the blastocyst, separating the cellular trophoblast from the blastocoele. This combination of mesoderm and trophoblast is the **chorion** (KŌ-rē-on) (see weeks 2 and 3, **Figure 29–5**).

When implantation first occurs, the nutrients absorbed by the trophoblast can easily reach the inner cell mass by simple diffusion. But as the embryo and the trophoblast enlarge, the distance between them increases, so diffusion alone can no longer keep pace with the demands of the developing embryo. Blood vessels now begin to develop within the mesoderm of the chorion, creating a rapid-transit system for nutrients that links the embryo with the trophoblast.

The appearance of blood vessels in the chorion is the first step in the creation of a functional placenta. By the third week of development, the mesoderm extends along the core of each trophoblastic villus, forming **chorionic villi** in contact with maternal tissues (**Figures 29–5** [weeks 3 through 10] and **29–6**). These villi continue to enlarge and branch, creating an intricate network within the endometrium. Embryonic blood vessels develop within each villus. Blood flow through those chorionic vessels begins early in the third week of development, when the embryonic heart starts beating. The blood supply to the chorionic villi arises from the allantoic arteries and veins.

As the chorionic villi enlarge, more maternal blood vessels are eroded. Maternal blood now moves slowly through complex lacunae lined by the syncytial trophoblast. Chorionic blood vessels pass close by, and gases and nutrients diffuse between the embryonic and maternal circulations across the layers of the trophoblast. Recall that fetal hemoglobin has a higher affinity for oxygen than does maternal hemoglobin, enabling fetal hemoglobin to strip oxygen from maternal hemoglobin. ↩ p. 845 Maternal blood then reenters the venous system of the mother through the broken walls of small uterine veins. No mixing of maternal and fetal blood occurs, because layers of trophoblast always separate the two.

Placentation

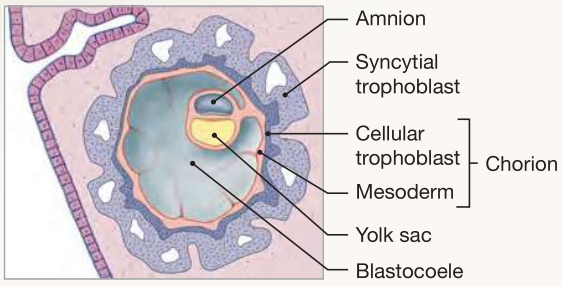
At first, the entire blastocyst is surrounded by chorionic villi. The chorion continues to enlarge, expanding like a balloon within the endometrium. By week 4, the embryo, amnion, and yolk sac are suspended within an expansive, fluid-filled chamber (**Figure 29–5**). The **body stalk,** the connection between embryo and chorion, contains the distal portions of the allantois and blood vessels that carry blood to and from the placenta. The narrow connection between the endoderm of the embryo and the yolk sac is called the **yolk stalk.** The formation of the yolk stalk and body stalk are illustrated in the *Atlas*. ATLAS: Embryology Summary 19: The Development of the Digestive System

The placenta does not continue to enlarge indefinitely. Regional differences in placental organization begin to develop as expansion of the placenta creates a prominent bulge in the endometrial surface. This relatively thin portion of the endometrium, called the **decidua capsularis** (dē-SID-ū-uh kap-sū-LA-ris; *deciduus*, a falling off), no longer exchanges nutrients, and the chorionic villi in the region disappear (**Figures 29–5** [week 5] and **29–6a**). Placental functions are now concentrated in a disc-shaped area in the deepest portion of the endometrium, a region called the **decidua basalis** (bā-SĀ-lis). The rest of the uterine endometrium, which has no contact with the chorion, is called the **decidua parietalis.**

Figure 29–5 Extraembryonic Membranes and Placenta Formation.

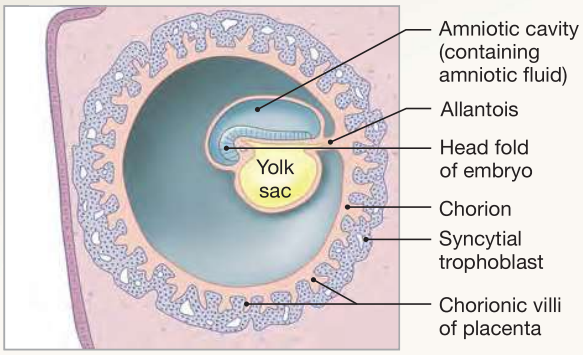
1 Week 2

Migration of mesoderm around the inner surface of the trophoblast creates the chorion. Mesodermal migration around the outside of the amniotic cavity, between the ectodermal cells and the trophoblast, forms the amnion. Mesodermal migration around the endodermal pouch creates the yolk sac.



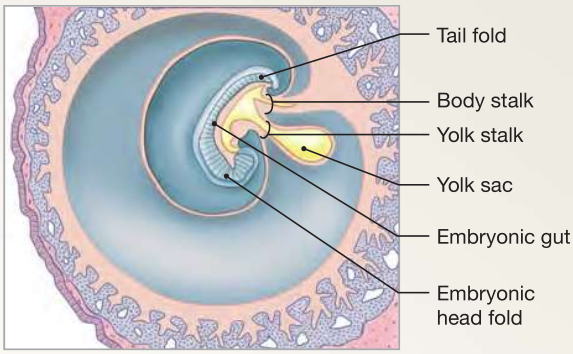
2 Week 3

The embryonic disc bulges into the amniotic cavity at the head fold. The allantois, an endodermal extension surrounded by mesoderm, extends toward the trophoblast.



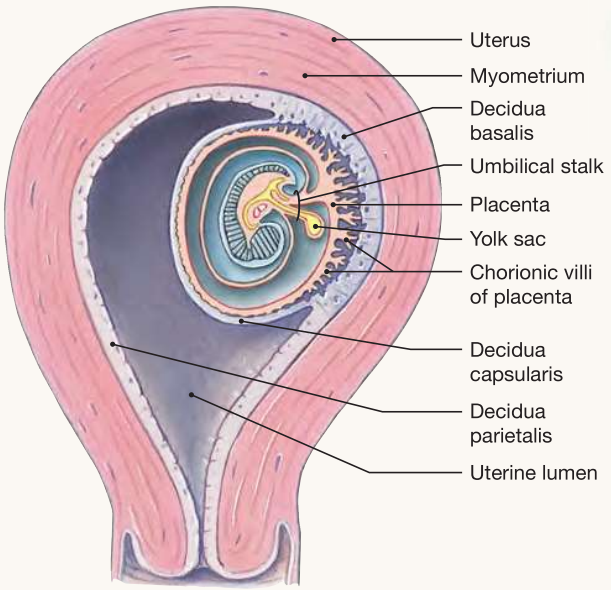
3 Week 4

The embryo now has a head fold and a tail fold. Constriction of the connections between the embryo and the surrounding trophoblast narrows the yolk stalk and body stalk.



4 Week 5

The developing embryo and extraembryonic membranes bulge into the uterine cavity. The trophoblast pushing out into the uterine lumen remains covered by endometrium but no longer participates in nutrient absorption and embryo support. The embryo moves away from the placenta, and the body stalk and yolk stalk fuse to form an umbilical stalk.



5 Week 10

The amnion has expanded greatly, filling the uterine cavity. The fetus is connected to the placenta by an elongated umbilical cord that contains a portion of the allantois, blood vessels, and the remnants of the yolk stalk.

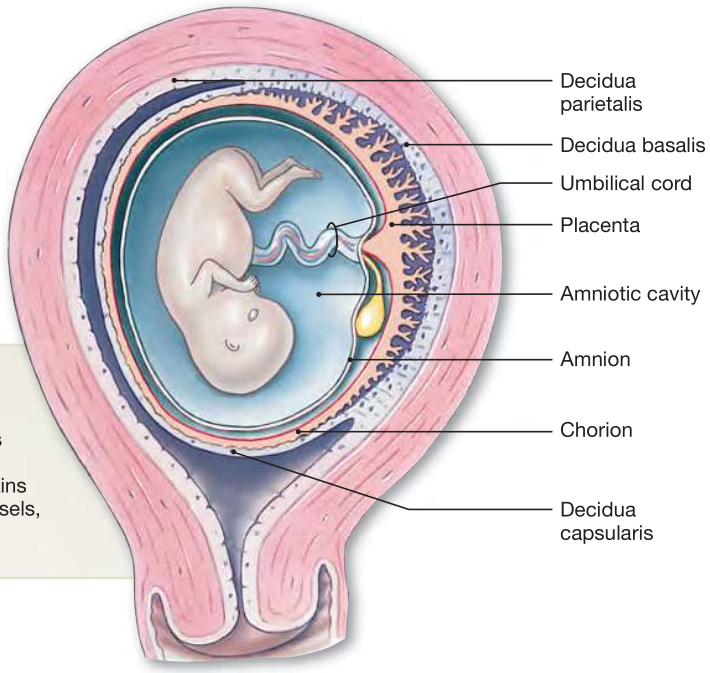
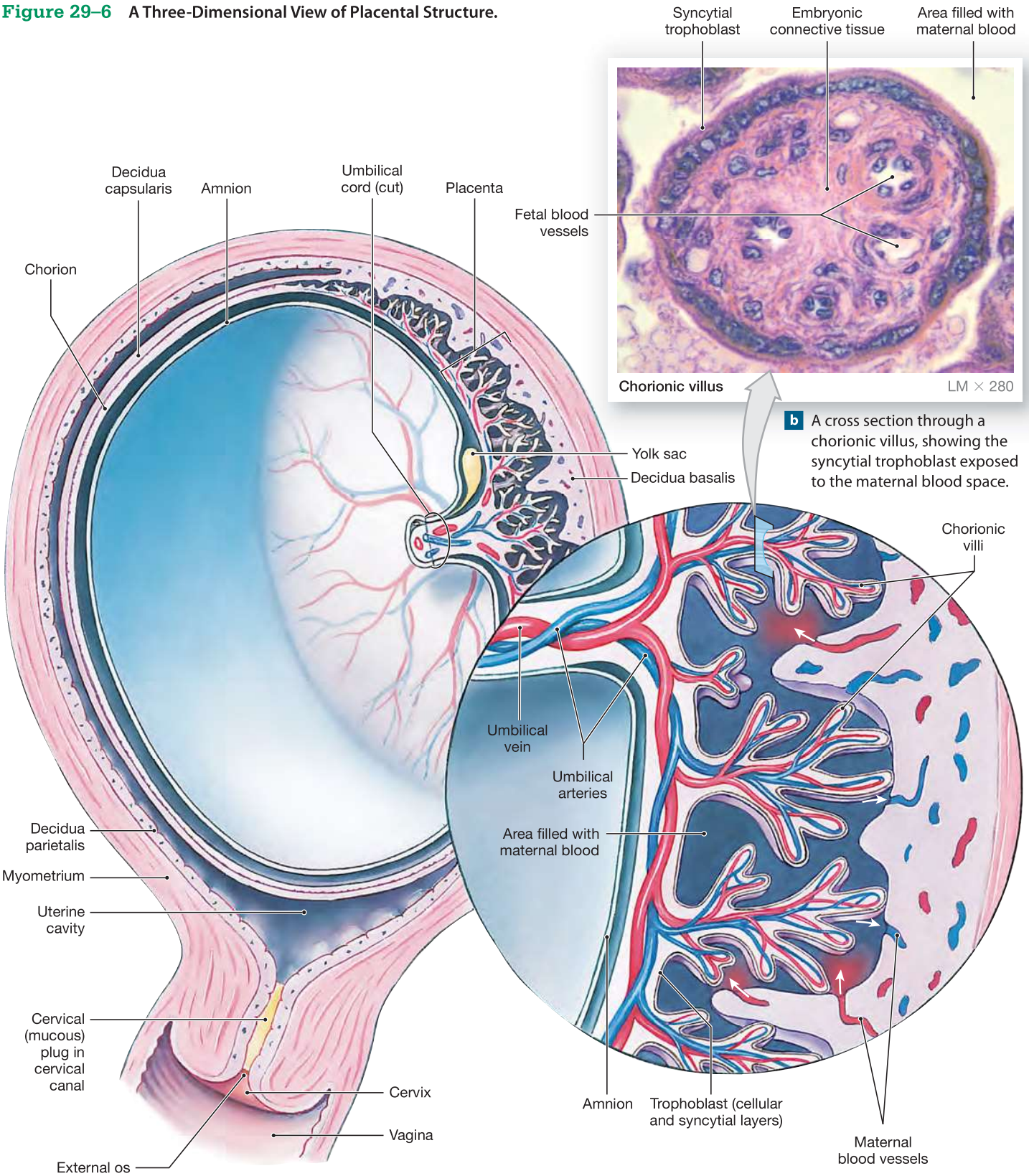


Figure 29–6 A Three-Dimensional View of Placental Structure.



b A cross section through a chorionic villus, showing the syncytial trophoblast exposed to the maternal blood space.

a A view of the uterus after the fetus has been removed and the umbilical cord cut. Arrows in the enlarged view indicate the direction of blood flow. Blood flows into the placenta through ruptured maternal arteries and then flows around chorionic villi, which contain fetal blood vessels.

As the end of the first trimester approaches, the fetus moves farther from the placenta (see weeks 5 and 10, **Figure 29–5**). The fetus and placenta remain connected by the **umbilical cord,** or *umbilical stalk*, which contains the allantois, the placental blood vessels, and the yolk stalk.

Tips & Tricks

Like a deep-sea diver's air hose or a space-walking astronaut's tether, the umbilical cord supplies the fetus with life-sustaining substances and removes waste products.

Placental Circulation

Figure 29–6a illustrates circulation at the placenta near the end of the first trimester. Blood flows to the placenta through the paired **umbilical arteries** and returns in a single **umbilical vein.** ↩ p. 755 The chorionic villi provide the surface area for active and passive exchanges of gases, nutrients, and waste products between the fetal and maternal bloodstreams. The blood in the umbilical arteries is deoxygenated and contains waste products generated by tissues. At the placenta, oxygen supplies are replenished, organic nutrients added, and carbon dioxide and other organic waste products removed.

The placenta places a considerable demand on the maternal cardiovascular system, and blood flow to the uterus and placenta is extensive. If the placenta is torn or otherwise damaged, the consequences may prove fatal to both fetus and mother.

The Endocrine Placenta

In addition to its role in the nutrition of the fetus, the placenta acts as an endocrine organ. Several hormones—including *human chorionic gonadotropin*, *human placental lactogen*, *placental prolactin*, *relaxin*, *progesterone*, and *estrogens*—are synthesized by the syncytial trophoblast and released into the maternal bloodstream.

Human Chorionic Gonadotropin. The hormone **human chorionic gonadotropin (hCG)** appears in the maternal bloodstream soon after implantation. The presence of hCG in blood or urine samples provides a reliable indication of pregnancy. Kits sold for the early detection of pregnancy are sensitive to the presence of this hormone.

In function, hCG resembles luteinizing hormone (LH), because it maintains the integrity of the corpus luteum and promotes the continued secretion of progesterone. As a result, the endometrial lining remains perfectly functional, and menses does not normally occur. In the absence of hCG, the pregnancy ends, because another uterine cycle begins and the functional zone of the endometrium disintegrates.

In the presence of hCG, the corpus luteum persists for three to four months before gradually decreasing in size and secretory function. The decline in luteal function does not trigger the return of uterine cycles, because by the end of the first trimester, the placenta actively secretes both estrogens and progesterone.

Human Placental Lactogen and Placental Prolactin. Human placental lactogen (hPL), or *human chorionic somatomammotropin (hCS)*, helps prepare the mammary glands for milk production. It also has a stimulatory effect on other maternal tissues comparable to that of growth hormone (GH), ensuring that glucose and protein are available for the fetus. At the mammary glands, the conversion from inactive to active status requires the presence of placental hormones (hPL, **placental prolactin,** estrogen, and progesterone) as well as several maternal hormones (GH, prolactin, and thyroid hormones). We consider the hormonal control of mammary gland function in a later section.

Relaxin. Relaxin is a peptide hormone that is secreted by the placenta and the corpus luteum during pregnancy. Relaxin (1) increases the flexibility of the pubic symphysis, permitting the pelvis to expand during delivery; (2) causes the dilation of the cervix, making it easier for the fetus to enter the vaginal canal; and (3) suppresses the release of oxytocin by the hypothalamus and delays the onset of labor contractions.

Progesterone and Estrogens. After the first trimester, the placenta produces sufficient amounts of progesterone to maintain the endometrial lining and continue the pregnancy. As the end of the third trimester approaches, estrogen production by the placenta accelerates. As we will see in a later section, the rising estrogen levels play a role in stimulating labor and delivery.

Embryogenesis

Shortly after gastrulation begins, the body of the embryo begins to separate itself from the rest of the embryonic disc. The body of the embryo and its internal organs now start to form. This process, called **embryogenesis,** begins as folding and differential growth of the embryonic disc produce a bulge that projects into the amniotic cavity (**Figure 29–5**). This projection is known as the **head fold;** similar movements lead to the formation of a **tail fold** (**Figure 29–5**).

The embryo is now physically as well as developmentally distinct from the embryonic disc and the extraembryonic membranes. The definitive orientation of the embryo can now be seen, complete with dorsal and ventral surfaces and left and right sides. **Table 29–2** provides an overview of the subsequent

development of the major organs and body systems. The changes in proportions and appearance that occur between the second developmental week and the end of the first trimester are summarized in **Figure 29–7**.

