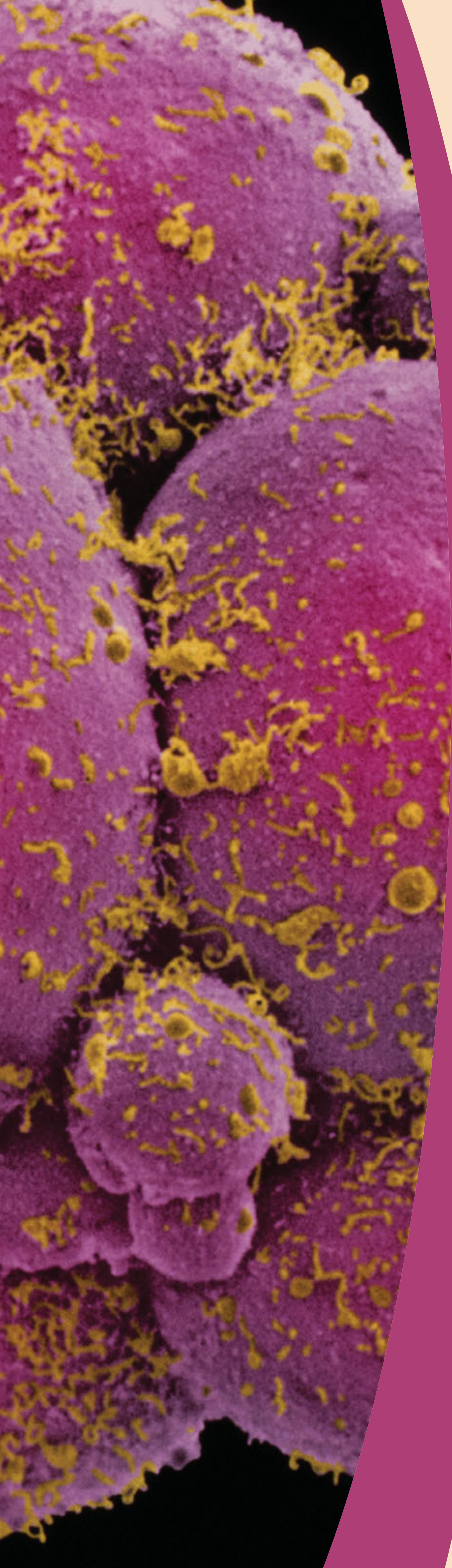
Basic Embryology 3



In just 38 weeks, from conception to birth, a single fertilized egg cell develops into a fully formed human being. The body will not change this much again during its remaining life span of 70 to 90 years. This chapter introduces you to human **embryology,** the study of the origin and development of an individual person. A knowledge of basic embryological events and structures is especially valuable as you begin your study of human anatomy. By knowing how the body methodically assembles itself, you will better understand adult anatomy. Moreover, embryology helps to explain the origin of many birth defects, anatomical abnormalities that are evident in about 3% of live births.

Eight-cell embryo (colored SEM).

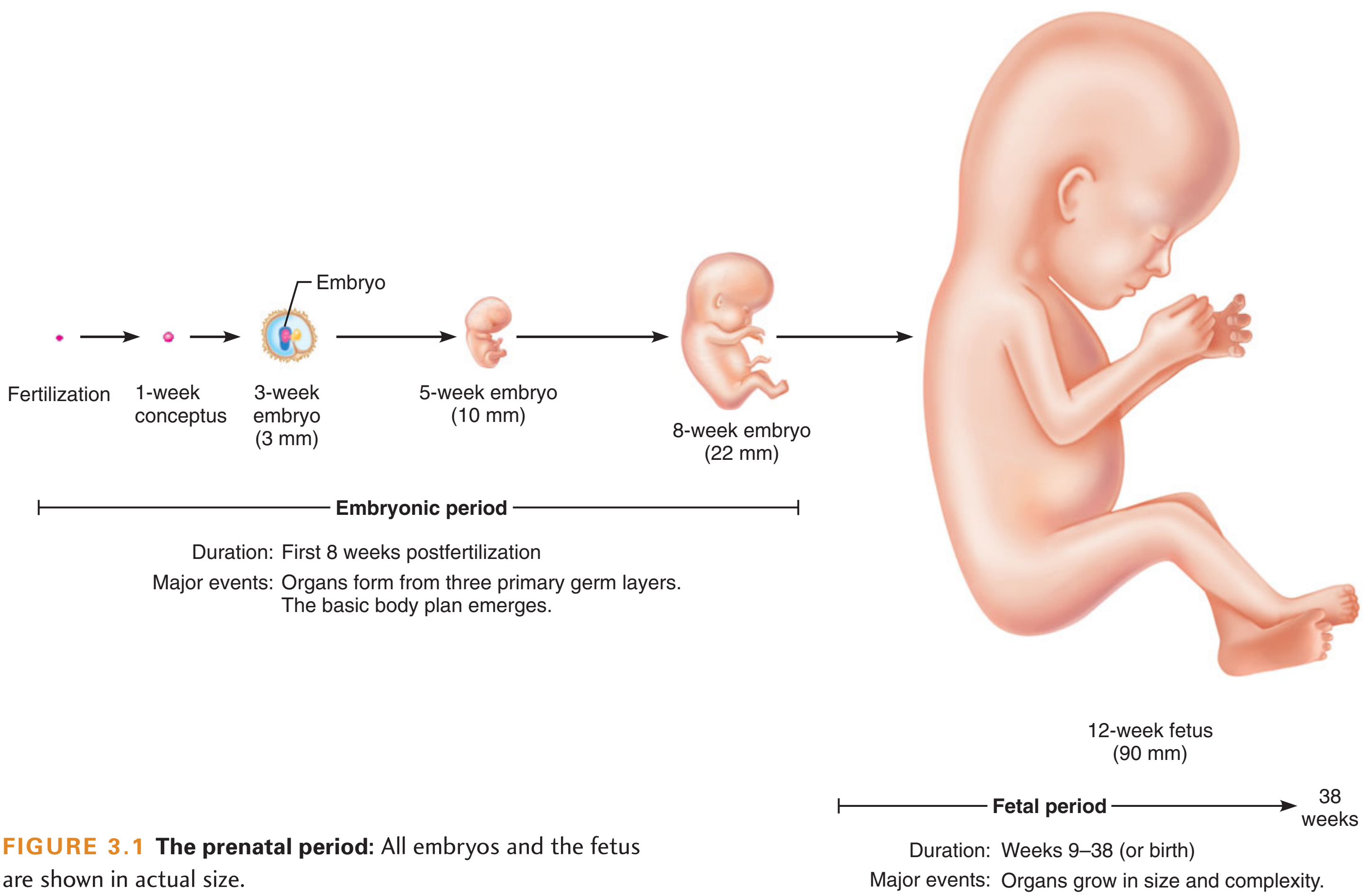


FIGURE 3.1 The prenatal period: All embryos and the fetus are shown in actual size.