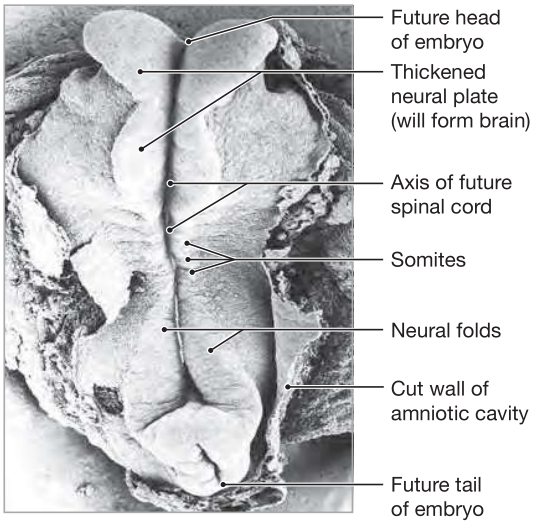
The first trimester is a critical period for development, because events in the first 12 weeks establish the basis for **organogenesis,** the process of organ formation. The major features of organogenesis in each organ system are described in Embryology Summaries 6–21 in the *Atlas*. Important developmental milestones are indicated in **Table 29–2**.

Checkpoint

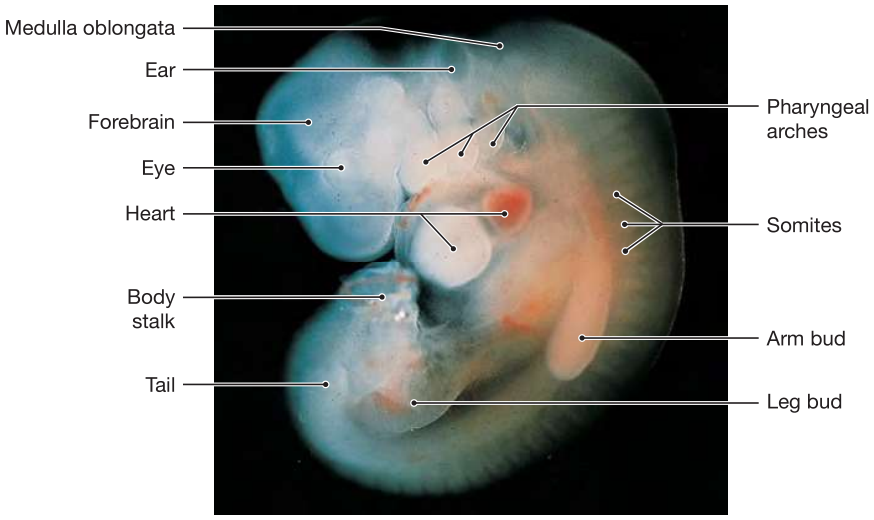
8. What is the developmental fate of the inner cell mass of the blastocyst?
9. Improper development of which of the extraembryonic membranes would affect the cardiovascular system?
10. Sue's pregnancy test indicates the presence of elevated levels of the hormone hCG (human chorionic gonadotropin). Is she pregnant?
11. What are two important functions of the placenta?

See the blue Answers tab at the back of the book.

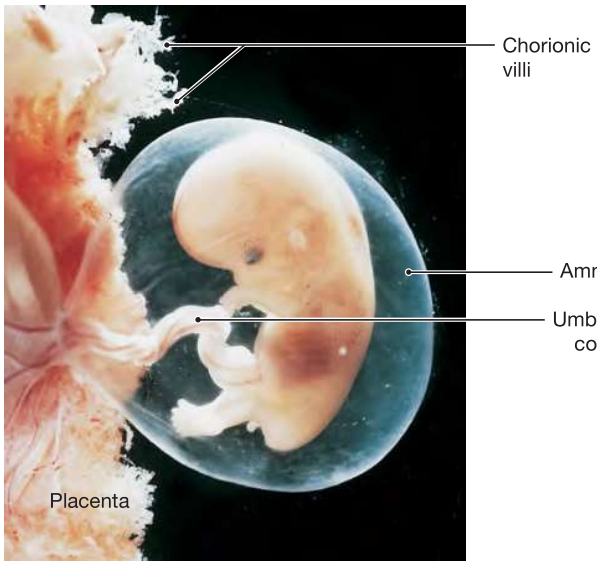
Figure 29–7 The First 12 Weeks of Development. ATLAS: Plate 90a



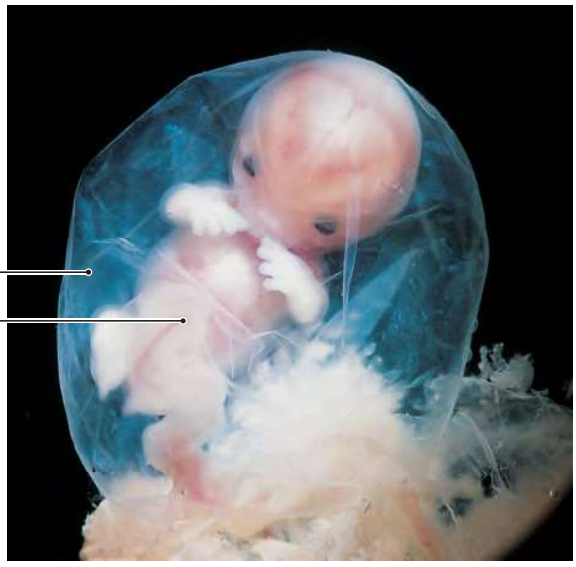
a Week 2. An SEM of the superior surface of a monkey embryo at 2 weeks of development. A human embryo at this stage would look essentially the same.



b Week 4. Fiberoptic view of human development at week 4.



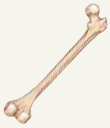
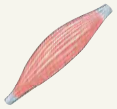
c Week 8. Fiberoptic view of human development at week 8.



d Week 12. Fiberoptic view of human development at week 12.

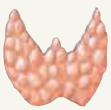
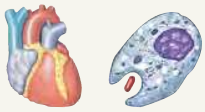
Table 29–2 An Overview of Prenatal Development

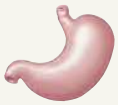
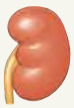
Background Material
ATLAS: Embryology Summaries 1–4:
The Development of Tissues
The Development of Epithelia
The Development of Connective Tissues
The Development of Organ Systems

Gestational Age (Months)	Size and Weight	Integumentary System	Skeletal System	Muscular System	Nervous System	Special Sense Organs
1	5 mm (0.2 in.), 0.02 g (0.00004 lb)		(b) Formation of somites	(b) Formation of somites	(b) Formation of neural tube	(b) Formation of eyes and ears
2	28 mm (1.1 in.), 2.7 g (0.00595 lb)	(b) Formation of nail beds, hair follicles, sweat glands	(b) Formation of axial and appendicular cartilages	(c) Rudiments of axial musculature	(b) CNS, PNS organization, growth of cerebrum	(b) Formation of taste buds, olfactory epithelium
3	78 mm (3.1 in.), 26 g (0.0573 lb)	(b) Epidermal layers appear	(b) Spreading of ossification centers	(c) Rudiments of appendicular musculature	(c) Basic spinal cord and brain structure	
4	133 mm (5.2 in.), 0.15 kg (0.33 lb)	(b) Formation of hair, sebaceous glands (c) Sweat glands	(b) Articulations (c) Facial and palatal organization	Fetal movements can be felt by the mother	(b) Rapid expansion of cerebrum	(c) Basic eye and ear structure (b) Formation of peripheral receptors
5	185 mm (7.3 in.), 0.46 kg (1.01 lb)	(b) Keratin production, nail production			(b) Myelination of spinal cord	
6	230 mm (9.1 in.), 0.64 kg (1.41 lb)			(c) Perineal muscles	(b) Formation of CNS tract (c) Layering of cortex	
7	270 mm (10.6 in.), 1.492 kg (3.284 lb)	(b) Keratinization, formation of nails, hair				(c) Eyelids open, retinas sensitive to light
8	310 mm (12.2 in.), 2.274 kg (5.003 lb)		(b) Formation of epiphyseal cartilages			(c) Taste receptors functional
9	346 mm (13.6 in.), 3.2 kg (7.04 lb)					
Early postnatal development		Hair changes in consistency and distribution	Formation and growth of epiphyseal cartilages continue	Muscle mass and control increase	Myelination, layering, CNS tract formation continue	
Location of relevant text and illustrations		ATLAS: Embryology Summary 5	Ch. 6: pp. 179–182 Ch. 7: pp. 215–216 ATLAS: Embryology Summaries 6,7,8	ATLAS: Embryology Summary 9	Ch. 14: pp. 450–451 ATLAS: Embryology Summaries 10,11,12	ATLAS: Embryology Summary 13

Note: (b) = beginning; (c) = completion.


Gestational Age (Months)	Endocrine System	Cardiovascular and Lymphatic Systems	Respiratory System	Digestive System	Urinary System	Reproductive System
1		(b) Heartbeat	(b) Formation of trachea and lungs	(b) Formation of intestinal tract, liver, pancreas (c) Yolk sac	(c) Allantois	
2	(b) Formation of thymus, thyroid, pituitary, adrenal glands	(c) Basic heart structure, major blood vessels, lymph nodes and ducts (b) Blood formation in liver	(b) Extensive bronchial branching into mediastinum (c) Diaphragm	(b) Formation of intestinal subdivisions, villi, salivary glands	(b) Formation of kidneys (metanephros)	(b) Formation of mammary glands
3	(c) Thymus, thyroid gland	(b) Tonsils, blood formation in bone marrow		(c) Gallbladder, pancreas		(b) Formation of gonads, ducts genitalia; oogonia in female
4		(b) Migration of lymphocytes to lymphoid organs; blood formation in spleen			(b) Degeneration of embryonic kidneys (mesonephros)	
5		(c) Tonsils	(c) Nostrils open	(c) Intestinal subdivisions		
6	(c) Adrenal glands	(c) Spleen, liver, bone marrow	(b) Formation of alveoli	(c) Epithelial organization, glands		
7	(c) Pituitary gland			(c) Intestinal plicae circulares		(b) Descent of testes in male; primary oocytes in prophase I of meiosis in female
8			Complete pulmonary branching and alveolar structure		(c) Nephron formation	Descent of testes complete at or near time of birth
9						
Early postnatal development		Cardiovascular changes at birth; immune response gradually becomes fully operational				
Location of relevant text and illustrations	ATLAS: Embryology Summary 14	Ch. 19: pp. 648, 657 Ch. 21: pp. 755–757 ATLAS: Embryology Summaries 15,16,17	Ch. 23: p. 854 ATLAS: Embryology Summary 18	Ch. 24: pp. 846–866 ATLAS: Embryology Summary 19	ATLAS: Embryology Summary 20	Ch. 28: pp. 1033–1034 ATLAS: Embryology Summary 21

Note: (b) = beginning; (c) = completion.

29-5 ◗ During the second and third trimesters, maternal organ systems support the developing fetus, and the uterus undergoes structural and functional changes

By the end of the first trimester (**Figure 29–7d**), the rudiments of all the major organ systems have formed. Over the next three months, the fetus will grow to a weight of about 0.64 kg (1.4 lb). Encircled by the amnion, the fetus grows faster than the surrounding placenta during this second trimester. When the mesoderm on the outer surface of the amnion contacts the mesoderm on the inner surface of the chorion, these layers fuse, creating a compound *amniochorionic membrane*. **Figure 29–8a** shows a four-month-old fetus; **Figure 29–8b** shows a six-month-old fetus.

During the third trimester, most of the organ systems become ready to perform their normal functions without maternal assistance. The rate of growth starts to slow, but in absolute terms this trimester sees the largest weight gain. In the last three months of gestation, the fetus gains about 2.6 kg (5.7 lb), reaching a full-term weight of approximately 3.2 kg (7 lb). The Embryology Summaries in the *Atlas* illustrate organ system development in the second and third trimesters, and highlights are noted in **Table 29–2**.

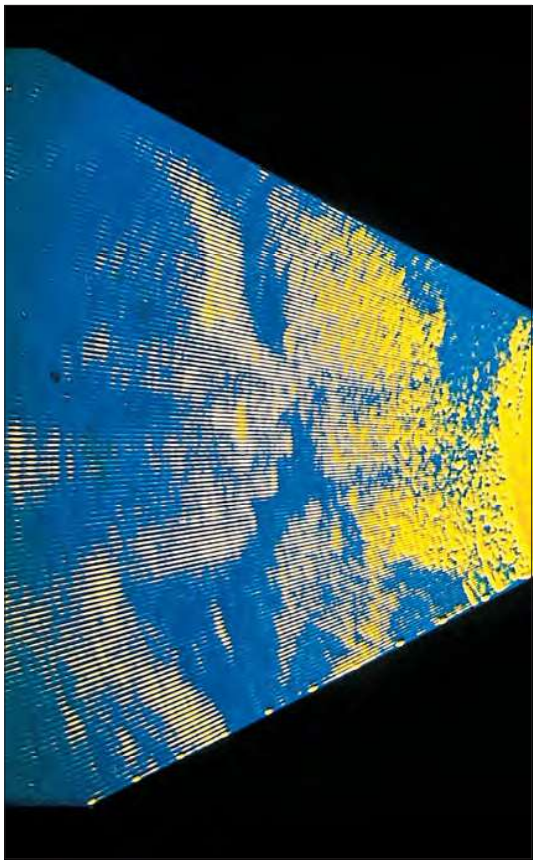
At the end of gestation, a typical uterus will have undergone a tremendous increase in size. **Figure 29–9a–c** shows the positions of the uterus, fetus, and placenta from 16 weeks to *full term* (nine months). When the pregnancy is at full term, the uterus and fetus push many of the maternal abdominal organs out of their normal positions (**Figure 29–9c,d**).

Pregnancy and Maternal Systems

The developing fetus is totally dependent on maternal organ systems for nourishment, respiration, and waste removal. Maternal systems perform these functions in addition to their normal operations. For example, the mother must absorb enough oxygen, nutrients, and vitamins for herself *and* for her fetus, and she must eliminate all the wastes that are generated. Although this is not a burden over the initial weeks of gestation,

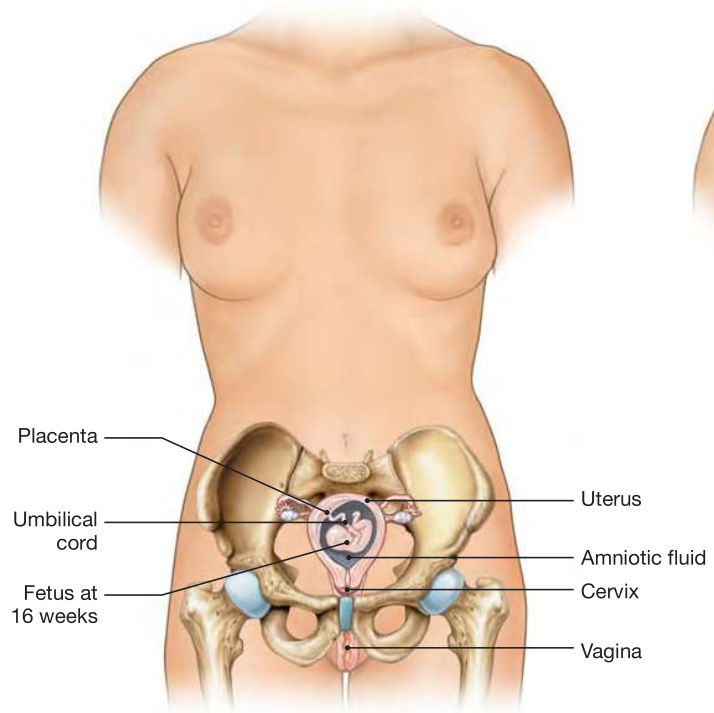
Figure 29–8 The Second and Third Trimesters. ATLAS: Plate 90b

a A four-month-old fetus, seen through a fiberoptic endoscope

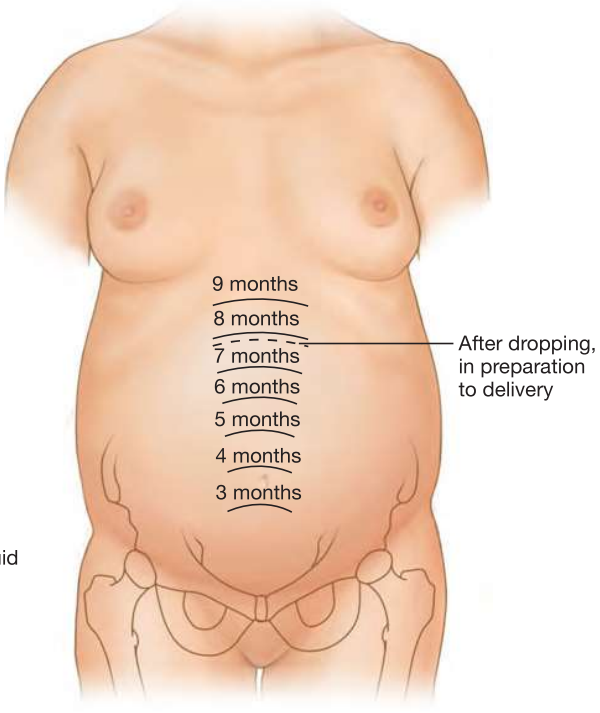


b Head of a six-month-old fetus, revealed through ultrasound

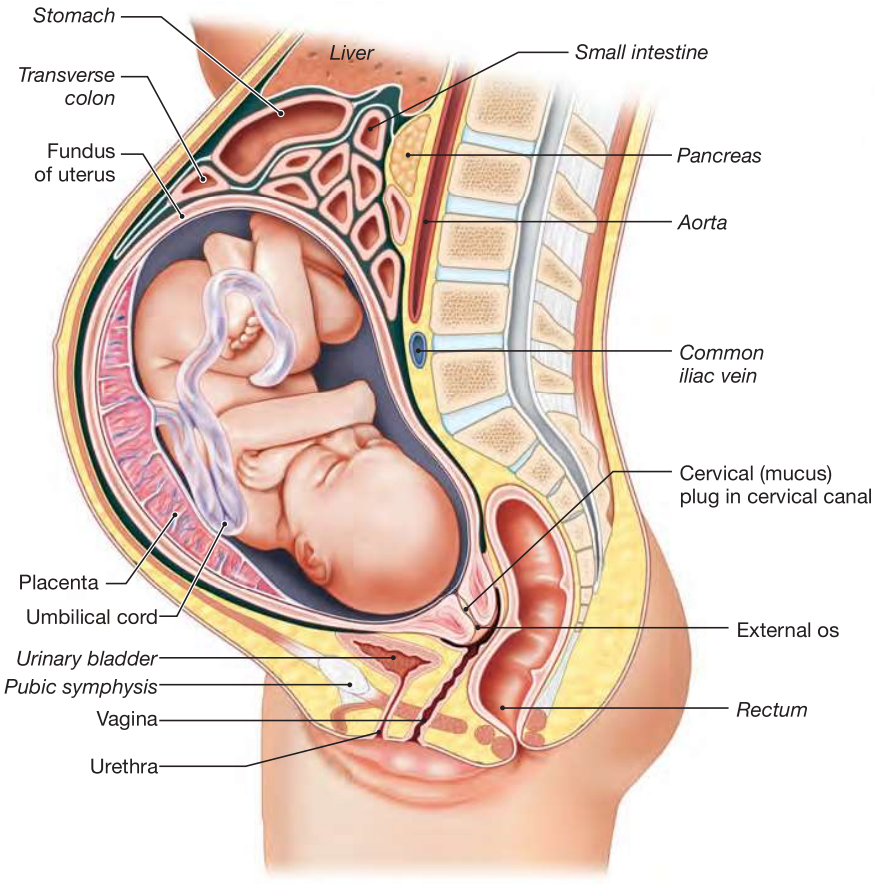
Figure 29–9 Growth of the Uterus and Fetus.



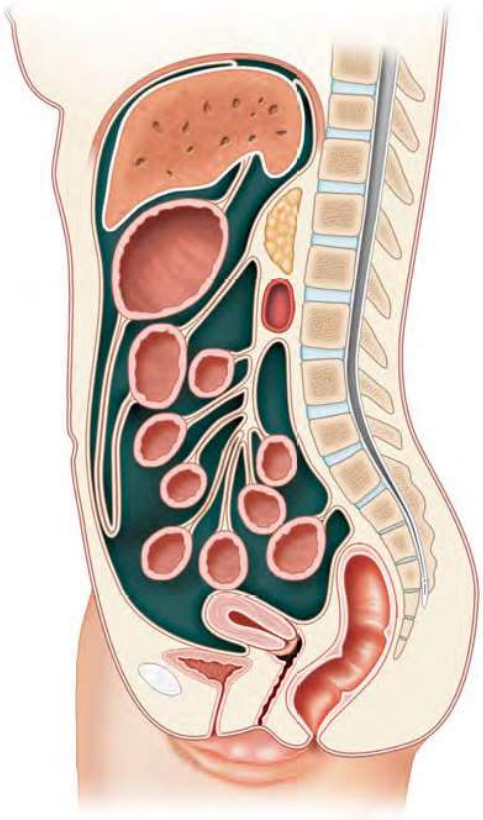
a Pregnancy at 16 weeks, showing the positions of the uterus, fetus, and placenta.



b Pregnancy at three months to nine months (full term), showing the superior-most position of the uterus within the abdomen.



c Pregnancy at full term. Note the positions of the uterus and full-term fetus within the abdomen, and the displacement of abdominal organs.



d A sectional view through the abdominopelvic cavity of a woman who is not pregnant.

Clinical Note

Abortion **Abortion** is the termination of a pregnancy. Most references distinguish among spontaneous, therapeutic, and induced abortions. Most **spontaneous abortions,** or *miscarriages*, result from developmental problems (such as chromosomal defects in the embryo) or from hormonal problems, including abnormally low LH production by the maternal pituitary gland, reduced LH sensitivity at the corpus luteum, insufficient progesterone sensitivity in the endometrium, or insufficient placental production of hCG. Spontaneous abortions occur in at least 15 percent of recognized pregnancies. **Therapeutic abortions** are performed when continued pregnancy poses a threat to the life of the mother.

Induced abortions, or *elective abortions*, are performed at the woman's request. Induced abortions remain the focus of considerable controversy. Most induced abortions involve unmarried or adolescent women. The ratio of abortions to deliveries for married women is 1:10, whereas it is nearly 2:1 for unmarried women and adolescents. In most states, induced abortions are legal during the first three months after conception; under certain conditions, induced abortions may be permitted until the fifth or sixth month. Abortion statistics are difficult to obtain, and in the United States, only two sources provide reliable data: the federally funded CDC and the privately funded Alan Guttmacher Institute. However, California, Louisiana, and New Hampshire do not have to report abortion data to the federal government, so the CDC statistics are incomplete.

the demands placed on the mother become significant as the fetus grows. For the mother to survive under these conditions, maternal systems must compensate for changes introduced by the fetus. In practical terms, the mother must breathe, eat, and excrete for two. The major changes that occur in maternal systems include the following:

- *Maternal respiratory rate goes up and tidal volume increases.* As a result, the mother's lungs deliver the extra oxygen required, and remove the excess carbon dioxide generated by the fetus.
- *Maternal blood volume increases.* This increase occurs because blood flowing into the placenta reduces the volume in the rest of the systemic circuit, and because fetal metabolic activity both lowers blood P_{O_2} and elevates P_{CO_2}. The latter combination stimulates the production of renin and erythropoietin, leading to an increase in maternal blood volume through mechanisms detailed in Chapter 21 (see **Figure 21–18,** p. 735). By the end of gestation, maternal blood volume has increased by almost 50 percent.
- *Maternal requirements for nutrients climb 10–30 percent.* Pregnant women tend to have increased appetites because they must nourish both themselves and their fetus.
- *Maternal glomerular filtration rate increases by roughly 50 percent.* This increase, which corresponds to the increase in blood volume, accelerates the excretion of metabolic wastes generated by the fetus. Because the volume of urine produced increases and the weight of the uterus presses down on the urinary bladder, pregnant women need to urinate frequently.
- *The uterus undergoes a tremendous increase in size.* Structural and functional changes in the expanding uterus are so important that we will discuss them in a separate section.
- *The mammary glands increase in size, and secretory activity begins.* Mammary gland development requires a combination of hormones, including human placental lactogen and placental prolactin from the placenta, and prolactin (PRL), estrogens, progesterone, GH, and thyroxine from maternal endocrine organs. By the end of the sixth month of pregnancy, the mammary glands are fully developed and begin to produce clear secretions that are stored in the duct system and may be expressed from the nipple.

Structural and Functional Changes in the Uterus

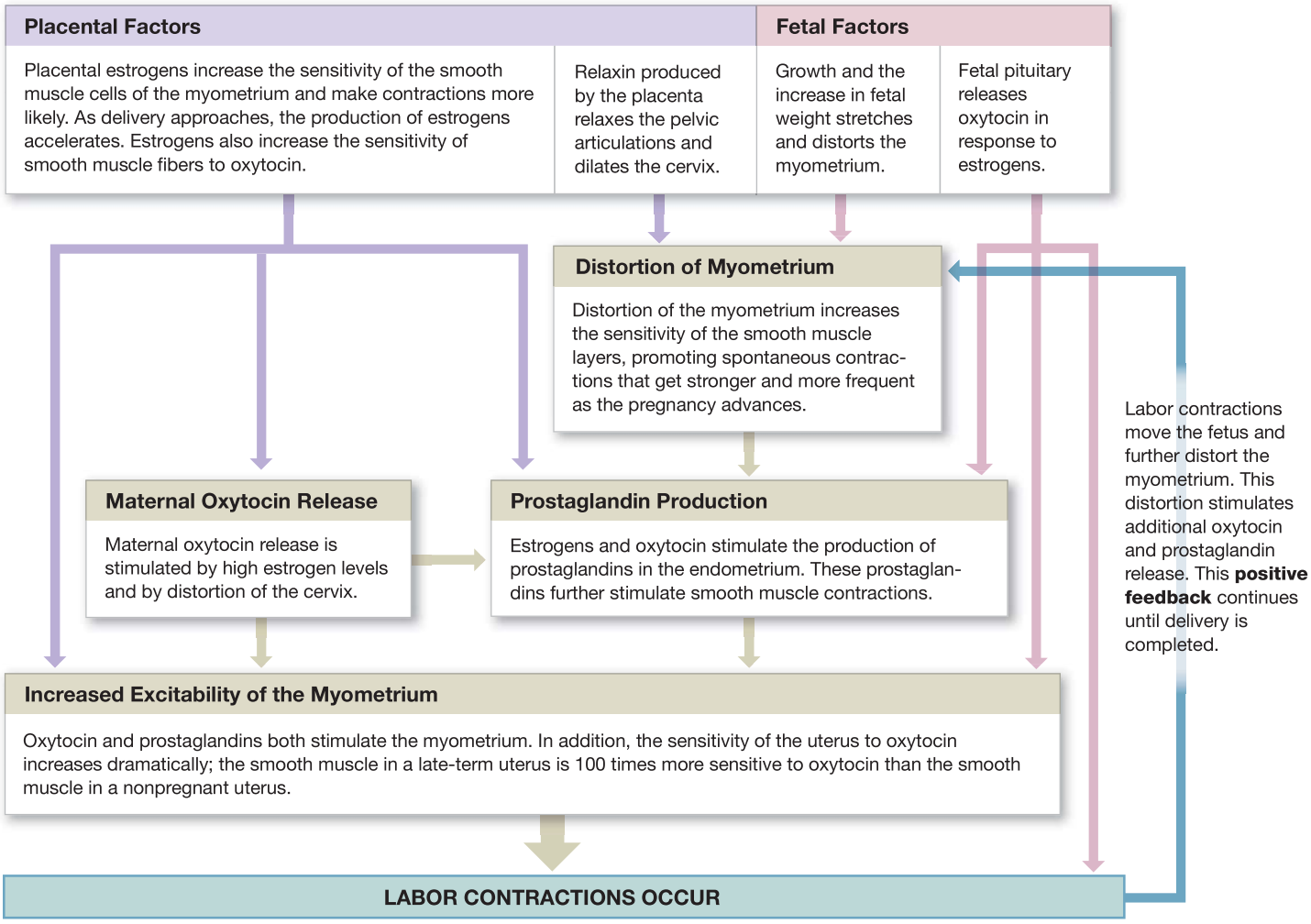
At the end of gestation, a typical uterus has grown from 7.5 cm (3 in.) in length and 30–40 g (1–1.4 oz) in weight to 30 cm (12 in.) in length and 1100 g (2.4 lb) in weight. The uterus may then contain 2 liters of fluid, plus fetus and placenta, for a total weight of roughly 6–7 kg (13–15.4 lb). This remarkable expansion occurs through the enlargement (hypertrophy) of existing cells, especially smooth muscle fibers, rather than by an increase in the total number of cells.

The tremendous stretching of the uterus is associated with a gradual increase in the rate of spontaneous smooth muscle contractions in the myometrium. In the early stages of pregnancy, the contractions are weak, painless, and brief. Evidence indicates that progesterone released by the placenta has an inhibitory effect on uterine smooth muscle, preventing more extensive and more powerful contractions. Placental and fetal factors are involved in the initiation of labor and delivery (**Figure 29–10**).

Late in pregnancy, some women experience occasional spasms in the uterine musculature, but these contractions are neither regular nor persistent. Such contractions are called **false labor. True labor** begins when biochemical and mechanical factors reach a point of no return. After nine months of gestation, multiple factors interact to initiate true labor. Once **labor contractions** have begun in the myometrium, positive feedback ensures that they will continue until delivery has been completed.

When labor begins, the fetal pituitary gland secretes oxytocin, which is then released into the maternal bloodstream at the placenta. This may be the actual trigger for the onset of true labor, as it increases myometrial contractions and prostaglandin production, on top of the priming effects of estrogens and maternal oxytocin.

Figure 29–10 Factors Involved in the Initiation of Labor and Delivery.



Checkpoint

12. Why do pregnant women experience breathing difficulty?
13. Identify three major factors opposing the calming action of progesterone on the uterus.
14. Why does a mother's blood volume increase during pregnancy?

See the blue Answers tab at the back of the book.

29-6 Labor consists of the dilation, expulsion, and placental stages

The goal of labor is **parturition** (par-toor-ISH-un), the forcible expulsion of the fetus. During true labor, each contraction begins near the top of the uterus and sweeps in a wave toward the cervix. The contractions are strong and occur at regular intervals. As parturition approaches, the contractions increase in force and frequency, changing the position of the fetus and moving it toward the cervical canal.

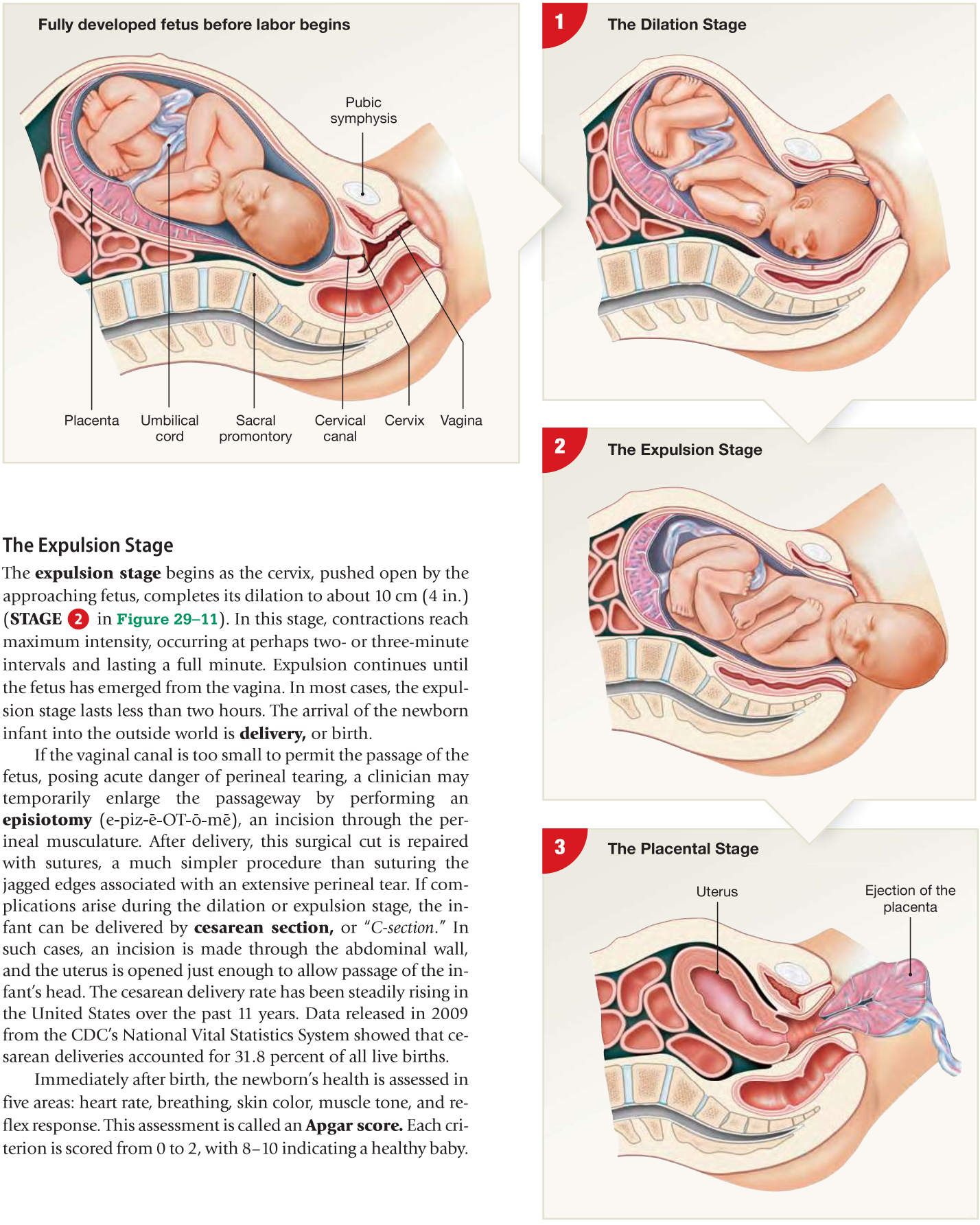
Stages of Labor

Labor has traditionally been divided into three stages: the *dilation stage*, the *expulsion stage*, and the *placental stage* (**Figure 29–11**).