STAGES OF PRENATAL DEVELOPMENT

- ➤ List the practical and clinical reasons for studying embryology.
- ➤ Distinguish the embryonic period from the fetal period of development.

The **prenatal period** (pre-na′tal; "before birth") is the time between conception (the union of an egg and a sperm cell) and birth. It is divided into two stages **(Figure 3.1)**: The **embryonic period** spans the first 8 weeks, and the **fetal** (fe′tal) **period** encompasses the remaining 30 weeks. The embryonic period is an exceptionally busy one. By its end, all major organs are in place, and the **embryo,*** the early form of the body, looks distinctly human. In the longer fetal period that follows, the organs of the **fetus** (fe′tus; "the young in the womb") grow larger and more complex.

THE BASIC BODY PLAN

- ➤ Sketch the basic structural plan of the adult body, which is established during the embryonic period.

*Technically, the embryo is the stage in prenatal development between the third or fourth and eighth weeks, inclusive. However, the term *embryo* can be used informally to encompass all stages in the embryonic period.

To simplify the treatment of embryology, this chapter limits the discussion to the derivation of the basic adult body plan. Recall that in Chapter 1, pp. 10–11, the basic body plan was described as a tube within a tube. This basic plan, which is evident by month 2 of development, is illustrated in **Figure 3.2**; the outer body wall makes up the outer tube and the inner tube in this section through the abdomen is the digestive tube. These two tubes are separated by a serous cavity. In the abdomen, this cavity is the peritoneal cavity. In the figure, note the following adult structures:

1. **Skin.** The skin has two layers: an outer layer called the *epidermis* and an inner, leathery layer called the *dermis*.
2. **Outer body wall.** The outer body wall consists mostly of trunk muscles. Dorsally, it also contains the vertebral column, through which the spinal cord runs. Ribs attach to each bony vertebra in the thoracic region of the trunk wall.
3. **Body cavity and inner tube.** The inner tube is composed of the respiratory and digestive structures (see Figure 1.5, p. 10). This section through the abdomen shows the peritoneal cavity, lined by visceral and parietal serosae, surrounding the digestive tube (stomach, intestines, and so on). The digestive tube has a muscular wall and is lined internally by a sheet of cells. This lining is shown in yellow in Figure 3.2.

   In the thoracic region the body plan is similar. The respiratory structures form from the inner tube. The body

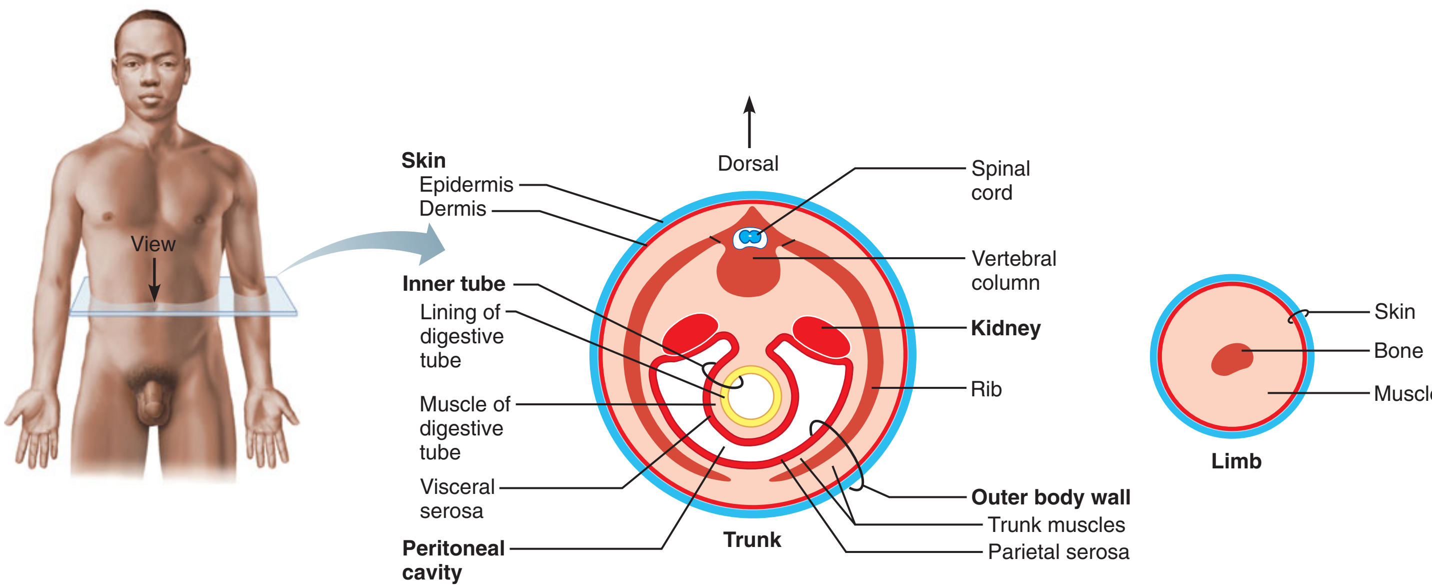


FIGURE 3.2 The adult human body plan (simplified cross section). The development of this body plan is traced in this chapter. The blue, red, and yellow colors denote derivation from the three basic embryonic germ layers. See the discussion on p. 56 and Figure 3.9 for more information.

cavities in the thorax are the pleural cavity around the lungs and the pericardial cavity surrounding the heart. Parietal and visceral serosae line these cavities as well. These relationships were introduced in Chapter 1, p. 12.

4. **Kidneys and gonads.** The kidneys lie directly deep to the dorsal body wall, in the lumbar region of the back posterior to the parietal serosa. The gonads (testes or ovaries) originate in a similar position but migrate to other parts of the body during the fetal period.
5. **Limbs.** The limbs consist mostly of bone, muscle, and skin.

You can see how this adult body plan takes shape by following the events of month 1 of human development.

check your understanding

1. During which prenatal period is the basic body plan established?
2. What abdominal structures form from the inner tube?
3. Using the directional terms introduced in Chapter 1 (Table 1.1, p. 8), describe the position of the kidneys in reference to the peritoneal cavity.

For answers, see Appendix B.

THE EMBRYONIC PERIOD

Week 1: From Zygote to Blastocyst

➤ Describe the earliest stage of development, from zygote to blastocyst (week 1).

Each month, one of a fertile woman's two ovaries releases an immature egg, called an *oocyte* **(Figure 3.3)**. This cell is normally drawn into a *uterine tube* (fallopian tube), which provides a direct route to the uterus (womb). **Fertilization** of an oocyte by a sperm generally occurs in the lateral third of the uterine tube. The fertilized oocyte, now called a **zygote** (zi′gōt; "a union"), is moved toward the uterus. Along the way, it divides repeatedly to produce two cells, then four cells, then eight cells, and so on. Because there is not much time for cell growth between divisions, the resulting cells become smaller and smaller. This early division sequence, called **cleavage,** provides the large number of cells needed as building blocks for the embryo.