The Dilation Stage

The **dilation stage** begins with the onset of true labor, as the cervix dilates and the fetus begins to shift toward the cervical canal (**STAGE 1** in **Figure 29–11**), moved by gravity and uterine contractions. This stage is highly variable in length but typically lasts eight or more hours. At the start of the dilation stage, labor contractions last up to half a minute and occur once every 10–30 minutes; their frequency increases steadily. Late in this stage, the amniochorionic membrane ruptures, an event sometimes referred to as "having one's water break." If this event occurs before other events of the dilation stage, the life of the fetus may be at risk from infection. If the risk is sufficiently great, labor can be induced.

Figure 29–11 The Stages of Labor.



The Expulsion Stage

The **expulsion stage** begins as the cervix, pushed open by the approaching fetus, completes its dilation to about 10 cm (4 in.) (**STAGE** 2 in **Figure 29–11**). In this stage, contractions reach maximum intensity, occurring at perhaps two- or three-minute intervals and lasting a full minute. Expulsion continues until the fetus has emerged from the vagina. In most cases, the expulsion stage lasts less than two hours. The arrival of the newborn infant into the outside world is **delivery,** or birth.

If the vaginal canal is too small to permit the passage of the fetus, posing acute danger of perineal tearing, a clinician may temporarily enlarge the passageway by performing an **episiotomy** (e-piz-ē-OT-ō-mē), an incision through the perineal musculature. After delivery, this surgical cut is repaired with sutures, a much simpler procedure than suturing the jagged edges associated with an extensive perineal tear. If complications arise during the dilation or expulsion stage, the infant can be delivered by **cesarean section,** or "*C-section*." In such cases, an incision is made through the abdominal wall, and the uterus is opened just enough to allow passage of the infant's head. The cesarean delivery rate has been steadily rising in the United States over the past 11 years. Data released in 2009 from the CDC's National Vital Statistics System showed that cesarean deliveries accounted for 31.8 percent of all live births.

Immediately after birth, the newborn's health is assessed in five areas: heart rate, breathing, skin color, muscle tone, and reflex response. This assessment is called an **Apgar score.** Each criterion is scored from 0 to 2, with 8–10 indicating a healthy baby.

The Placental Stage

During the **placental stage** of labor, muscle tension builds in the walls of the partially empty uterus, which gradually decreases in size (**STAGE** 3 in Figure 29–11). This uterine contraction tears the connections between the endometrium and the placenta. In general, within an hour of delivery, the placental stage ends with the ejection of the placenta, or *afterbirth*. The disruption of the placenta is accompanied by a loss of blood, but associated uterine contraction compresses the uterine vessels and usually restricts this flow. Because maternal blood volume has increased greatly during pregnancy, the blood loss that does occur can normally be tolerated without difficulty.

Premature Labor

Premature labor occurs when true labor begins before the fetus has completed normal development. The newborn's chances of surviving are directly related to its body weight at delivery. Even with massive supportive efforts, newborns weighing less than 400 g (14 oz) at birth will not survive, primarily because their respiratory, cardiovascular, and urinary systems are unable to support life without aid from maternal systems. As a result, the dividing line between spontaneous abortion and **immature delivery** is usually set at 500 g (17.6 oz), the normal weight near the end of the second trimester.

Most fetuses born at 25–27 weeks of gestation (a birth weight under 600 g or 21.1 oz) die despite intensive neonatal care; moreover, survivors have a high risk of developmental abnormalities. **Premature delivery** usually refers to birth at 28–36 weeks (a birth weight over 1 kg or 2.2 lb). With care, these newborns have a good chance of surviving and developing normally.

Difficult Deliveries

By the end of gestation in most pregnancies, the fetus has rotated within the uterus to transit the birth canal headfirst, facing the mother's sacrum. In about 6 percent of deliveries, the fetus faces the mother's pubis instead. These babies can be delivered normally, given enough time, but risks to infant and mother are reduced by a *forceps delivery*. Forceps resemble large, curved salad tongs that can be separated for insertion into the vaginal canal, one side at a time. Once in place, they are reunited and used to grasp the head of the fetus. An intermittent pull is applied, so that the forces on the head resemble those of normal delivery.

In 3–4 percent of deliveries, the legs or buttocks of the fetus enter the vaginal canal first. Such deliveries are **breech births.** Risks to the fetus are higher in breech births than in normal deliveries, because the umbilical cord can become constricted, cutting off placental blood flow.

The head is normally the widest part of the fetus; the mother's cervix may dilate enough to pass the baby's legs and body, but not the head. This entrapment compresses the umbilical cord, prolongs delivery, and subjects the fetus to severe distress and potential injury. If attempts to reposition the fetus or promote further dilation are unsuccessful over the short term, delivery by cesarean section may be required.

Multiple Births

Multiple births (twins, triplets, quadruplets, and so forth) can occur for several reasons. The ratio of twin births to single births in the U.S. population is roughly 1:89. "Fraternal," or **dizygotic** (dī-zī-GOT-ik), twins develop when two separate oocytes were ovulated and subsequently fertilized. Because chromosomes are shuffled during meiosis, the odds against any two zygotes from the same parents having identical genes exceed 1 in 8.4 million. Seventy percent of twins are dizygotic.

"Identical," or **monozygotic,** twins result either from the separation of blastomeres early in cleavage or from the splitting of the inner cell mass before gastrulation. In either event, the genetic makeup of the twins is identical because both formed from the same pair of gametes. Triplets, quadruplets, and larger multiples can result from multiple ovulations, blastomere splitting, or some combination of the two. For unknown reasons, the rates of naturally occurring multiple births fall into a pattern: Twins occur in 1 of every 89 births, triplets in 1 of every 89^2 (or 7921) births, quadruplets in 1 of every 89^3 (704,969) births, and so forth. The incidence of multiple births can be increased by exposure to fertility drugs that stimulate the maturation of abnormally large numbers of follicles.

Pregnancies with multiple fetuses pose special problems because the strains on the mother are multiplied. The chances of premature labor are increased, and the risks to the mother are higher than for single births. Increased risks also extend to the fetuses during gestation, and to the newborns, because even at full term such newborns have lower-than-average birth weights. They are also more likely to have problems during delivery. For example, in more than half of twin deliveries, one or both fetuses enter the vaginal canal in an abnormal position.

If the splitting of the blastomeres or of the embryonic disc is not complete, **conjoined** *(Siamese)* **twins** may develop. These genetically identical twins typically share some skin, a portion of the liver, and perhaps other internal organs as well. When the fusion is minor, the infants can be surgically separated with some success. Most conjoined twins with more extensive fusions fail to survive delivery.

Checkpoint

15. **Name the three stages of labor.**
16. **Differentiate between immature delivery and premature delivery.**
17. **Supply the biological terms for fraternal twins and identical twins.**

See the blue Answers tab at the back of the book.

29-7 Postnatal stages are the neonatal period, infancy, childhood, adolescence, maturity, and senescence

Developmental processes do not cease at delivery, because newborns have few of the anatomical, functional, or physiological characteristics of mature adults. The course of postnatal development typically includes five **life stages:** (1) the *neonatal period*, (2) *infancy*, (3) *childhood*, (4) *adolescence*, and (5) *maturity*. Each stage is typified by a distinctive combination of characteristics and abilities. These stages are familiar parts of human experience. Although each stage has distinctive features, the transitions between them are gradual, and the boundaries indistinct. At maturity, development ends and the process of aging, or *senescence*, begins.

The Neonatal Period, Infancy, and Childhood

The **neonatal period** extends from birth to one month thereafter. **Infancy** then continues to two years of age, and **childhood** lasts until **adolescence,** the period of sexual and physical maturation. Two major events are under way during these developmental stages:

1. The organ systems (except those associated with reproduction) become fully operational and gradually acquire the functional characteristics of adult structures.
2. The individual grows rapidly, and body proportions change significantly.

Pediatrics is the medical specialty that focuses on postnatal development from infancy through adolescence. Infants and young children cannot clearly describe the problems they are experiencing, so pediatricians and parents must be skilled observers. Standardized tests are used to assess developmental progress relative to average values.

The Neonatal Period

Physiological and anatomical changes occur as the fetus completes the transition to the status of newborn, or **neonate.** Before delivery, dissolved gases, nutrients, wastes, hormones, and antibodies were transferred across the placenta. At birth, the neonate must become relatively self-sufficient, performing respiration, digestion, and excretion using its own specialized organs and organ systems. The transition from fetus to neonate can be summarized as follows:

- At birth, the lungs are collapsed and filled with fluid. Filling them with air requires a massive and powerful inhalation. ↩ p. 854
- When the lungs expand, the pattern of cardiovascular circulation changes due to alterations in blood pressure and flow rates. The ductus arteriosus closes, isolating the pulmonary and systemic trunks. Closure of the foramen ovale separates the atria of the heart, completing the separation of the pulmonary and systemic circuits. ↩ p. 755
- The typical neonatal heart rate (120–140 beats per minute) and respiratory rate (30 breaths per minute) are considerably higher than in adults. In addition, the metabolic rate per unit of body weight in neonates is roughly twice that of adults.
- Before birth, the digestive system remains relatively inactive, although it does accumulate a mixture of bile secretions, mucus, and epithelial cells. This collection of debris, called *meconium*, is excreted during the first few days of life. Over that period, the newborn begins to nurse.
- As waste products build up in the arterial blood, the kidneys excrete them. Glomerular filtration is normal, but the neonate cannot concentrate urine to any significant degree. As a result, urinary water losses are high, and neonatal fluid requirements are proportionally much greater than those of adults.
- The neonate has little ability to control its body temperature, particularly in the first few days after delivery. As the infant grows larger and its insulating subcutaneous adipose "blanket" gets thicker, its metabolic rate also rises. Daily and even hourly shifts in body temperature continue throughout childhood. ↩ p. 947

Over the entire neonatal period, the newborn is dependent on nutrients contained in milk, typically breast milk secreted by the maternal mammary glands.

Lactation and the Mammary Glands. By the end of the sixth month of pregnancy, the mammary glands are fully developed, and the gland cells begin to produce a secretion known as **colostrum** (kō-LOS-trum). Ingested by the infant during the first two or three days of life, colostrum contains more proteins and far less fat than breast milk. Many of the proteins are antibodies that may help the infant ward off infections until its own immune system becomes fully functional. In addition, the mucins present in both colostrum and milk can inhibit the replication of a family of viruses *(rotaviruses)* that can cause dangerous forms of gastroenteritis and diarrhea in infants.

As colostrum production drops, the mammary glands convert to milk production. Breast milk consists of water, proteins, amino acids, lipids, sugars, and salts. It also contains large quantities of *lysozyme*—an enzyme with antibiotic properties. In terms of energy, human milk provides about 750 kilocalories per liter. The secretory rate varies with the demand, but a 5–6-kg (11–13-lb) infant usually requires about 850 mL (3.6 cups) of milk per day. (The production of milk throughout this period is maintained through the combined actions of several hormones, as detailed in Chapter 18. ↩ p. 607)

Milk becomes available to infants through the **milk let-down reflex** (Figure 29–12). The milk let-down reflex continues to function until *weaning*, withdrawing mother's milk, typically one to two years after birth. Milk production ceases soon after, and the mammary glands gradually return to a resting state. Earlier weaning is a common practice in the United States, where women take advantage of commercially prepared milk- or soy-based infant formulas that closely approximate the composition of natural breast milk. The major difference between such substitutes and natural milk is that the substitutes lack antibodies and lysozyme, which play important roles in maintaining the health of the infant. Consequently, early weaning is associated with an increased risk of infections and allergies in the infant.

Infancy and Childhood

The most rapid growth occurs during prenatal development, and the growth rate declines after delivery. Growth during infancy and childhood occurs under the direction of circulating hormones, notably growth hormone, adrenal steroids, and thyroid hormones. These hormones affect each tissue and organ in specific ways, depending on the sensitivities of the individual cells. As a result, growth does not occur uniformly, so body proportions gradually change. The head, for example, is relatively large at birth but decreases in proportion with the rest of the body as the child grows to adulthood (Figure 29–13).

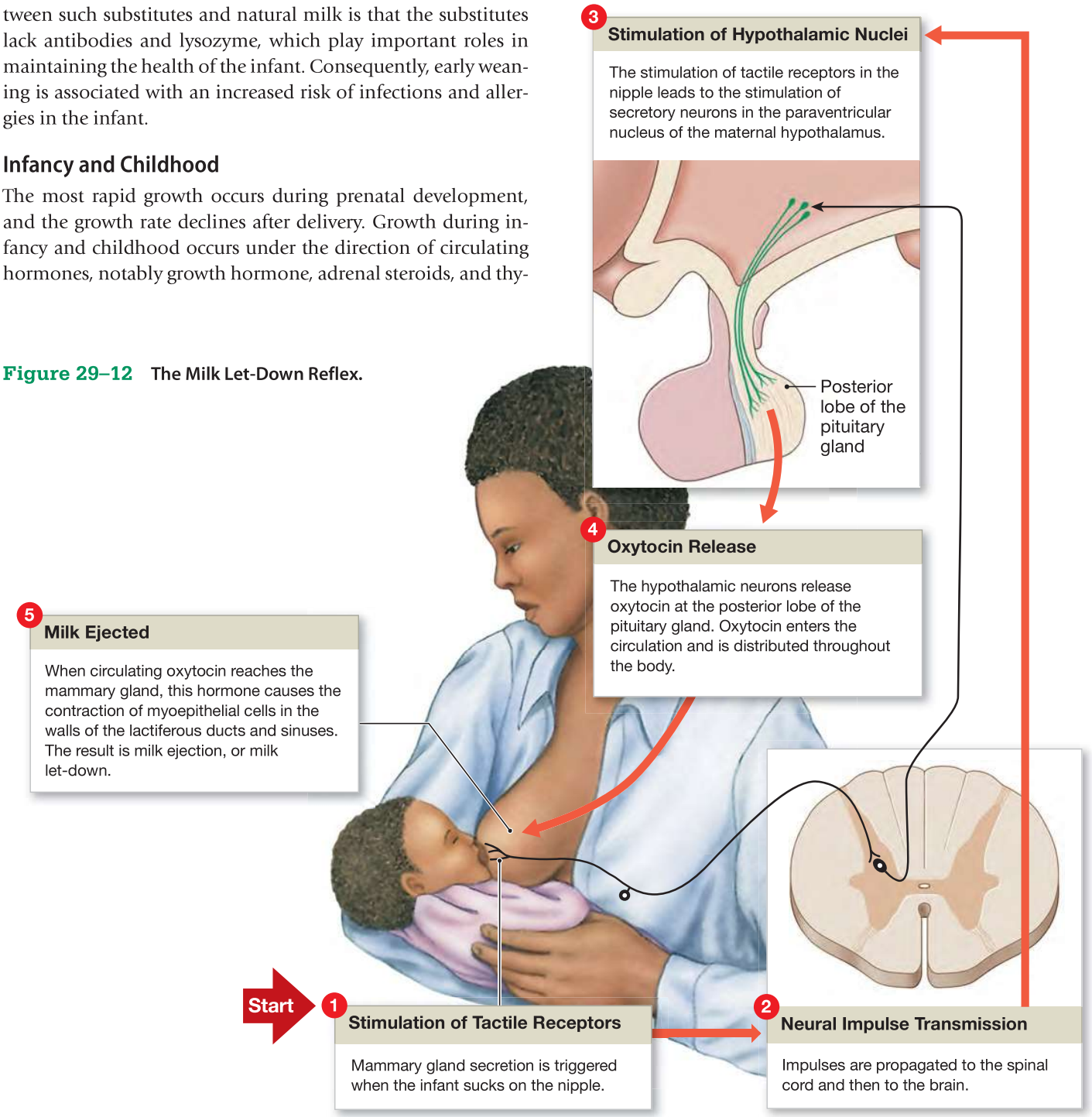
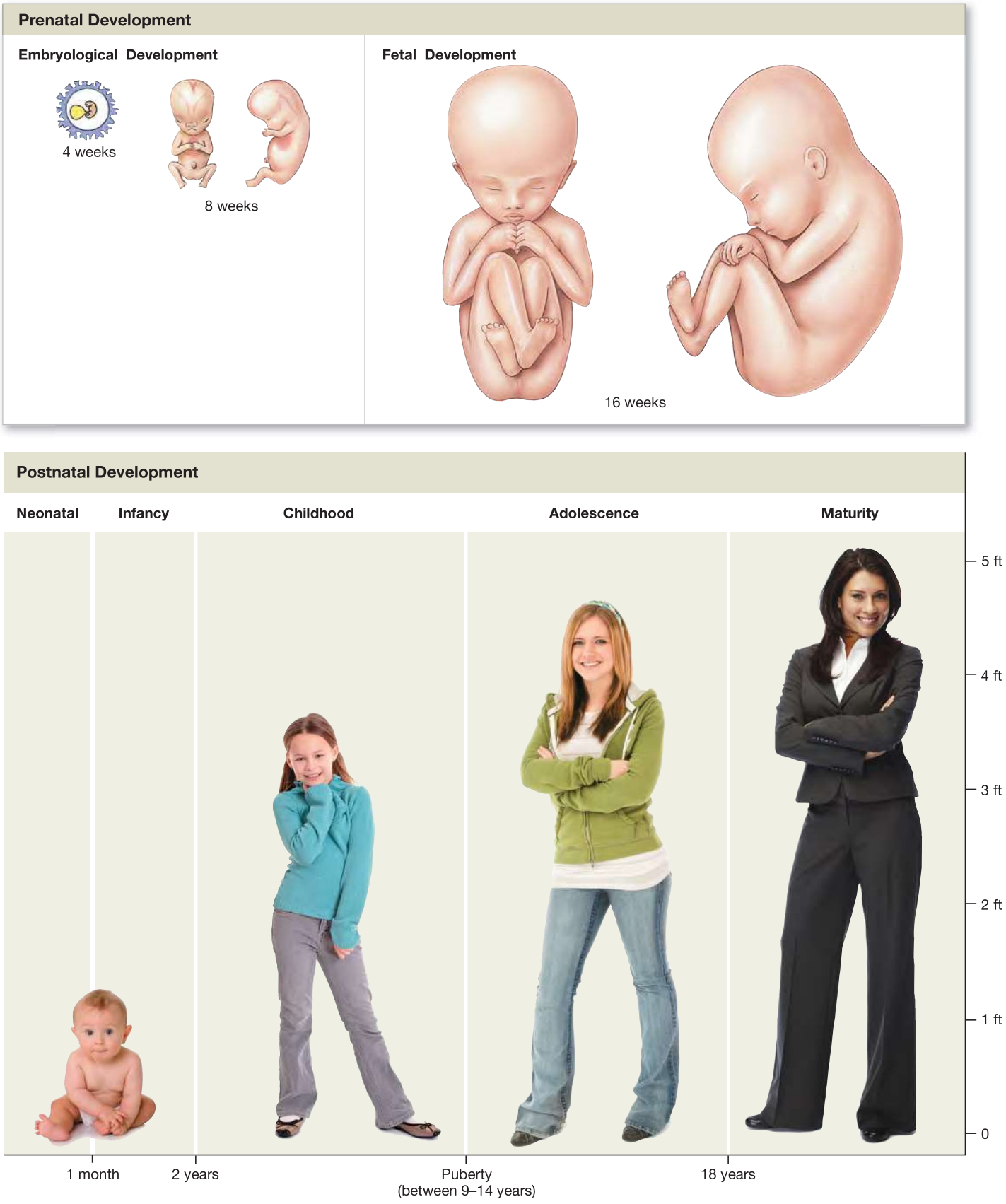