About 72 hours* after fertilization, cleavage has generated a solid cluster of 12–16 cells called a **morula** (mor′u-lah; "mulberry"). During day 4, the late morula—now consisting of about 60 cells—enters the uterus. It takes up fluid, which gathers into a central cavity. This new fluid-filled structure is called a **blastocyst** (blas′to-sist; *blasto* = bud or sprout; *cyst* = bag).

Two distinct types of cells are obvious in the blastocyst stage (Figure 3.3e). A cluster of cells on one side of the blastocyst cavity is called the **inner cell mass,** and the layer of cells surrounding the cavity is called the **trophoblast** (trōf′o-blast; *tropho* = nourishment). The inner cell mass will form the embryo, and the trophoblast will help form the placenta, the structure that transfers nutrients from the mother to the fetus. This chapter focuses on the inner cell mass and the embryo; the trophoblast and placenta are discussed along with the female reproductive system in Chapter 25.

The blastocyst stage lasts about 3 days, from day 4 to day 7. For most of this time, the blastocyst floats freely in the cavity of the uterus, but on day 6, it starts to burrow into the wall of the

*All dates given for the developmental events in this chapter are *average* times. Actual dates vary by 1–2 days or more among different pregnancies.

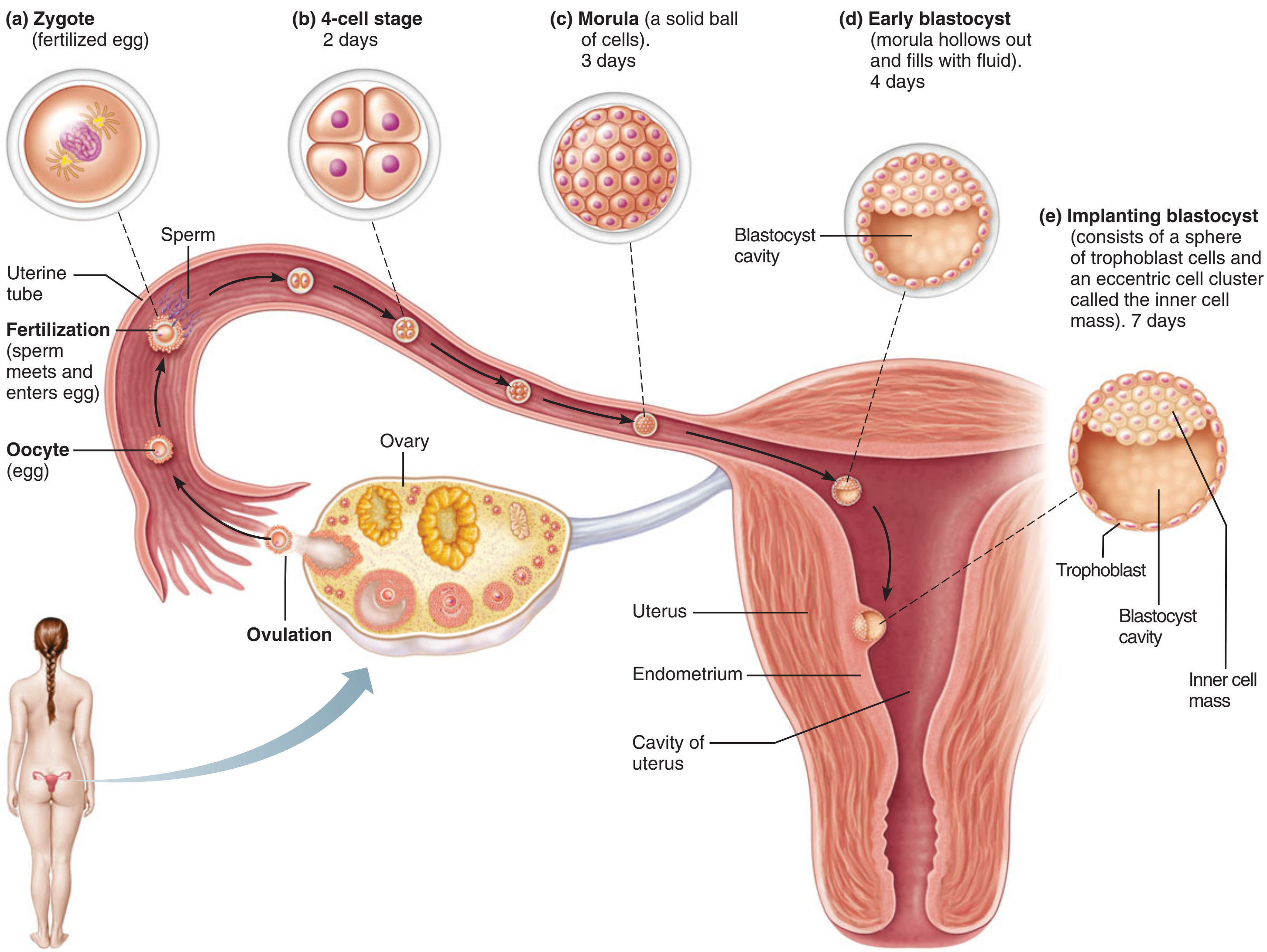


FIGURE 3.3 Fertilization and the events of the first 6 days of development. The ovary, uterus, and uterine tubes, which lie in the mother's pelvis, are shown in posterior view. An egg (oocyte) is released into the peritoneal cavity (ovulation) and taken up by the uterine tube, where it undergoes fertilization to become a zygote **(a)**. Then, as it moves through the uterine tube and into the uterus, it passes through the four-cell stage **(b)** and the morula **(c)** and blastocyst **(d)** stages. Finally, the blastocyst implants into the wall of the uterus **(e),** as shown in detail in the next figure. Parts (d) and (e) show the blastocyst cut in half to reveal the inside.

uterus (Figure 3.4). This process, called **implantation,** takes about a week to complete. In implantation, the trophoblast layer erodes inward until the entire blastocyst is embedded in the uterine wall.

In some pregnancies, the inner cell mass of a single blastocyst splits into two during the early stages of cleavage of week 1 or week 2. This produces identical twins, also called monozygotic twins (*monozygotic* = from one zygote). Worldwide, the birth rate for identical twins is approximately 4 per 1000 births.

Week 2: The Two-Layered Embryo

➤ Describe how the embryo becomes a two-layered disc (week 2).

Figure 3.4d shows the embryo about 9 days after fertilization. The inner cell mass has now divided into two sheets of cells, the **epiblast** (ep′ĭ-blast; *epi* = over, upon) and the **hypoblast** (hi′po-blast; *hypo* = under, beneath). Extensions of these cell sheets form two fluid-filled sacs (Figure 3.4d–e) resembling two balloons touching one another, with the epiblast and hypoblast at the area of contact. Together, the epiblast and hypoblast make up the **bilaminar** ("two-layered") **embryonic disc,** which will give rise to the whole body.

The sac formed by an extension of the epiblast is the *amniotic* (am″ne-ot′ik) *sac*. The outer membrane of the amniotic sac is called the **amnion,** and the internal **amniotic sac cavity** is filled with *amniotic fluid*. This fluid buffers the

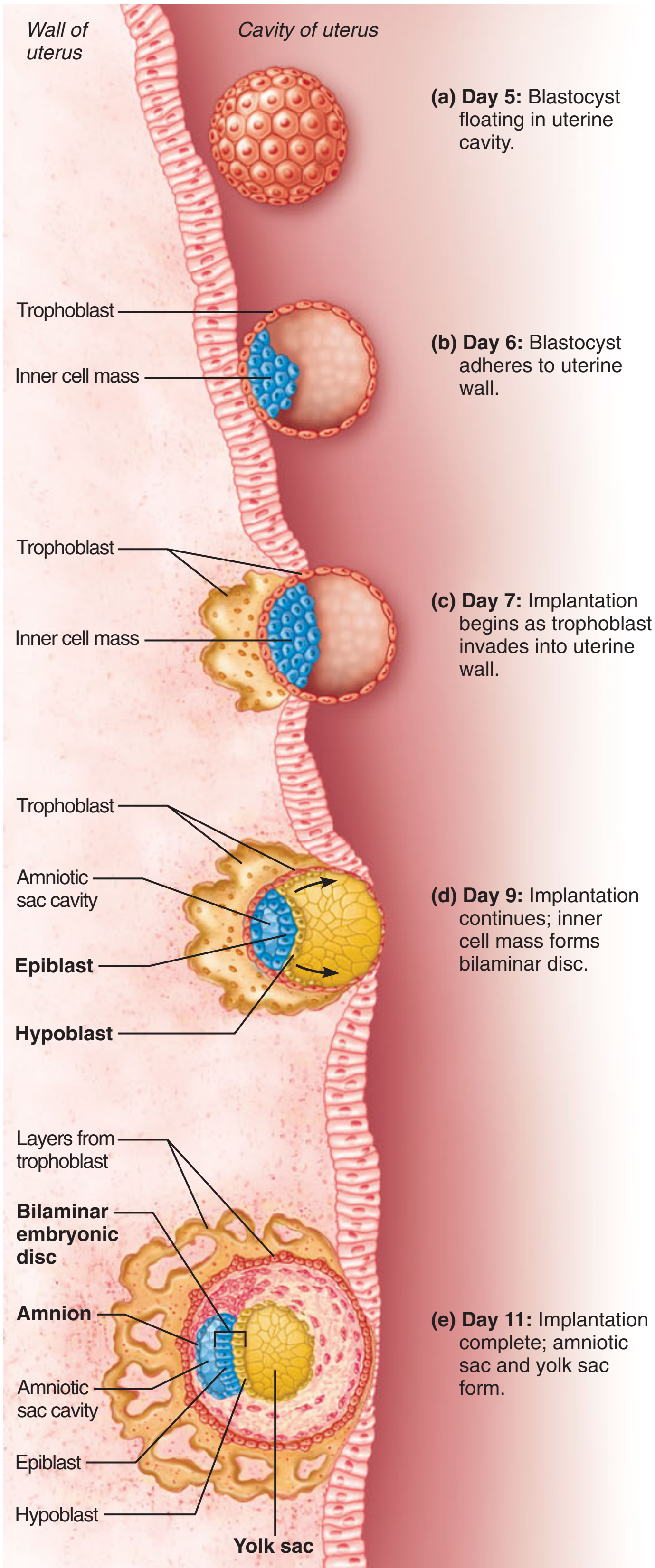


FIGURE 3.4 Implantation of the blastocyst during week 2 of development. The embryos are shown in section (cut in half).

developing embryo and fetus from physical shock until the time of birth. You may have heard the expression, "The mother's water broke just before she gave birth." This refers to the rupture of the amniotic sac and release of its amniotic fluid near the start of labor, the process that expels the mature fetus from the uterus.

The **yolk sac,** formed by an extension of the hypoblast, holds a very small amount of yolk, which is insignificant as a food source. The human yolk sac, however, is important because the digestive tube forms from part of it (see p. 55). Furthermore, tissue around the yolk sac gives rise to the earliest blood cells and blood vessels (see Chapter 18, "The Blood Throughout Life" section).

Week 3: The Three-Layered Embryo

➤ Explain gastrulation and the formation of the three germ layers (week 3).

The Primitive Streak and the Three Germ Layers

During week 3, the embryo grows from a two-layered disc to a three-layered (trilaminar) disc. This process, called **gastrulation** (gas″troo-la′shun), forms the three *primary germ* layers—ectoderm, mesoderm, and endoderm—the layers from which all body tissues develop. The germ layer begins to form on days 14–15, when a raised groove called the **primitive streak** appears on the dorsal surface of the epiblast **(Figure 3.5)**. Epiblast cells migrate inward at this streak. On days 14–15 the first cells that migrate through the primitive streak displace the cells of the underlying hypoblast to become the **endoderm.** Then, starting on day 16, the ingressing epiblast cells form a new layer between epiblast and endoderm, the **mesoderm.** The epiblast cells that remain on the embryo's dorsal surface make up the **ectoderm.** In this way, the three primary germ layers of the body are established, all derived from epiblast cells. The structures formed from each germ layer are color-coded in the figures throughout this chapter: Structures formed from ectoderm are colored blue; those derived from mesoderm are red; and structures formed from endoderm are yellow.

The three germ layers differ in their tissue structure. (Recall from Chapter 1 that a tissue is a collection of similar cells that perform a common function.) Ectoderm and endoderm are *epithelial tissues,* or *epithelia*—sheets of tightly joined cells (p. 4). Mesoderm, by contrast, is a *mesenchyme tissue* (mes′eng-kīm; *mesen* = middle; *chyme* = fluid). A mesenchyme is any embryonic tissue with star-shaped cells that do not attach to one another. Thus, mesenchyme cells are free to migrate widely within the embryo.

The Notochord

At one end of the primitive streak is a swelling called the **primitive node** (Figure 3.5e). The epiblast cells that move through the primitive node migrate straight anteriorly. These mesodermal cells, along with a few cells from the underlying endoderm, form a rod called the **notochord**