Figure 29–12 The Milk Let-Down Reflex.

Figure 29–13 Growth and Changes in Body Form and Proportion. The views at 4, 8, and 16 weeks of gestation are presented at actual size. Notice the changes in body form and proportions as development proceeds. For example, the head, which contains the brain and sense organs, is proportionately large at birth.



Adolescence and Maturity

Adolescence begins at **puberty,** the period of sexual maturation, and ends when growth is completed. Three major hormonal events interact at the onset of puberty:

1. The hypothalamus increases its production of gonadotropin-releasing hormone (GnRH). Evidence indicates that this increase is dependent on adequate levels of *leptin*, a hormone released by adipose tissues. ↩ p. 628
2. Endocrine cells in the anterior lobe of the pituitary gland become more sensitive to the presence of GnRH, and circulating levels of FSH and LH rise rapidly.
3. Ovarian or testicular cells become more sensitive to FSH and LH, initiating (1) gamete production, (2) the secretion of sex hormones that stimulate the appearance of secondary sex characteristics and behaviors, and (3) a sudden acceleration in the growth rate, culminating in closure of the epiphyseal cartilages.

The age at which puberty begins varies. In the United States today, puberty generally starts at about age 12 in boys and 11 in girls, but the normal ranges are broad (10–15 in boys, 9–14 in girls). Many body systems alter their activities in response to circulating sex hormones and to the presence of growth hormone, thyroid hormones, prolactin, and adrenocortical hormones, so sex-specific differences in structure and function develop. At puberty, endocrine system changes induce characteristic changes in various body systems:

- *Integumentary System.* Testosterone stimulates the development of terminal hairs on the face and chest, whereas under estrogen stimulation those follicles continue to produce fine hairs. The hairline recedes under testosterone stimulation. Both testosterone and estrogen stimulate terminal hair growth in the axillae and in the genital area. Androgens, which are present in both sexes, also stimulate sebaceous gland secretion and may cause acne. Adipose tissues respond differently to testosterone than to estrogens, and this difference produces changes in the distribution of subcutaneous body fat. In women, the combination of estrogens, prolactin, growth hormone, and thyroid hormones promotes the initial development of the mammary glands. Although the duct system becomes more elaborate, true secretory alveoli do not develop, and much of the growth of the breasts during this period reflects increased deposition of fat rather than glandular tissue.
- *Skeletal System.* Both testosterone and estrogen accelerate bone deposition and skeletal growth. In the process, they promote closure of the epiphyseal cartilages and thus place a limit on growth in height. Girls generally do not grow as tall as boys because estrogens cause more rapid epiphyseal cartilage closure than does testosterone, and the period of skeletal growth is briefer in girls than in boys. Girls grow most rapidly between ages 10 and 13, whereas boys grow most rapidly between ages 12 and 15.
- *Muscular System.* Sex hormones stimulate the growth of skeletal muscle fibers, increasing strength and endurance. The effects of testosterone greatly exceed those of the estrogens, and the increased muscle mass accounts for significant sex differences in body mass, even for males and females of the same height. The stimulatory effects of testosterone on muscle mass has led to the use of anabolic steroids among competitive athletes of both sexes.
- *Nervous System.* Sex hormones affect central nervous system centers concerned with sexual drive and sexual behaviors. These centers differentiated in sex-specific ways during the second and third trimesters, when the fetal gonads secrete either testosterone (in males) or estrogens (in females). The surge in sex hormone secretion at puberty activates the CNS centers.
- *Cardiovascular System.* Testosterone stimulates erythropoiesis, thereby increasing blood volume and the hematocrit. In females whose uterine cycles have begun, the iron loss associated with menses increases the risk of developing iron-deficiency anemia. Late in each uterine cycle, estrogens and progesterone promote the movement of water from plasma into interstitial fluid, leading to an increase in tissue water content. Estrogens decrease plasma cholesterol levels and slow the formation of plaque. As a result, premenopausal women have a lower risk of atherosclerosis than do adult men.
- *Respiratory System.* Testosterone stimulates disproportionate growth of the larynx and a thickening and lengthening of the vocal cords. These changes cause a gradual deepening of the voice of males compared with those of females.
- *Reproductive System.* In males, testosterone stimulates the functional development of the accessory reproductive glands, such as the prostate gland and seminal glands, and helps promote spermatogenesis. In females, estrogens target the uterus, promoting a thickening of the myometrium, increasing blood flow to the endometrium, and stimulating cervical mucus production. Estrogens also promote the functional development of accessory reproductive organs in females. The first few uterine cycles may or may not be accompanied by ovulation. After the initial stage, the woman will be fertile, even though growth and physical maturation will continue for several years.

After puberty, the continued background secretion of estrogens or androgens maintains the foregoing sex-specific differences. In both sexes, growth continues at a slower pace until age 18–21, by which time most of the epiphyseal cartilages have closed. The boundary between adolescence and maturity is

hazy, because it has physical, emotional, and behavioral components. Adolescence is often said to be over when growth stops, in the late teens or early twenties. The individual is then considered physically mature.

Senescence

Although physical growth may stop at maturity, physiological changes continue. The sex-specific differences produced at puberty are retained, but further changes occur when sex hormone levels decline at menopause or the male climacteric. p. 1069 All these changes are part of the process of **senescence** (*senesco*, to grow old), or aging, which reduces the functional capabilities of the individual. Even in the absence of such factors as disease or injury, senescence-related changes at the molecular level ultimately lead to death.

Table 29–3 summarizes the age-related changes in physiological systems discussed in earlier chapters. Taken together, these changes both reduce the functional abilities of the individual and affect homeostatic mechanisms. As a result, the elderly are less able to make homeostatic adjustments in response to internal or environmental stresses. The risks of contracting a variety of infectious diseases are proportionately increased as immune function deteriorates. This deterioration leads to drastic physiological changes that affect all internal systems. Death ultimately occurs when some combination of stresses cannot be countered by the body's existing homeostatic mechanisms.

Table 29–3 Effects of Aging on Organ Systems

The characteristic physical and functional changes that are part of the aging process affect all organ systems. Examples discussed in previous chapters include the following:

- A loss of elasticity in the skin that produces sagging and wrinkling. p. 164
- A decline in the rate of bone deposition, leading to weak bones, and degenerative changes in joints that make them less mobile. pp. 192, 273
- Reductions in muscular strength and ability. p. 368
- Impairment of coordination, memory, and intellectual function. pp. 541–542
- Reductions in the production of, and sensitivity to, circulating hormones. p. 630
- Appearance of cardiovascular problems and a reduction in peripheral blood flow that can affect a variety of vital organs. p. 758
- Reduced sensitivity and responsiveness of the immune system, leading to infection, cancer, or both. p. 806
- Reduced elasticity in the lungs, leading to decreased respiratory function. p. 855
- Decreased peristalsis and muscle tone along the digestive tract. p. 909
- Decreased peristalsis and muscle tone in the urinary system, coupled with a reduction in the glomerular filtration rate. p. 990
- Functional impairment of the reproductive system, which eventually becomes inactive when menopause or the male climacteric occurs. p. 1069

Physicians attempt to forestall death by adjusting homeostatic mechanisms or removing the sources of stress. **Geriatrics** (*geras*, old age) is the medical specialty that deals with the problems associated with aging. Physicians trained in geriatrics are known as **geriatricians.** Problems commonly encountered by geriatricians include infections, cancers, heart disease, strokes, arthritis, senile dementia, and anemia—conditions directly related to age-induced changes in vital systems.

Checkpoint

18. **Name the postnatal stages of development.**
19. **Describe the time frame for each of the following stages: neonatal period, infancy, and adolescence.**
20. **What is the difference between colostrum and breast milk?**
21. **Increases in the blood levels of GnRH, FSH, LH, and sex hormones mark the onset of which stage of development?**

See the blue Answers tab at the back of the book.

29-8 Genes and chromosomes determine patterns of inheritance

Chromosomes contain DNA and proteins, and genes are functional segments of DNA. Each gene carries the information needed to direct the synthesis of a specific polypeptide. Chromosome structure and the functions of genes were introduced in Chapter 3. pp. 80–85 Every nucleated somatic cell in your body carries copies of the original 46 chromosomes present when you were a zygote. Those chromosomes and their component genes constitute your **genotype** (JĒN-ō-tīp; *geno-*, gene).

Through development and differentiation, the instructions contained in the genotype are expressed in many ways. No single cell or tissue uses all the information and instructions contained in the genotype. For example, in muscle fibers, the genes involved in the formation of excitable membranes and contractile proteins are active, whereas in cells of the pancreatic islets, a different set of genes operates. Collectively, however, the instructions contained in your genotype determine the anatomical and physiological characteristics that make you a unique individual. Those anatomical and physiological characteristics constitute your **phenotype** (FĒ-nō-tīp; *phaino*, to display). In architectural terms, the genotype is a set of plans, and the phenotype is the finished building. Specific elements in your phenotype, such as hair and eye color, skin tone, and foot size, are called phenotypic *traits*, or *characters*.

Your genotype is derived from the genotypes of your parents. Yet you are not an exact copy of either parent; nor are you an easily identifiable mixture of their characteristics. Our discussion of genetics begins with the basic patterns of inheritance and their implications. We then examine the mechanisms re-

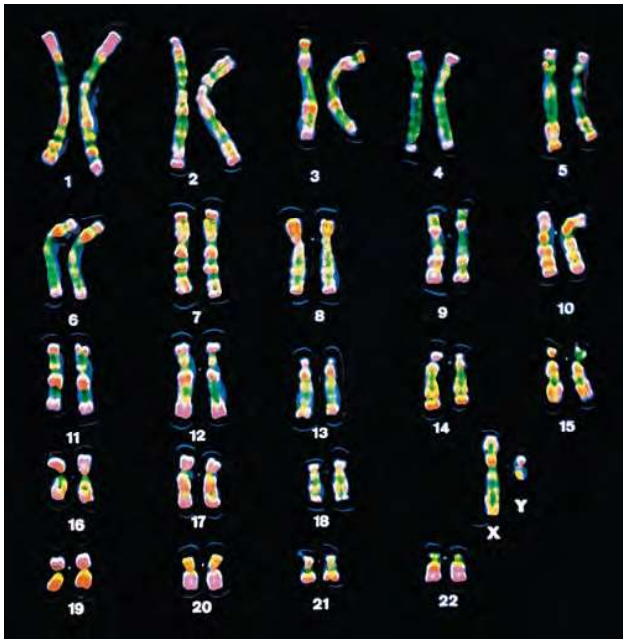
sponsible for regulating the activities of the genotype during prenatal development.

Patterns of Inheritance

The 46 chromosomes carried by each somatic cell in human beings occur in pairs: Every somatic cell contains 23 pairs of chromosomes. At amphimixis, the spermatozoon supplies one member of each pair, and the ovum supplies the other. The two members of each pair are known as **homologous** (huh-MOL-ō-gus) **chromosomes.** Twenty-two of those pairs are called **autosomal** (aw-tō-SŌ-mul) **chromosomes.** Most of the genes of the autosomal chromosomes affect somatic characteristics, such as hair color and skin pigmentation. The chromosomes of the 23rd pair are called the **sex chromosomes;** one of their functions is to determine whether the individual is genetically male or female. **Figure 29–14** shows the **karyotype** (*karyon*, nucleus + *typos*, mark), or entire set of chromosomes, of a normal male. The discussion that follows concerns the inheritance of traits carried on the autosomal chromosomes. We will examine the patterns of inheritance via the sex chromosomes in a later section.

The two chromosomes in a homologous autosomal pair have the same structure and carry genes that affect the same traits. Suppose that one member of the pair contains three genes in a row, with the first gene determining hair color, the second eye color, and the third skin pigmentation. The other chromosome (or *homolog*) carries genes that affect the same traits, and the genes are in the same sequence. The genes are also located at equivalent positions on their respective chromosomes. A gene's position on a chromosome is called a **locus** (LŌ-kus; plural, *loci*).

Figure 29–14 **A Human Karyotype.** The 23 pairs of somatic cell chromosomes from a normal male.



The two chromosomes in a pair may not carry the same *form* of each gene, however. The various forms of a given gene are called **alleles** (uh-LĒLZ). These *alternate forms* determine the precise effect of the gene on your phenotype. If the two chromosomes of a homologous pair carry the same allele of a particular gene, you are **homozygous** (hō-mō-ZĪ-gus; *homos*, the same) for the trait affected by that gene. That allele will then indeed be expressed in your phenotype. For example, if you receive a gene for curly hair from your father and a gene for curly hair from your mother, you will be homozygous for curly hair—and you will have curly hair. About 80 percent of an individual's genome consists of homozygous alleles. In **simple inheritance,** the phenotype is determined by interactions between a single pair of alleles.