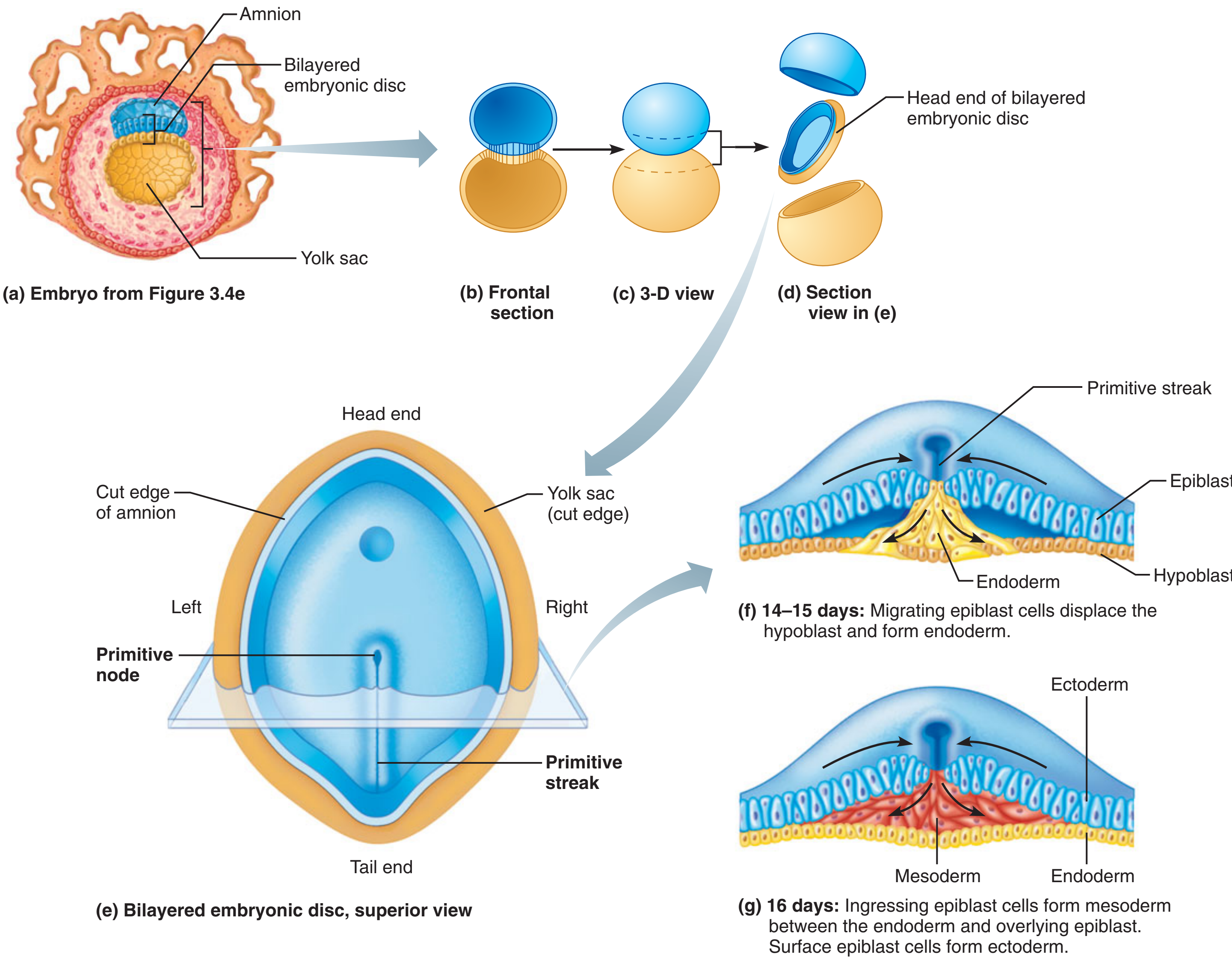


FIGURE 3.5 The primitive streak stage. Diagrams **(a)** through **(d)** show orientation of the bilaminar disc shown in (e). **(e)** The primitive streak appears on the epiblast on about day 14. **(f, g)** Sections through the embryonic disc at the location shown in (e).

(Figure 3.6a). The notochord defines the body *axis* (the midline that divides the left and right sides of the body). It extends the length of the body and is the site of the future vertebral column. The notochord appears on day 16, and by day 18 it reaches the future head region.

Neurulation

As the notochord develops, it signals the overlying ectoderm to start forming the spinal cord and brain, an event called **neurulation** (nu″roo-la′shun) (central column of Figure 3.7). Specifically, the ectoderm in the dorsal midline thickens into a **neural plate,** and then starts to fold inward as a **neural groove.** This groove deepens until a hollow **neural tube** is pinched off into the body. Closure of the neural tube begins at the end of week 3 in the region that will become the neck and then proceeds both cranially (toward the head or crown) and caudally (toward the tail or rump). Complete closure occurs by the end of week 4. The cranial part of this neural tube becomes the brain, and the rest becomes the spinal cord.

As shown in Figure 3.7b, **neural crest** cells are pulled into the body along with the invaginating neural tube. The neural crest cells originate from ectodermal cells on the lateral ridges (neural folds) of the neural plate, and they come to lie just external to the closed neural tube. The neural crest forms the sensory nerve cells and some other important structures, as described on p. 56.

The ability of one group of cells to influence the developmental direction of other cells is called **induction.** The influence of the notochord on the formation of the neural tube is an example of induction. In fact, the notochord initiates a chain reaction of inductions that continue throughout development. Disruption in any of these inductive processes can result in developmental abnormalities. The genes and molecules that signal these inductive events are currently being identified.

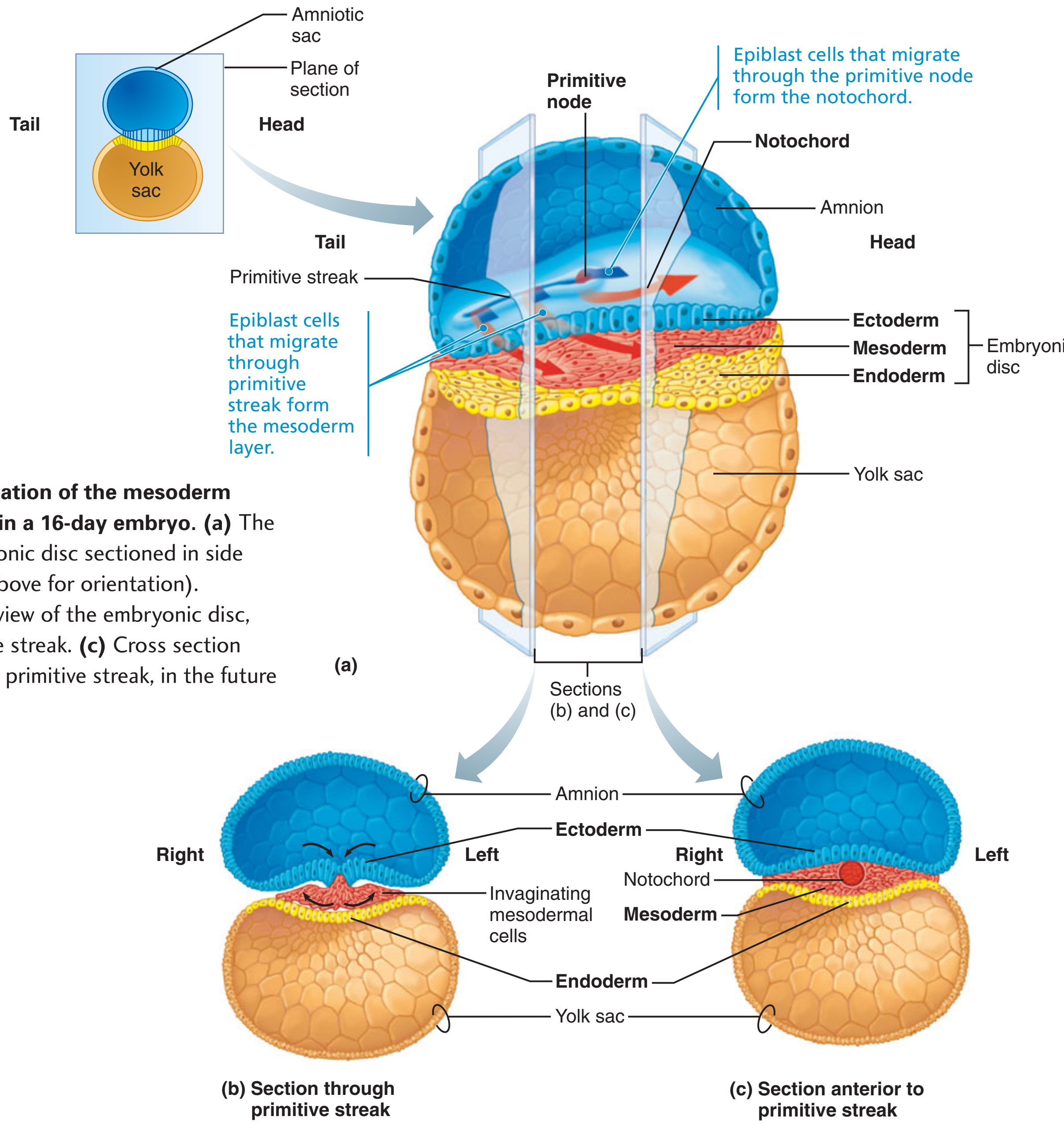


FIGURE 3.6 Formation of the mesoderm and the notochord in a 16-day embryo. (a) The three-layered embryonic disc sectioned in side view (see the inset above for orientation). **(b)** Cross-sectional view of the embryonic disc, through the primitive streak. **(c)** Cross section taken anterior to the primitive streak, in the future thorax.

NEURAL TUBE DEFECTS Neural tube defects result from failure of the neural tube to close completely. The most common neural tube defects are spina bifida and anencephaly. **Spina bifida** results when the neural tube does not close completely, causing malformation of the spinal cord, spine, and spinal nerves. Depending on the location and extent of the defect, resulting disabilities range from mild (lower body weakness and pain, bowel and bladder dysfunction) to severe (paralysis below the area of defect and complications from hydrocephalus, excessive fluid buildup on the brain). **Anencephaly** results when the neural tube fails to close in the head. The brain does not develop, and the baby is either stillborn or dies within a few hours after birth. Up to 70% of neural tube defects have been linked to low maternal levels of folic acid. It is recommended that women of childbearing age consume 400 micrograms (0.4 mg) of folic acid daily. In addition to vitamin supplementation, good sources of folic acid include green leafy vegetables, whole-grain cereals, and nuts. Taking supplements prior to pregnancy is important because the neural tube forms in the third week of development, often before a woman knows she is pregnant.

The Mesoderm Begins to Differentiate

In the middle of week 3, the mesoderm lies lateral to the notochord on both sides of the body (Figure 3.7a) and extends cranially to caudally (from head to tail, or crown to rump).

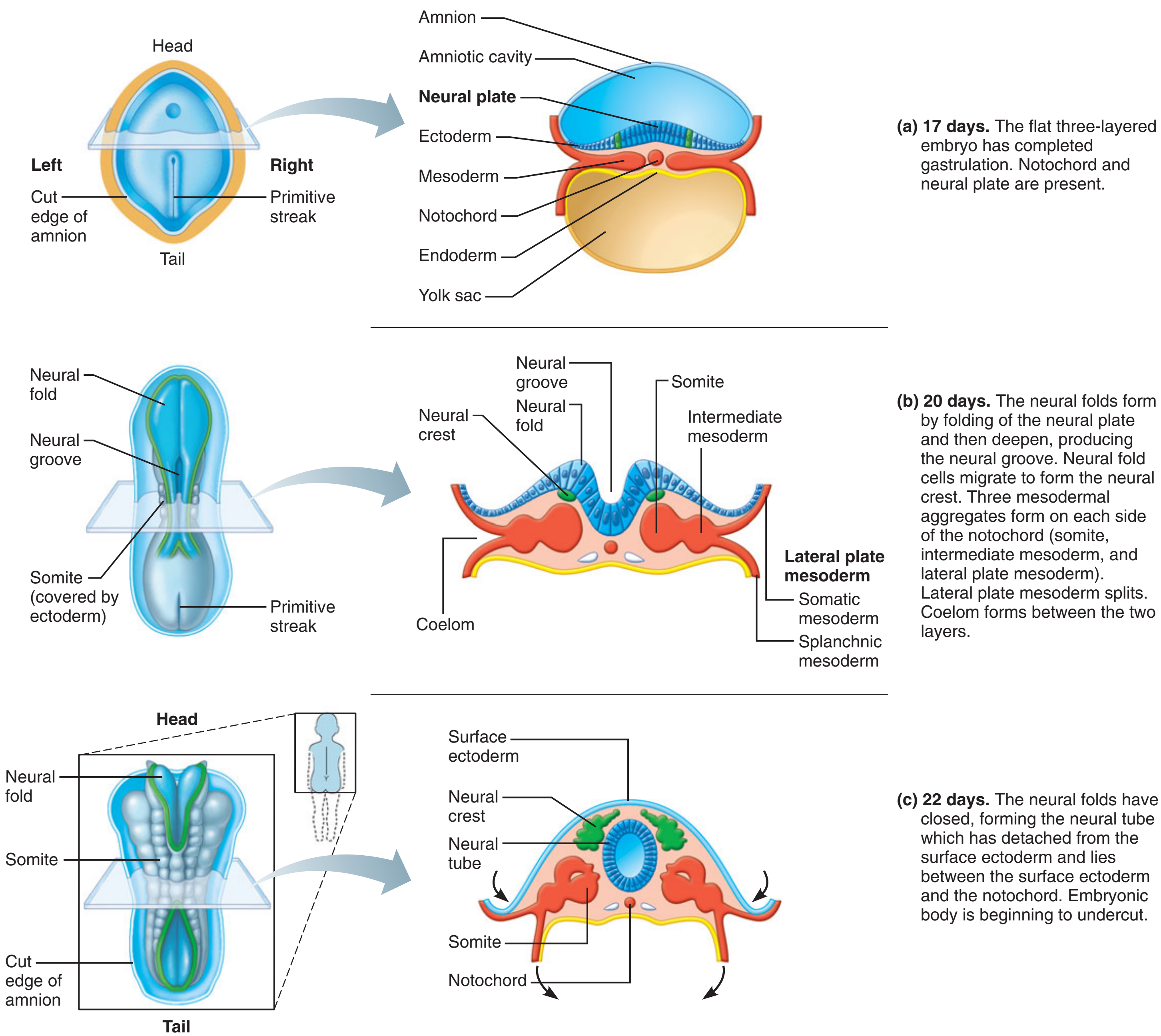


FIGURE 3.7 Neurulation and mesoderm differentiation, week 3. (a–c) At left, dorsal surface views of the embryo. At right, transverse sections through the entire embryo showing formation of the neural tube and mesoderm differentiation.