Interactions between Alleles

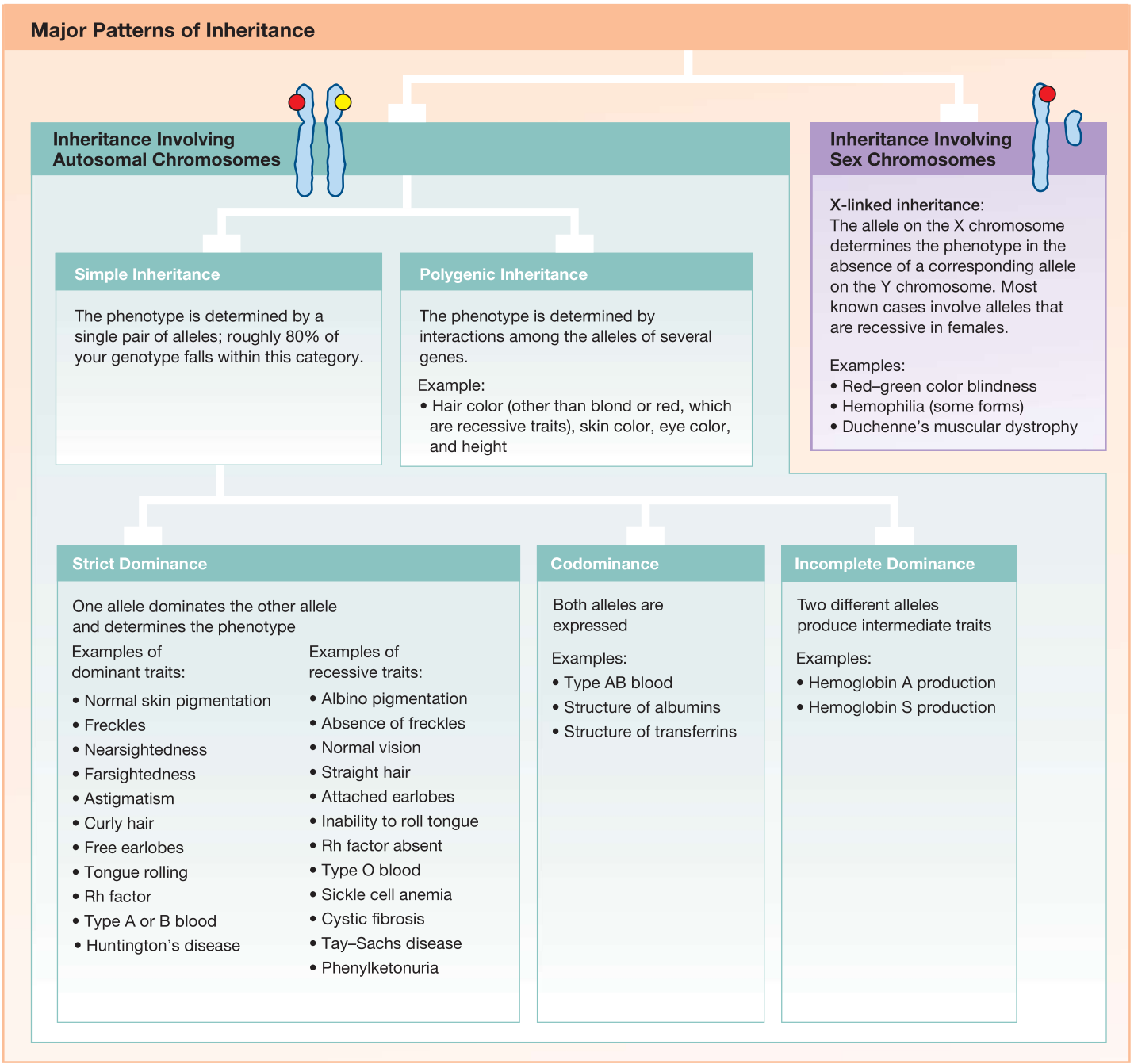
Because the chromosomes of a homologous pair have different origins, one paternal and the other maternal, they do not necessarily carry the same alleles. If you have two different alleles for the same gene, you are **heterozygous** (het-er-ō-ZĪ-gus; *heteros*, other) for the trait determined by that gene. The phenotype that results from a heterozygous genotype depends on the nature of the interaction between the corresponding alleles. The potential interactions are diagrammed in **Figure 29–15**, which includes examples of normal and abnormal phenotypic traits. For example, if you received a gene for curly hair from your father, but a gene for straight hair from your mother, whether *you* will have curly hair, straight hair, or even wavy hair depends on the relationship between the alleles for those traits:

- In **strict dominance,** an allele that is **dominant** will be expressed in the phenotype, *regardless of any conflicting instructions carried by the other allele*. For instance, an individual with only one allele for freckles will have freckles, because that allele is dominant over the "nonfreckle" allele. An allele that is **recessive** will be expressed in the phenotype only if that same allele is present on *both chromosomes* of a homologous pair. For example, in Chapter 5 we learned that albino individuals cannot synthesize the yellow-brown pigment *melanin*. ↩ p. 149 The presence of one allele that directs melanin production will result in normal color. Two recessive alleles must be present to produce an albino individual. A single gene can have many different alleles *in a population*, some dominant and others recessive. An individual can have a maximum of only two alleles—one from the mother and the other one from the father. If both parents have the same alleles, then an individual has only one kind of allele, but two copies of it, and is thus, homozygous.
- In **incomplete dominance,** heterozygous alleles produce a phenotype that is intermediate (not completely dominant) to the phenotypes of individuals who are homozygous for

one allele or the other. A good example is a gene that affects the shape of red blood cells. Individuals with homozygous alleles that carry instructions for normal adult hemoglobin A have red blood cells of normal shape. Individuals with homozygous alleles for hemoglobin S, an abnormal form, have red blood cells that become sickle-shaped in peripheral capillaries when the P_{O_2} decreases. These individuals develop *sickle cell anemia*. ↩ p. 646 Individuals who are heterozygous for this trait do not develop anemia but their red blood cells may sickle when tissue oxygen levels are extremely low.

- In **codominance,** an individual who is heterozygous (has different alleles) for a given trait exhibits both phenotypes for that trait. Blood type in humans is determined by codominance. The alleles for type A and type B blood are dominant over the allele for type O blood, but a person with one type A allele and one type B allele has type AB blood, not A or B. Type AB blood has *both* type A antigens

Figure 29–15 Major Patterns of Inheritance.



and type B antigens. The distinction between incomplete dominance and codominance is not always clear-cut. For example, a person who has alleles for hemoglobin A and hemoglobin S shows incomplete dominance for RBC shape, but codominance for hemoglobin. Each red blood cell contains a mixture of hemoglobin A and hemoglobin S.

Penetrance and Expressivity

Differences in genotype lead to distinct variations in phenotype, but the relationships are not always predictable. The presence of a particular pair of alleles does not affect the phenotype in the same way in every individual. **Penetrance** is the percentage of individuals with a particular genotype that show the "expected" phenotype. The effects of that genotype in other individuals may be overridden by the activity of other genes or by environmental factors. For example, *emphysema*, a respiratory disorder discussed in Chapter 23, has been linked to a specific abnormal genotype. ↩ p. 855 However, about 20 percent of the individuals with this genotype do not develop emphysema, and thus the penetrance of this genotype is approximately 80 percent. The effects of environmental factors are apparent: Most people who develop emphysema are cigarette smokers.

If a given genotype *does* affect the phenotype, it can do so to various degrees, again depending on the activity of other genes or environmental stimuli. For example, even though identical twins have the same genotype, they do not have exactly the same fingerprints. The extent to which a particular allele is expressed when it is present is termed its **expressivity.**

Environmental effects on genetic expression are particularly evident during embryological and fetal development. Drugs, including certain antibiotics, alcohol, and nicotine in cigarette smoke, can disrupt fetal development. Factors that result in abnormal development are called **teratogens** (TER-uh-tō-jenz).

Predicting Inheritance

When an allele can be neatly characterized as dominant or recessive, you can predict the characteristics of individuals on the basis of their parents' alleles.

In such calculations, dominant alleles are traditionally indicated by capitalized abbreviations, and recessive alleles by lowercase abbreviations. For a given trait, the possibilities are indicated by *AA* (homozygous dominant), *Aa* (heterozygous), or *aa* (homozygous recessive). Each gamete involved in fertilization contributes a single allele for a given trait. That allele must be one of the two alleles contained by all cells in the parent's body. Consider, for example, the possible offspring of an albino mother and a father with normal skin pigmentation. Because albinism is a recessive trait, the maternal alleles are abbreviated *aa*. No matter which of her oocytes is fertilized, it will carry the recessive *a* allele. The father has normal pigmentation, a dominant trait. He is therefore either homozygous *or* heterozygous for this trait, because both *AA* and *Aa* will produce the same phenotype: normal skin pigmentation. Every sperm produced by a homozygous father will carry the *A* allele. In contrast, half the sperm produced by a heterozygous father will carry the dominant allele *A*, and the other half will carry the recessive allele *a*.

A simple box diagram known as a **Punnett square** enables us to predict the probabilities that children will have particular characteristics by showing the various combinations of parental alleles they can inherit. In the Punnett squares shown in **Figure 29–16**, the maternal alleles for skin pigmentation are listed along the horizontal axis, and the paternal ones along the vertical axis. The combinations of alleles are indicated in the small boxes. **Figure 29–16a** shows the possible offspring of an *aa* mother and an *AA* father. All the children must have the genotype *Aa*, so all will have normal skin pigmentation. Compare these results with those of **Figure 29–16b**, for a heterozygous father (*Aa*) and an *aa* mother. The heterozygous male produces two types of gametes, *A* and *a*, and the secondary oocyte may be fertilized by either one. As a result, the probability is 50 percent that a child of such a father will inherit the genotype *Aa* and so have normal skin pigmentation. The probability of inheriting the genotype *aa*, and thus having the albino phenotype, is also 50 percent.

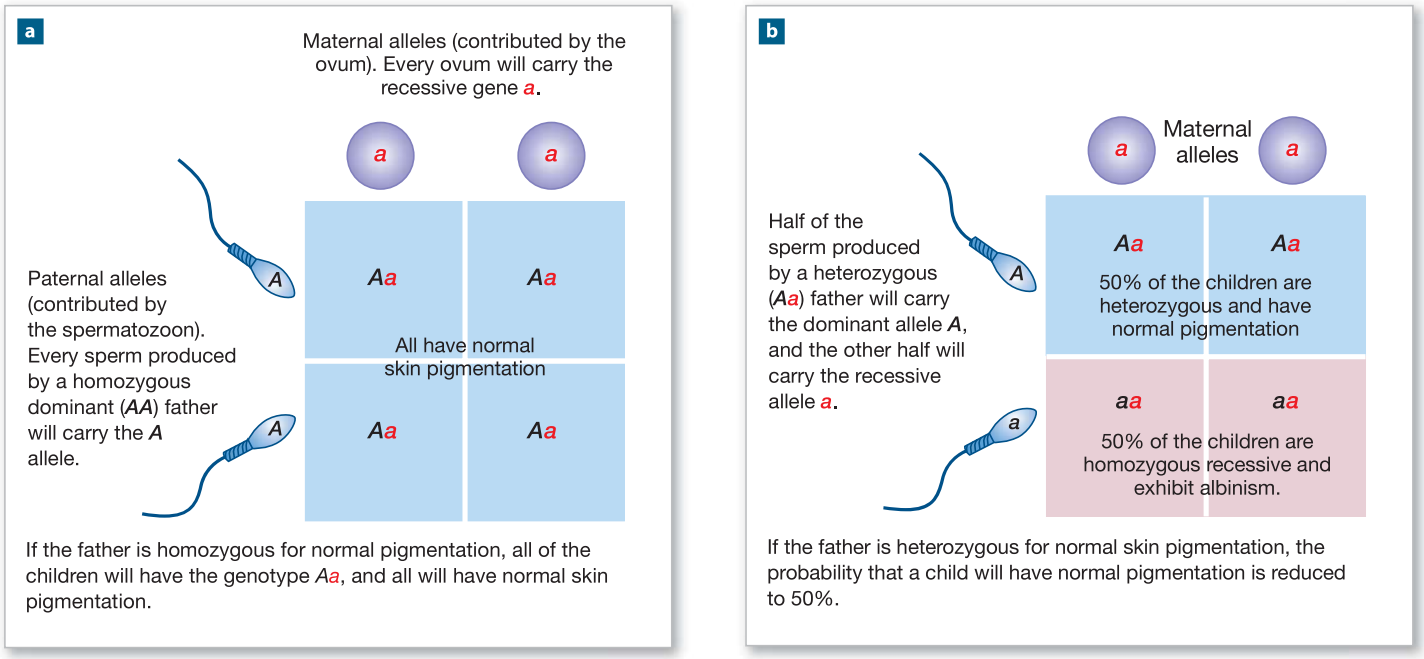
A Punnett square can also be used to draw conclusions about the identity and genotype of a parent. For example, in our scenario, a man with the genotype *AA* cannot be the father of an albino child (*aa*).

We can predict the frequency of appearance of any inherited disorder that results from simple inheritance by using a Punnett square. Although they are rare in terms of overall numbers, more than 1200 inherited disorders have been identified that reflect the presence of one or two abnormal alleles for a single gene.

Phenotypic traits are sometimes determined by interactions among several genes. Such interactions constitute **polygenic inheritance.** Because the resulting phenotype depends not only on the nature of the alleles but how those alleles interact, you cannot predict the presence or absence of phenotypic traits using a simple Punnett square. In *suppression*, one gene suppresses the other, so that the second gene has no effect on the phenotype. In *complementary gene action*, dominant alleles on two genes interact to produce a phenotype different from that seen when one gene contains recessive alleles. The risks of developing several important adult disorders, including hypertension and coronary artery disease, are linked to polygenic inheritance.

Many of the developmental disorders responsible for fetal deaths and congenital malformations result from polygenic inheritance. In these cases, an individual's genetic composition does not by itself determine the onset of the disease. Instead, the conditions regulated by these genes establish a susceptibility to particular environmental influences. Thus, not every individual with the genetic tendency for a certain condition will

Figure 29–16 Predicting Phenotypic Characters by Using Punnett Squares.



develop that condition. It is therefore difficult to track polygenic conditions through successive generations. However, because many inherited polygenic conditions are *likely* (but not *guaranteed*) to occur, steps can be taken to prevent a crisis. For example, you can reduce hypertension by controlling your diet and fluid volume, and you can prevent coronary artery disease by lowering your serum cholesterol levels.

Sources of Individual Variation

Just as you are not a copy of either of your parents, neither are you a mixture of their characteristics. One reason for this was noted in Chapter 28: During meiosis, maternal and paternal chromosomes are randomly distributed, so each gamete has a unique combination of maternal and paternal chromosomes. Thus, you may have an allele for curly hair from your father and an allele for straight hair from your mother, even though your sister received an allele for straight hair from each of your parents. Only in very rare cases will an individual receive both alleles from one parent. The few documented cases appear to have resulted when duplicate maternal chromatids failed to separate during meiosis II and the corresponding chromosome provided by the sperm did not participate in amphimixis. This condition, called *uniparental disomy*, generally remains undetected, because the individuals are phenotypically normal.

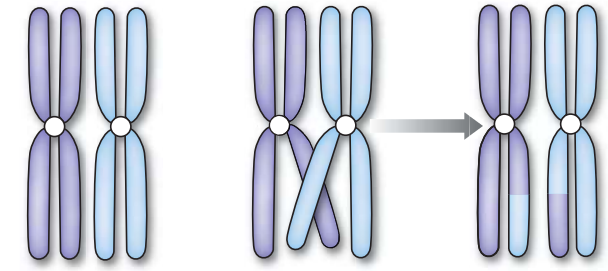
Genetic Recombination

During meiosis, various changes can occur in chromosome structure, producing gametes with chromosomes that differ from those of each parent. This phenomenon, called **genetic recombination,** greatly increases the range of possible variation among gametes, and thus among members of successive generations, whose genotypes are formed by the combination of gametes in fertilization. Genetic recombination can also complicate the tracing of the inheritance of genetic disorders.

In one normal form of recombination, parts of chromosomes become rearranged in synapsis during meiosis (**Figure 29–17**). When tetrads form, adjacent chromatids may overlap, an event called **crossing over.** The chromatids may then break, and the overlapping segments trade places. In general, the genetic exchange between homologous chromosomes is called crossing over, and between nonhomologous chromosomes it is called **translocation.**

During recombination, portions of chromosomes may break away and be lost, or *deleted*. This is an abnormal event, which can have severe or even lethal effects on the zygote depending on the nature of the lost genes. However a lack of specific gene expression in a zygote is not necessarily due to chromosomal aberrations or deletions. Genes can be present, yet be prevented from being fully expressed. A genetic phenomenon called **genomic imprinting** is particularly impor-

Figure 29–17 Crossing Over and Recombination.



a Tetrad at synapsis. Synapsis, with the formation of a tetrad during meiosis

b Crossing over. Crossing over of portions of two homologous chromosomes

c Recombination. The exchange of corresponding segments and groups of genes increases chromosomal variation among the gametes produced.

tant in the early embryo. Imprinting does not change the DNA itself; instead it results in specific (and usually reversible) chemical modifications of DNA and its associated proteins. These changes then dictate whether the gene is expressed or not (silenced). As gametes mature, a proportion of their genes develop characteristic, maternal and paternal specific, imprinting "patterns". These patterns persist after fertilization and can regulate whether or not the maternally or the paternally derived gene is transcribed during embryo development. Many of the estimated 150 genes known to be affected by genomic imprinting regulate many aspects of early development, including rates of prenatal and postnatal growth, behavior, and language development. Imprinting is a normal process that acts as a "volume control" for parental genes since it results in one active copy of an imprinted gene. Incorrectly imprinted genes can have the same effect as deletion of the same gene. This is exemplified by two human genetic disorders linked to genes in a specific portion of chromosome 15 and their differential imprinting during sperm or oocyte formation. *Angelman syndrome*, which results in hyperactivity, severe mental retardation, and seizures, occurs when the maternal genes are inactive; and *Prader–Willi syndrome*, which results in short stature, reduced muscle tone and skin pigmentation, underdeveloped gonads, and some degree of mental retardation, occurs when paternal genes are inactive.

Recombination that produces abnormal chromosome shapes or numbers is lethal for the zygote in almost all cases. Roughly 10 percent of zygotes have **chromosomal abnormalities**—that is, damaged, broken, missing, or extra copies of chromosomes—but only about 0.5 percent of newborns have such abnormalities. Few individuals with chromosomal abnormalities survive to full term; *Down's syndrome (trisomy 21)*, which involves one of the smallest chromosomes in human beings, is an exception. In addition to contributing to prenatal mortality, chromosomal abnormalities produce a variety of serious clinical conditions. The high mortality rate and the severity of the problems reflect the fact that large numbers of genes have been added or deleted. Women who become pregnant later in life run a higher risk of birth defects and miscarriage due to chromosomal abnormalities in the oocyte. It seems that the longer the oocyte remains suspended in meiosis I, the more likely are recombination errors when meiosis is completed.