By the end of this week, the mesoderm has divided into three regions.

1. **Somites** (so′mītz; "bodies"). The mesoderm closest to the notochord begins as paraxial mesoderm (par″ak′se-al; "near the body axis"). Starting cranially and proceeding caudally, the paraxial mesoderm divides into a series of blocks called *somites* (Figure 3.7b). The somites are visible in surface view as a row of subectodermal bulges on each side of the back (see the dorsal views on the left side of Figure 3.7b and c). The somites are the first body segments, and about 40 pairs develop by the end of week 4.

2. **Intermediate mesoderm.** This begins as a continuous strip of tissue just lateral to the paraxial mesoderm. Influenced by the segmentation of the somites, the intermediate mesoderm divides into spherical segments in a cranial-to-caudal sequence (Figure 3.7b). Each segment of intermediate mesoderm attaches to a somite.

3. **Lateral plate.** This, the most lateral part of the mesoderm, never divides into segments (Figure 3.7b and c). The lateral plate begins as one layer, but soon splits into two. A wedge of space is formed between these two sheets. This space is called the **coelom** (se′lum; "cavity"). The two

resulting divisions of the lateral plate are the **somatic mesoderm** (so-mat′ik; "body"), next to the ectoderm, and the **splanchnic mesoderm** (splangk′nik; "viscera"), next to the endoderm. The coelom that intervenes between the splanchnic and somatic mesoderm will become the serous cavities of the ventral body cavity, namely the peritoneal, pericardial, and pleural cavities (see Figure 1.7).

When you compare the cross sections in Figure 3.7 with the adult body plan in Figure 3.2, you might begin to see a few similarities, especially if you match structures according to their colors. For example, the blue ectoderm becomes the epidermis of the skin, the neural tube becomes the spinal cord, and the yellow endoderm becomes the lining of the digestive tube. The main difference between the 3-week embryo and the adult body is that the embryo is still a flat disc. The three-dimensional, cylindrical body shape forms during week 4.

check your understanding

4. Describe gastrulation. During what week of embryonic development does it occur?
5. What structure induces the formation of the neural tube?
6. What type or types of mesoderm cluster into segments along the body axis?

For answers, see Appendix B.

Week 4: The Body Takes Shape

- Discuss how the body folds from a flat disc into its three-dimensional, tubular shape (week 4).
- In the week 4 embryo, clearly differentiate between the outer tube, the inner tube, and the coelom.
- List the main derivatives of ectoderm and endoderm.
- Identify the five regions of mesoderm and list the main derivatives of each region.

Folding

The embryo takes on a cylindrical shape when its sides fold medially and it lifts off the yolk sac and protrudes into the amniotic cavity **(Figure 3.8)**. This process resembles the folding of three stacked sheets of paper into a tube. At the same time, the head and tail regions fold under, as shown in Figure 3.8c. The embryonic disc bulges upward because it is growing so much faster than the yolk sac below it. Its lateral folding is caused by the fast growth of the somites. The folding at the head and tail is caused by expansion of the brain and lengthening of the spinal cord.

As a result of this folding, the embryo acquires a tadpole shape by day 24. As the embryo becomes cylindrical, it encloses a tubular part of the yolk sac, called the **primitive gut** (future digestive tube and respiratory structures: Figure 3.8d and Figure 1.5 on p. 10). This tube is lined by endoderm. The embryo remains attached to the yolk sac below by a duct located at the future navel. This duct becomes incorporated into the umbilical cord.

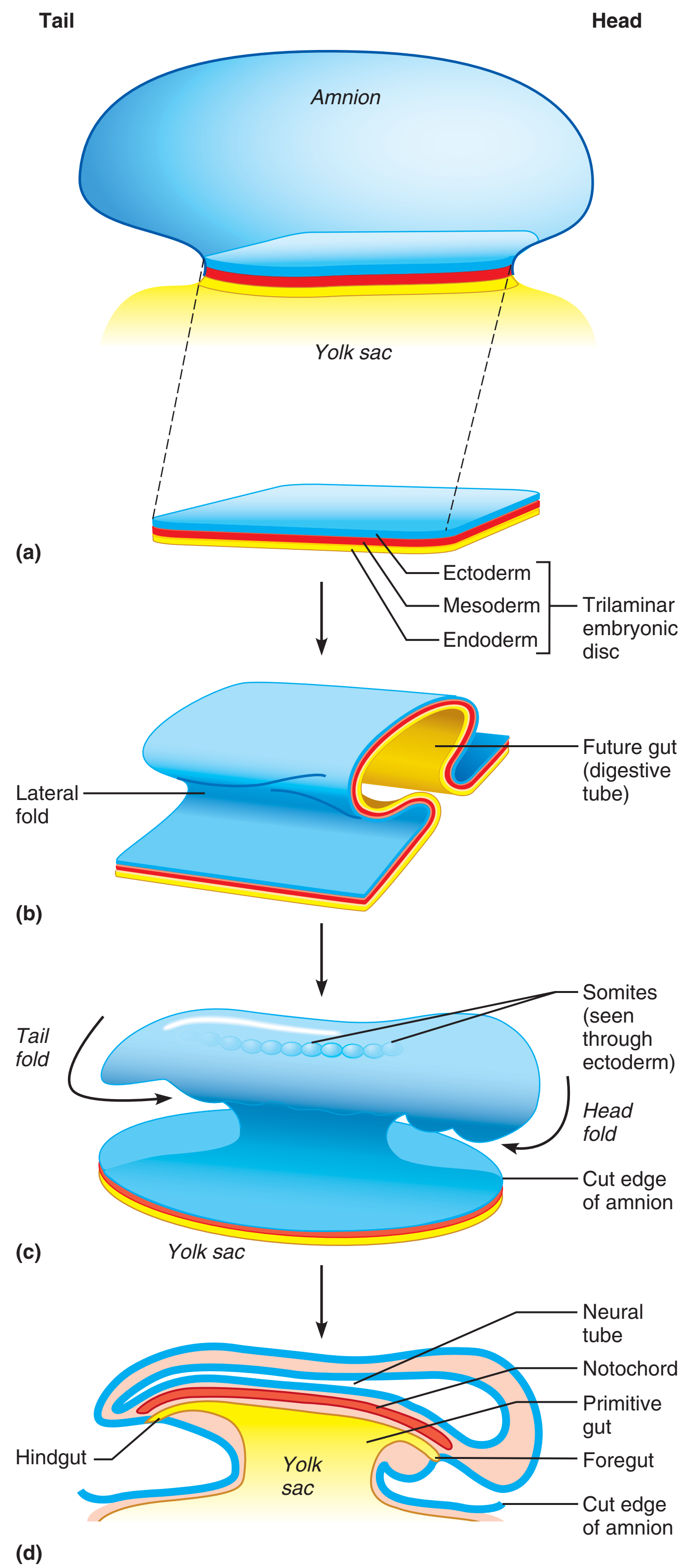


FIGURE 3.8 Folding of the embryo, lateral views. **(a)** Model of the flat three-layered embryo as three sheets of paper. **(b, c)** Folding begins with lateral folds, and then head and tail folds appear. **(d)** A 24-day embryo in sagittal section. Notice the primitive gut, which is derived from the yolk sac, and the dorsal notochord and neural tube.