Mutations

Variations at the level of the individual gene can result from *mutations*—changes in the nucleotide sequence of an allele. **Spontaneous mutations** are the result of random errors in DNA replication. Such errors are relatively common, but in most cases the error is detected and repaired by enzymes in the nucleus. Those errors that go undetected and unrepaired have the potential to change the phenotype in some way.

Mutations occurring during meiosis can produce gametes that contain abnormal alleles. These alleles may be dominant or recessive, and they may occur on autosomal chromosomes or on sex chromosomes. The vast majority of mutations make the zygote incapable of completing normal development. Mutation, rather than chromosomal abnormalities, is probably the primary cause of the high mortality rate among pre-embryos and embryos. (Roughly 50 percent of all zygotes fail to complete cleavage, and another 10 percent fail to reach the fifth month of gestation.)

If the abnormal allele is dominant but does not affect gestational survival, the individual's phenotype will show the effects of the mutation. If the abnormal allele is recessive and is on an autosomal chromosome, it will not affect the individual's phenotype as long as the zygote contains a normal allele contributed by the other parent at fertilization. Over generations, a recessive autosomal allele can spread through the population, remaining undetected until a fertilization occurs in which the two gametes contribute identical recessive alleles. This individual, who will be homozygous for the abnormal allele, will be the first to show the phenotypic effects of the original mutation. Individuals who are heterozygous for the abnormal allele but do not show the effects of the mutation are called **carriers.** Available genetic tests can determine whether an individual is a carrier for any of several autosomal recessive disorders, including Tay–Sachs disease. The information obtained from these tests can be useful in counseling prospective parents. For example, if both parents are carriers of the same disorder, they have a 25 percent probability of producing a child with the disease. This information may affect their decision to conceive.

Sex-Linked Inheritance

Unlike the other 22 chromosomal pairs, the sex chromosomes are never identical in appearance and gene content. There are two types of sex chromosomes: an **X chromosome** and a **Y chromosome.** X chromosomes are considerably larger and have more genes than do Y chromosomes. The Y chromosome includes dominant alleles specifying that an individual with that chromosome will be male. The normal pair of sex chromosomes in males is XY. Females do not have a Y chromosome; their sex chromosome pair is XX.

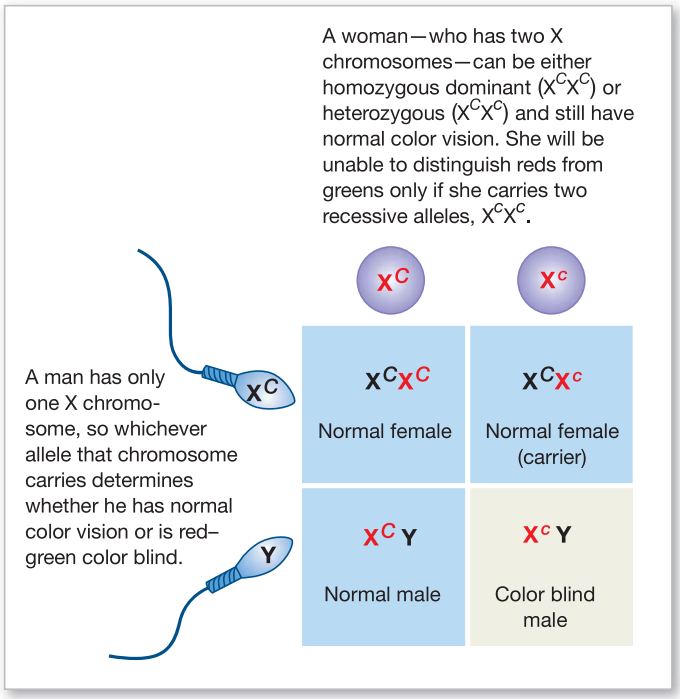
All oocytes carry an X chromosome, because the only sex chromosomes females have are X chromosomes. But each sperm carries either an X or a Y chromosome, because males have one of each and can pass along either one. As a Punnett square shows, the ratio of males to females in offspring should be 1:1. The birth statistics differ slightly from that prediction, with 106 males born for every 100 females. It has been suggested that more males are born because a sperm that carries the Y chromosome can reach the oocyte first, because that sperm does not have to carry the extra weight of the larger X chromosome.

The X chromosome also carries genes that affect somatic structures. These characteristics are called **X-linked** (or *sex-linked*), because in most cases there are no corresponding alleles on the Y chromosome. The inheritance of characteristics regulated by these genes does not follow the pattern of alleles on autosomal chromosomes.

The inheritance of color blindness exemplifies the differences between sex-linked inheritance and autosomal inheritance. The presence of a dominant allele, *C*, on the X chromosome results in normal color vision; a recessive allele, *c*, on the X chromosome results in red–green color blindness. A woman, with her two X chromosomes, can be either homozygous dominant (*CC*) or heterozygous (*Cc*) and still have normal color vision. She will be unable to distinguish reds from greens only if she carries two recessive alleles, *cc*. But a male has only one X chromosome, so whichever allele that chromosome carries determines whether he has normal color vision or is red–green color blind. The Punnett square in **Figure 29–18** reveals that the sons produced by a father with normal vision and a heterozygous (carrier) mother have a 50 percent chance of being red–green color blind, whereas any daughters have normal color vision. Recessive alleles on X chromosomes produce genetic disorders in males at a higher frequency than in females.

A number of other clinical disorders noted earlier in the text are X-linked traits, including certain forms of hemophilia, diabetes insipidus, and muscular dystrophy. In several instances, advances in molecular genetics techniques have enabled geneticists to localize the specific genes on the X chromosome. These techniques provide a reasonably direct method of screening for the presence of a particular condition before any signs or symptoms appear, and even before birth.

Figure 29–18 Inheritance of an X-Linked Trait.

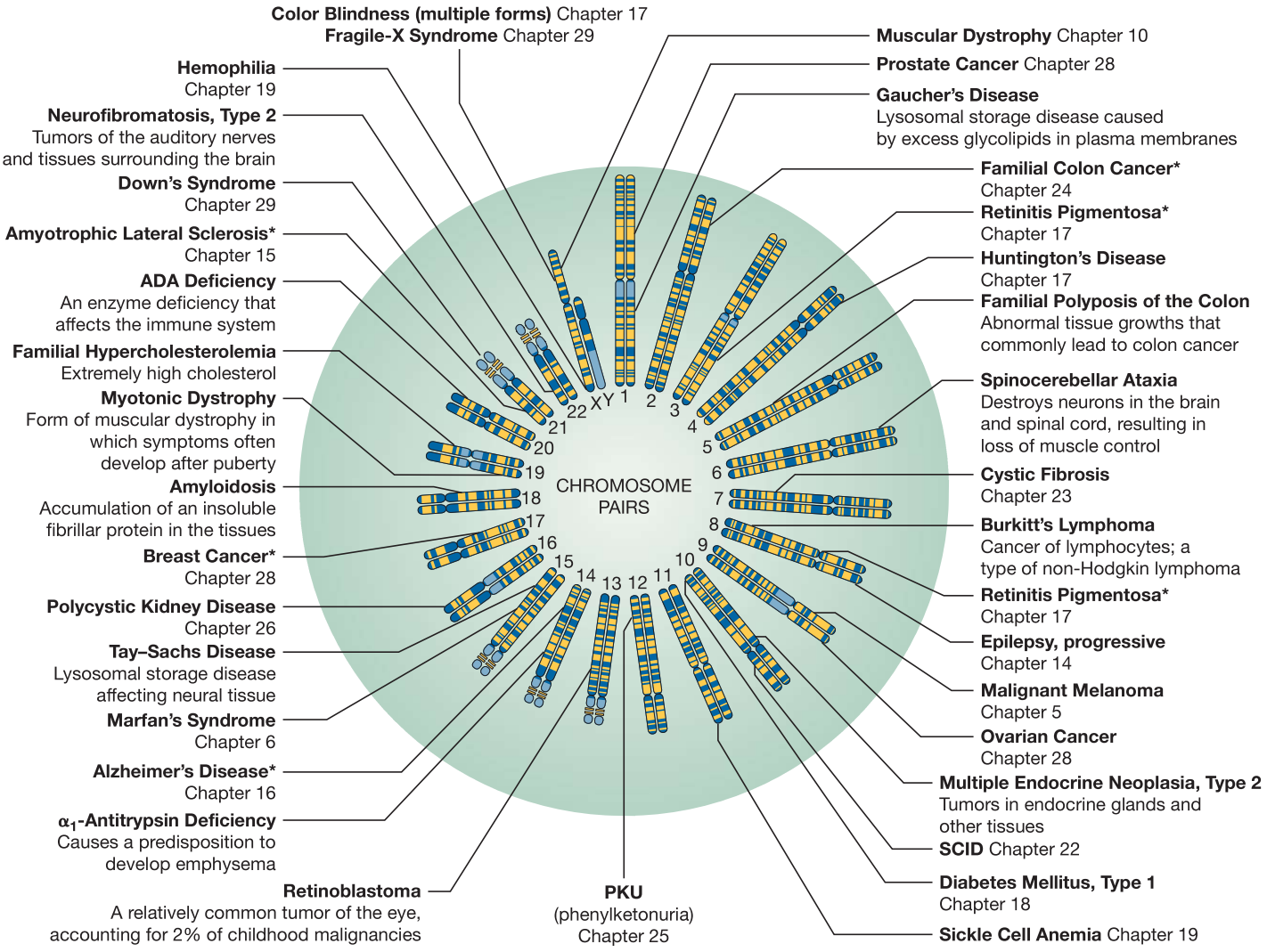


The Human Genome Project and Beyond

It has long been appreciated that all diseases—whether inherited or due to the body's responses to stresses, such as radiation, toxins, or pathogens—have a connection to chromosomes and genes. A much richer and fuller understanding of these relationships is now on the horizon, thanks to the biotechnological methods and techniques developed during the **Human Genome Project (HGP).** Funded by the National Institutes of Health and the Department of Energy, the project's goal was to make a written copy of the entire human **genome**—that is, the full set of genetic material (DNA), nucleotide by nucleotide, found in our chromosomes. Begun in 1990, the project was completed in 2003 with 99 percent of the entire genome listed as a finished, "high-quality sequence." A high-quality sequence is defined as a complete sequence of nucleotides, with no gaps or ambiguities and an error rate of less than one base per 10,000. The final HGP papers were published in 2006.

The first step in accessing the human genome was the preparation of a map of the individual chromosomes. **Karyotyping** (KAR-ē-ō-tīp-ing) is the determination of an individual's complete chromosomal complement (**Figure 29–14**). Each chromosome has characteristic banding patterns when stained with special dyes. The patterns are useful as reference points for the preparation of more detailed genetic maps, such as the one shown in **Figure 29–19**. The banding patterns

Figure 29–19 **A Map of Human Chromosomes.** The banding patterns of typical chromosomes in a male, and the locations of the genes associated with specific inherited disorders. The chromosomes are not drawn to scale.



themselves can be useful, as abnormal patterns are characteristic of some genetic disorders and several cancers.

The following are highlights of the Human Genome Project:

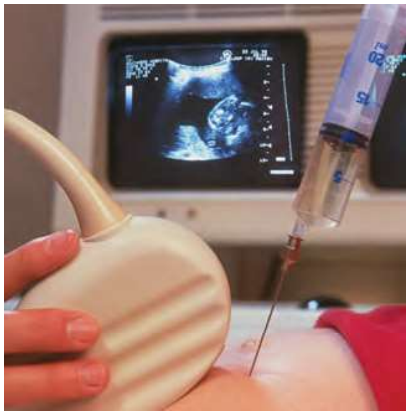
- All the chromosomes (23 pairs) have been completely sequenced.
- The total number of genes is now estimated at 20,000–25,000 genes. Almost 20,000 protein-coding genes are confirmed and, based on DNA segments, an additional 2188 more are predicted. (Defining a gene is not always straightforward. For example, small genes can easily be overlooked in a nucleotide sequence, a gene may code for more than one protein, some genes code for RNA, and two genes can overlap.)
- Although more than 99 percent of human nucleotide bases are the same in all people, there are about 1.4 million single-base differences, or single nucleotide polymorphisms (SNPs). Some of these SNPs are associated with specific diseases.
- Roughly 10,000 different single gene disorders have been described. Most are very rare, but collectively they may affect 1 in every 200 births. Over 900 of these disorders have been mapped on the genome, and several examples are included in **Figure 29–19**. Genetic screening and diagnostic tests for abnormal genes are now performed for many of these disorders.

Rogue chromosomes

Embryos that have abnormal autosomal chromosomes rarely survive. However, *translocation defects* and *trisomy* are two types of autosomal chromosome abnormalities that do not invariably result in prenatal death.

In a **translocation defect,** an exchange occurs between different (nonhomologous) chromosome pairs such that, for example, a piece of chromosome 8 may become attached to chromosome 14. The genes moved to their new position may function abnormally, becoming inactive or overactive. In a balanced translocation, where there is no net loss or gain of chromosomal material, embryos may survive.

In **trisomy,** a mistake occurs in meiosis. One of the gametes involved in fertilization carries an extra copy of one chromosome, so the zygote then has three copies of this chromosome rather than two. (The nature of the trisomy is indicated by the number of the chromosome involved. Thus, individuals with trisomy 13 have three copies of chromosome 13.) Zygotes with extra copies of chromosomes seldom survive. Individuals with trisomy 13 and trisomy 18 may survive until delivery but rarely live longer than a year. The notable exception is trisomy 21.



Trisomy 21, or **Down's syndrome,** is the most common viable chromosomal abnormality. Estimates of its incidence in the U.S. population range from 1.5 to 1.9 per 1000 births. Affected individuals exhibit mental retardation and characteristic physical malformations, including a facial appearance that gave rise to the term *mongolism*, once used to describe this condition. The degree of mental retardation ranges from moderate to severe. Anatomical problems affecting the cardiovascular system often prove fatal during childhood or early adulthood. Although some individuals survive to moderate old age, many develop Alzheimer's disease while still relatively young (before age 40).

For unknown reasons, there is a direct correlation between maternal age and the risk of having a child with trisomy 21. For a maternal age below 25, the incidence of Down's syndrome approaches 1 in 2000 births, or 0.05 percent. For maternal ages 30–34, the odds increase to 1 in 900, and over the next decade they go from 1 in 290 to 1 in 46, or more than 2 percent. These statistics are becoming increasingly significant because many women are delaying childbearing until their mid-thirties or later.

Abnormal numbers of sex chromosomes do not produce effects as severe as those induced by extra or missing autosomal chromosomes. In **Klinefelter's syndrome,** the individual carries the sex chromosome pattern XXY. The phenotype is male, but the extra X chromosome causes reduced androgen production. As a result, the testes fail to mature so the individuals are sterile, and the breasts are slightly enlarged. The incidence of this condition among newborn males averages 1 in 750 births.

Individuals with **Turner's syndrome** have only a single, female sex chromosome; their sex chromosome complement is abbreviated XO. This kind of chromosomal deletion is known as **monosomy.** The incidence of this condition at delivery has been estimated as 1 in 10,000 live births. The condition may not be recognized at birth, because the phenotype is normal female. But maturational changes do not appear at puberty. The ovaries are nonfunctional, and estrogen production occurs at negligible levels.

Fragile-X syndrome causes mental retardation, abnormal facial development, and enlarged testes in affected males. The cause is an abnormal X chromosome that contains a *genetic stutter*, an abnormal repetition of a single nucleotide triplet. The presence of the stutter in some way disrupts the normal functioning of adjacent genes and so produces the signs and symptoms of the disorder.

Many of these conditions can be detected before birth through the analysis of fetal cells. In **amniocentesis,** a sample of amniotic fluid is removed and the fetal cells it contains are analyzed. This procedure permits the identification of more than 20 congenital conditions, including Down's syndrome. The needle inserted to obtain a fluid sample is guided into position during an ultrasound procedure. ↩ p. 22 Unfortunately, amniocentesis has two major drawbacks:

1. Because the sampling procedure represents a potential threat to the health of fetus and mother alike, amniocentesis is performed only when known risk factors are present. Examples of risk factors are a family history of specific conditions, or in the case of Down's syndrome, maternal age over 35.
2. Sampling cannot safely be performed until the volume of amniotic fluid is large enough that the fetus will not be injured during the process. The usual time for amniocentesis is at 14–15 weeks of gestation. It may take several weeks to obtain results once samples have been collected, and by the time the results are received, an induced or therapeutic abortion may no longer be a viable option.

An alternative procedure known as **chorionic villus sampling (CVS)** analyzes cells collected from the chorionic villi late in the first trimester. CVS carries a slightly higher risk of miscarriage than amniocentesis, but may be preferable because it can be done earlier in gestation.

The completion of the sequence stimulated new approaches for diagnosing disease and predicting disease susceptibility. For example, in 2006, the Genes and Environment Initiative (GEI) was launched to understand the link between genes, the environment, and why certain individuals develop diseases. The GEI is a joint collaboration of the National Institute of Environmental Health Services (NIEHS) and the National Human Genome Research Institute (NHGRI). Together, they are conducting genetic studies of individuals with common conditions, such as tooth decay, cancer, diabetes, and heart disease, and their personal exposure to environmental factors such as sun and chemicals, diet, and physical activity. Also begun in 2006 is The Cancer Genome Atlas (TCGA), sponsored by the NHGRI and the National Cancer Institute. TCGA had an immediate goal—the compilation of an atlas of genetic changes (mutations) in three tumors: brain cancer (glioblastoma), lung cancer, and ovarian cancer. Research into 20 other types of cancer, including breast cancer and colon cancer, is now also receiving attention.

The Human Genome Project has identified the normal genetic composition of a "typical" human. Yet we all are variations on a basic theme. How do we decide what set of genes to accept as "normal"? Moreover, as we improve our abilities to manipulate our own genetic foundations, we will face many additional troubling ethical and legal dilemmas. Few people, for example, object to the insertion of a "correct" gene into somatic cells to cure a specific disease. But what if we could insert that modified gene into a gamete and change not only that individual, but all of his or her descendants as well? And what if the goal of manipulating the gene was not to correct or prevent any disorder, but instead to "improve" the individual by increasing his or her intelligence, height, or vision, or by altering some other phenotypic characteristic? Such difficult questions will not go away. In the years to come, we will have to find answers that are acceptable to us all.

Checkpoint

22. **Describe the relationship between genotype and phenotype.**
23. **Define heterozygous.**
24. **Curly hair is an autosomal dominant trait. What would be the phenotype of a person who is heterozygous for this trait?**
25. **Why are children not identical copies of their parents?**

See the blue Answers tab at the back of the book.

Related Clinical Terms

eclampsia: A condition in which one or more convulsions occur in a pregnant woman suffering from high blood pressure, often followed by coma and posing a threat to the health of mother and baby.

gamete intrafallopian transfer (GIFT): An assisted reproductive procedure in which a woman's eggs are removed, mixed with sperm, and replaced into the woman's uterine tube where the fertilization takes place, rather than in the laboratory.

infertility: The inability to achieve pregnancy after engaging in one year of appropriately timed intercourse.

in vitro fertilization: Fertilization outside the body, generally in a Petri dish.

neural tube defects (NTDs): Major birth defects caused by an abnormal development of the neural tube—the structure present during the embryonic stage that later becomes the central nervous system. These are very common birth defects that cause infant mortality and disability and include anencephaly and spina bifida.

placenta previa: Condition during pregnancy in which the placenta is abnormally placed so as to totally or partially cover the cervix.

placenta abruptio: Condition in which there is separation of the placenta from the uterine site of implantation before delivery of the baby.

preeclampsia: A condition in pregnancy characterized by sudden hypertension, albuminuria, and edema of the hands, feet, and face. It is the most common complication of pregnancy, affecting about 5 percent of pregnancies.

therapeutic cloning: A procedure that usually takes skin cells from a patient, and inserts a skin cell nucleus into a fertilized egg whose nucleus has been removed to create a new cell. That new cell divides repeatedly to form a blastocyst from which stem cells can be extracted to grow new tissue that is genetically matched to the patient.

Chapter Review

Study Outline

29-1 Development, marked by various stages, is a continuous process that occurs from fertilization to maturity p. 1077

1. **Development** is the gradual modification of anatomical structures and physiological characteristics from **conception** to maturity. The formation of different types of cells is **differentiation.**
2. **Prenatal development** occurs before birth; **postnatal development** begins at birth and continues to **maturity,** when aging begins. **Inheritance** is the transfer of genetically

determined characteristics from generation to generation. **Genetics** is the study of the mechanisms of inheritance.

29-2 Fertilization—the fusion of a secondary oocyte and a spermatozoon—forms a zygote p. 1077

3. **Fertilization,** or *conception*, normally occurs in the uterine tube within a day after ovulation. Spermatozoa cannot fertilize a secondary oocyte until they have undergone *capacitation*. *(Figure 29–1)*
4. The acrosomal caps of the spermatozoa release **hyaluronidase** and **acrosin**, enzymes required to penetrate the corona radiata and zona pellucida of the oocyte. When a single spermatozoon contacts the oocyte membrane, fertilization begins and **oocyte activation** follows. *(Figure 29–1)*
5. During activation, the oocyte completes meiosis II and thus becomes a functionally mature ovum. **Polyspermy** is prevented by membrane depolarization and the *cortical reaction*.
6. After activation, the **female pronucleus** and the **male pronucleus** fuse in a process called *amphimixis*. *(Figure 29–1)*

29-3 Gestation consists of three stages of prenatal development: the first, second, and third trimesters p. 1080

7. During prenatal development, differences in the cytoplasmic composition of individual cells trigger changes in genetic activity. The chemical interplay among developing cells is **induction.**
8. The nine-month **gestation** period can be divided into three **trimesters.**

29-4 Cleavage, implantation, placentation, and embryogenesis are critical events of the first trimester p. 1080

9. In the **first trimester, cleavage** subdivides the cytoplasm of the zygote in a series of mitotic divisions; the zygote becomes a **pre-embryo** and then a **blastocyst.** During **implantation,** the blastocyst becomes enclosed within the uterine endometrium. **Placentation** occurs as blood vessels form around the blastocyst and the **placenta** develops. **Embryogenesis** is the formation of a viable embryo.
10. The blastocyst consists of an outer **trophoblast** and an **inner cell mass.** *(Figure 29–2)*
11. Implantation occurs about seven days after fertilization as the blastocyst adheres to the uterine lining. *(Figure 29–3)*
12. As the trophoblast enlarges and spreads, maternal blood flows through open **lacunae.** After **gastrulation,** there is an **embryonic disc** composed of **endoderm**, **ectoderm**, and an intervening **mesoderm.** It is from these **germ layers** that the body systems differentiate. *(Figure 29–4; Table 29–1)*
13. Germ layers help form four **extraembryonic membranes**: the yolk sac, amnion, allantois, and chorion. *(Figure 29–5)*
14. The **yolk sac** is an important site of blood cell formation. The **amnion** encloses fluid that surrounds and cushions the developing embryo. The base of the **allantois** later gives rise to the urinary bladder. Circulation within the vessels of the **chorion** provides a rapid-transit system that links the embryo with the trophoblast. (*Figures 29–5, 29–6*)
15. **Chorionic villi** extend outward into the maternal tissues, forming an intricate, branching network through which maternal blood flows. As development proceeds, the **umbilical cord** connects the fetus to the placenta. The syncytial trophoblast synthesizes **human chorionic gonadotropin (hCG),** estrogens, progesterone, **human placental lactogen (hPL), placental prolactin,** and **relaxin.** *(Figure 29–6)*
16. The first trimester is critical, because events in the first 12 weeks establish the basis for **organogenesis** (organ formation). *(Figure 29–7; Table 29–2)*

29-5 During the second and third trimesters, maternal organ systems support the developing fetus, and the uterus undergoes structural and functional changes p. 1092

17. In the **second trimester,** the organ systems increase in complexity. During the **third trimester,** many of the organ systems become fully functional. *(Figure 29–8; Table 29–2)*
18. The fetus undergoes its largest weight gain in the third trimester. At the end of gestation, the fetus and the enlarged uterus displace many of the mother's abdominal organs. *(Figure 29–9)*
19. The developing fetus is totally dependent on maternal organs for nourishment, respiration, and waste removal. Maternal adaptations include increases in respiratory rate, tidal volume, blood volume, nutrient and vitamin intake, and glomerular filtration rate, as well as changes in the size of the uterus and mammary glands.
20. Progesterone produced by the placenta has an inhibitory effect on uterine muscles. Estrogens, oxytocin, and prostaglandins oppose its calming action. At some point, multiple factors interact to produce **labor contractions** in the uterine wall. *(Figure 29–10)*

29-6 Labor consists of the dilation, expulsion, and placental stages p. 1095

21. The goal of **true labor** is **parturition,** the forcible expulsion of the fetus.
22. Labor can be divided into three stages: the **dilation stage,** the **expulsion stage,** and the **placental stage.** The Apgar score is used to assess the overall health of a newborn. *(Figure 29–11)*
23. **Premature labor** may result in **premature delivery.**
24. Difficult deliveries can include *forceps deliveries* and **breech births**—deliveries in which the legs or buttocks of the fetus, rather than the head, enter the vaginal canal first.
25. Twin births are either **dizygotic** (fraternal) or **monozygotic** (identical).

29-7 Postnatal stages are the neonatal period, infancy, childhood, adolescence, maturity, and senescence p. 1098

26. Postnatal development involves a series of five **life stages:** the neonatal period, infancy, childhood, adolescence, and maturity. *Senescence* (aging) begins at maturity and ends in the death of the individual.
27. The **neonatal period** extends from birth to one month after. In the transition from fetus to **neonate,** the respiratory, circulatory, digestive, and urinary systems of the infant begin functioning independently. The newborn must also begin thermoregulation.
28. Mammary gland cells produce protein-rich **colostrum** during the neonate's first few days of life and then convert to milk production. These secretions are released as a result of the **milk let-down reflex.** *(Figure 29–12)*
29. Body proportions gradually change during **infancy** (from age one month to two years) and during **childhood** (from two years to puberty). *(Figure 29–13)*
30. **Adolescence** begins at **puberty,** when (1) the hypothalamus increases its production of GnRH, (2) circulating levels of FSH and LH rise rapidly, and (3) ovarian or testicular cells become

more sensitive to FSH and LH. These changes initiate gamete formation, the production of sex hormones, and a sudden increase in the growth rate. The hormonal changes at puberty, especially changes in sex hormone levels, produce sex-specific differences in the structure and function of many systems; these differences will be retained. Adolescence continues until growth is completed. Further changes occur when sex hormone levels decline at menopause or the male climacteric.

31. **Senescence** then begins, producing gradual reductions in the functional capabilities of all systems. *(Table 29–3)*

29-8 Genes and chromosomes determine patterns of inheritance p. 1102

32. Every somatic cell carries copies of the original 46 chromosomes in the zygote; these chromosomes and their component genes constitute the individual's **genotype.** The physical expression of the genotype is the individual's **phenotype.**
33. Every somatic human cell contains 23 pairs of chromosomes; each pair consists of **homologous chromosomes.** Twenty-two pairs are **autosomal chromosomes.** The chromosomes of the twenty-third pair are the **sex chromosomes;** they differ between the sexes. *(Figure 29–14)*
34. Chromosomes contain DNA, and genes are functional segments of DNA. The various forms of a given gene are called **alleles.** If both homologous chromosomes carry the same allele of a particular gene, the individual is **homozygous;** if they carry different alleles, the individual is **heterozygous.**
35. In **simple inheritance,** phenotypic traits are determined by interactions between a single pair of alleles. **Polygenic inheritance** involves interactions among alleles on several genes. *(Figure 29–15)*
36. Alleles are either **dominant** or **recessive,** depending on how their traits are expressed.
37. Combining maternal and paternal alleles in a **Punnett square** helps us predict the characteristics of offspring. *(Figure 29–16)*
38. **Genetic recombination,** the gene reshuffling (**crossing over** and **translocation)** that occurs during meiosis, increases the genetic variation of male and female gametes. *(Figure 29–17)*
39. **Spontaneous mutations** are the result of random errors in DNA replication. Such mutations can cause the production of abnormal alleles.
40. The two types of sex chromosomes are an **X chromosome** and a **Y chromosome.** The normal sex chromosome complement of males is XY; that of females is XX. The X chromosome carries **X-linked** *(sex-linked)* **genes,** which affect somatic structures but have no corresponding alleles on the Y chromosome. *(Figure 29–18)*
41. The **Human Genome Project** has mapped close to 25,000 human genes, including some of those responsible for inherited disorders. *(Figure 29–19)*

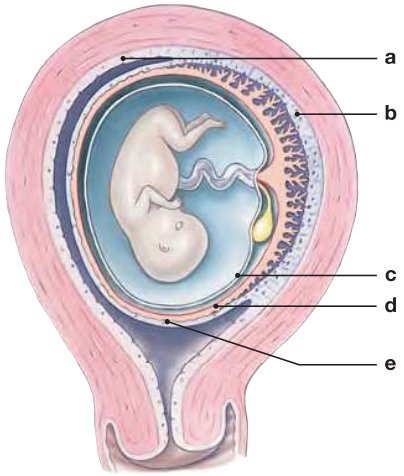
Review Questions

See the blue Answers tab at the back of the book.

LEVEL 1 Reviewing Facts and Terms

1. The chorionic villi
   (a) form the umbilical cord.
   (b) form the umbilical vein.
   (c) form the umbilical arteries.
   (d) increase the surface area available for exchange between the placenta and maternal blood.
   (e) form the portion of the placenta called the decidua capsularis.
2. Identify the two extraembryonic membranes and the three different regions of the endometrium at week 10 of development in the following diagram.

   (a) _____
   (b) _____
   (c) _____
   (d) _____
   (e) _____



3. The hormone that is the basis for a pregnancy test is
   (a) LH.
   (b) progesterone.
   (c) human chorionic gonadotropin (hCG).
   (d) human placental lactogen (hPL).
   (e) either c or d, depending on the type of test.
4. Recessive X-linked traits
   (a) are passed from fathers to their sons.
   (b) are more likely to be expressed in males.
   (c) always affect some aspect of the reproductive system.
   (d) are never expressed in females.
   (e) cannot be passed from mothers to daughters.
5. The stage of development that follows cleavage is the
   (a) blastocyst.
   (b) morula.
   (c) trophoblast.
   (d) blastocoele.
6. What developmental stage begins once the zygote arrives in the uterine cavity?
   (a) blastocyst
   (b) trophoblast
   (c) lacuna
   (d) blastomere
7. The structure(s) that allow(s) active and passive exchange between the fetal and maternal bloodstreams is/are the
   (a) yolk stalk.
   (b) chorionic villi.
   (c) umbilical veins.
   (d) umbilical arteries.

8. If an allele must be present on both the maternal and paternal chromosomes to affect the phenotype, the allele is said to be
   (a) dominant.
   (b) recessive.
   (c) complementary.
   (d) heterozygous.
9. Describe the changes that occur in the oocyte immediately after fertilization.
10. (a) What are the four extra-embryonic membranes?
    (b) From which germ layers do these membranes form, and what are their functions?
11. Identify the three stages of labor, and describe the events that characterize each stage.
12. List the factors involved in initiating labor contractions.
13. Identify the three life stages that occur between birth and approximately age 10. Describe the timing and characteristics of each stage.
14. What hormonal events are responsible for puberty? Which life stage does puberty initiate?

LEVEL 2 Reviewing Concepts

15. A normally pigmented woman whose father was an albino marries a normally pigmented man whose mother was an albino. What is the probability that they would have an albino child?
    (a) 50 percent
    (b) 25 percent
    (c) 12.5 percent
    (d) 6.25 percent
    (e) 100 percent
16. If a sperm cell lacked sufficient quantities of hyaluronidase, it would *not* be able to
    (a) move its flagellum.
    (b) penetrate the corona radiata.
    (c) become capacitated.
    (d) survive the environment of the female reproductive tract.
    (e) metabolize fructose.
17. Problems involving the formation of the chorion would affect
    (a) the embryo's ability to produce blood cells.
    (b) the formation of limbs.
    (c) the embryo's ability to derive nutrition from the mother.
    (d) lung formation.
    (e) the urinary system.
18. After implantation, how does the developing embryo obtain nutrients? What structures and processes are involved?
19. In addition to its role in the nutrition of the fetus, what are the primary endocrine functions of the placenta?
20. Discuss the changes that occur in maternal systems during pregnancy. Why are these changes functionally significant?
21. During true labor, what physiological mechanisms ensure that uterine contractions continue until delivery has been completed?
22. What physiological adjustments must an infant make during the neonatal period in order to survive?
23. Distinguish between the following paired terms:
    (a) genotype and phenotype
    (b) heterozygous and homozygous
    (c) simple inheritance and polygenic inheritance
24. Indicate the type of inheritance involved in each of the following situations.
    (a) Children who exhibit the trait have at least one parent who also exhibits it.
    (b) Children exhibit the trait even though neither parent exhibits it.
    (c) The trait is expressed more commonly in sons than in daughters.
    (d) The trait is expressed equally in daughters and sons.
25. GEI and TCGA are abbreviations for what studies that followed from the Human Genome Project? What are the general goals of each?

LEVEL 3 Critical Thinking and Clinical Applications

26. Hemophilia A, a condition in which blood does not clot properly, is a recessive trait located on the X chromosome (X^h). Suppose that a woman who is heterozygous for this trait (XX^h) mates with a normal male (XY). What is the probability that the couple will have hemophiliac daughters? What is the probability that the couple will have hemophiliac sons?
27. Joe and Jane desperately want to have children, and although they have tried for two years, they have not been successful. Finally, each of them consults a physician, and it turns out that Joe suffers from oligospermia (a low sperm count). He confides to you that he doesn't understand why this would interfere with his ability to have children since he remembers from biology class that it only takes one sperm to fertilize an egg. What would you tell him?
28. Cathy has just given birth to a little girl. When the nurses take the infant back to the nursery and try to feed her, she becomes cyanotic, a condition characterized by bluish discoloration of the skin. The episode passes, but when the infant is bathed, she becomes cyanotic again. Blood gas levels indicate that arterial blood is only 60 percent saturated. Physical examination reveals no structural deformities involving the respiratory or digestive system. What might be causing the problem?
29. Sally gives birth to a baby with a congenital deformity of the stomach. Sally believes that her baby's affliction is the result of a viral infection she suffered during her third trimester. Is this a possibility? Explain.