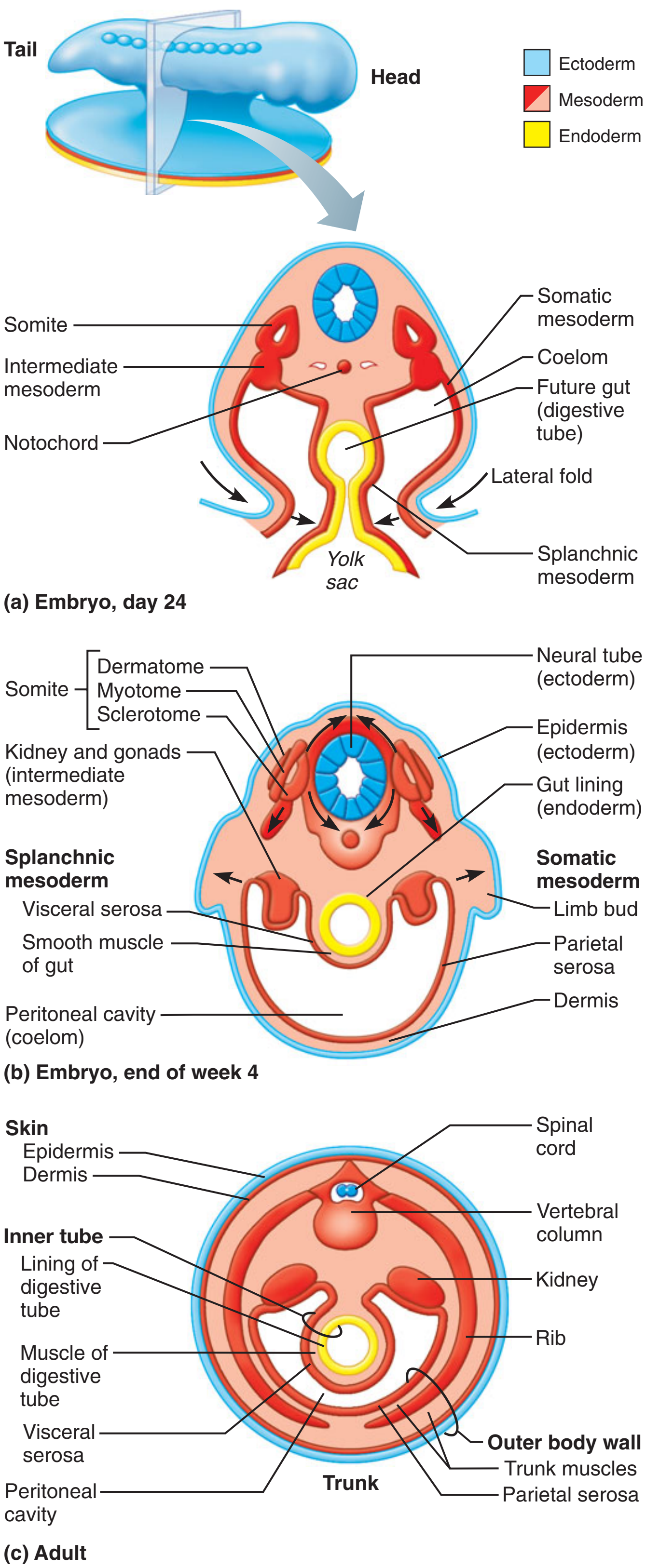


FIGURE 3.9 The germ layers in week 4 and their adult derivatives. The basic adult body plan (c) is established in week 4 (a–b). **(a)** Folding continues as the embryo forms into a cylinder and lifts up off the yolk sac. The right and left lateral folds will join ventrally. **(b)** The cylindrical human body plan on day 28. This cross section is taken from the trunk region, where the posterior limb buds (future legs) attach. **(c)** Simplified cross section through the abdomen of an adult.

Derivatives of the Germ Layers

By day 28, the basic human body plan has been attained (Figure 3.9). Figure 3.9b is a cross section through the trunk of a 1-month-old embryo, which you can compare directly to the adult body section (Figure 3.9c). This comparison will help you understand the adult derivatives of the germ layers. These derivatives are summarized in Figure 3.10.

Derivatives of Ectoderm The ectoderm becomes the brain, spinal cord, and epidermis of the skin. The early epidermis, in turn, produces the hair, fingernails, toenails, sweat glands, and the oil glands of the skin. Neural crest cells, from ectoderm, give rise to the sensory nerve cells. Furthermore, much of the neural crest breaks up into a mesenchyme tissue, which wanders widely through the embryonic body. These wandering neural crest derivatives produce such varied structures as the pigment-producing cells in the skin (melanocytes) and the bones of the face.

Derivatives of Endoderm The endoderm becomes the inner epithelial lining of the gut tube and its derivatives: the respiratory tubes, digestive organs, and the urinary bladder. It also gives rise to the secretory cells of glands that develop from gut-lining epithelium, such as the liver and pancreas.

Derivatives of the Mesoderm and Notochord The mesoderm has a complex fate, so you may wish to start by reviewing its basic parts in Figure 3.9: the somites, intermediate mesoderm, and somatic and splanchnic lateral plate mesoderm. Also note the location of the notochord.

The *notochord* gives rise to an important part of the spinal column, the springy cores of the discs between the vertebrae. These spherical centers, each called a *nucleus pulposus* (pul-po′sus), give the vertebral column some bounce as we walk.

Each of the *somites* divides into three parts (Figure 3.9b). One part is the **sclerotome** (skle′ro-tōm; "hard piece"). Its cells migrate medially, gather around the notochord and the neural tube, and produce the vertebra and rib at the associated level. The most lateral part of each somite is a **dermatome** ("skin piece"). Its cells migrate externally until they lie directly deep to the ectoderm, where they form the dermis of the skin in the dorsal part of the body. The third part of each somite is the **myotome** (mi′o-tōm; "muscle piece"), which stays behind after the sclerotome and dermatome migrate away. Each myotome grows ventrally until it extends the entire dorsal-to-ventral height of the trunk. Myotomes become the segmented trunk musculature of the body wall (Figures 1.5b and 3.10). Additionally, the ventral parts of myotomes grow into the limb buds and form the muscles of the limbs.

The *intermediate mesoderm,* lateral to each somite, forms the kidneys and the gonads. By comparing Figures 3.9b and

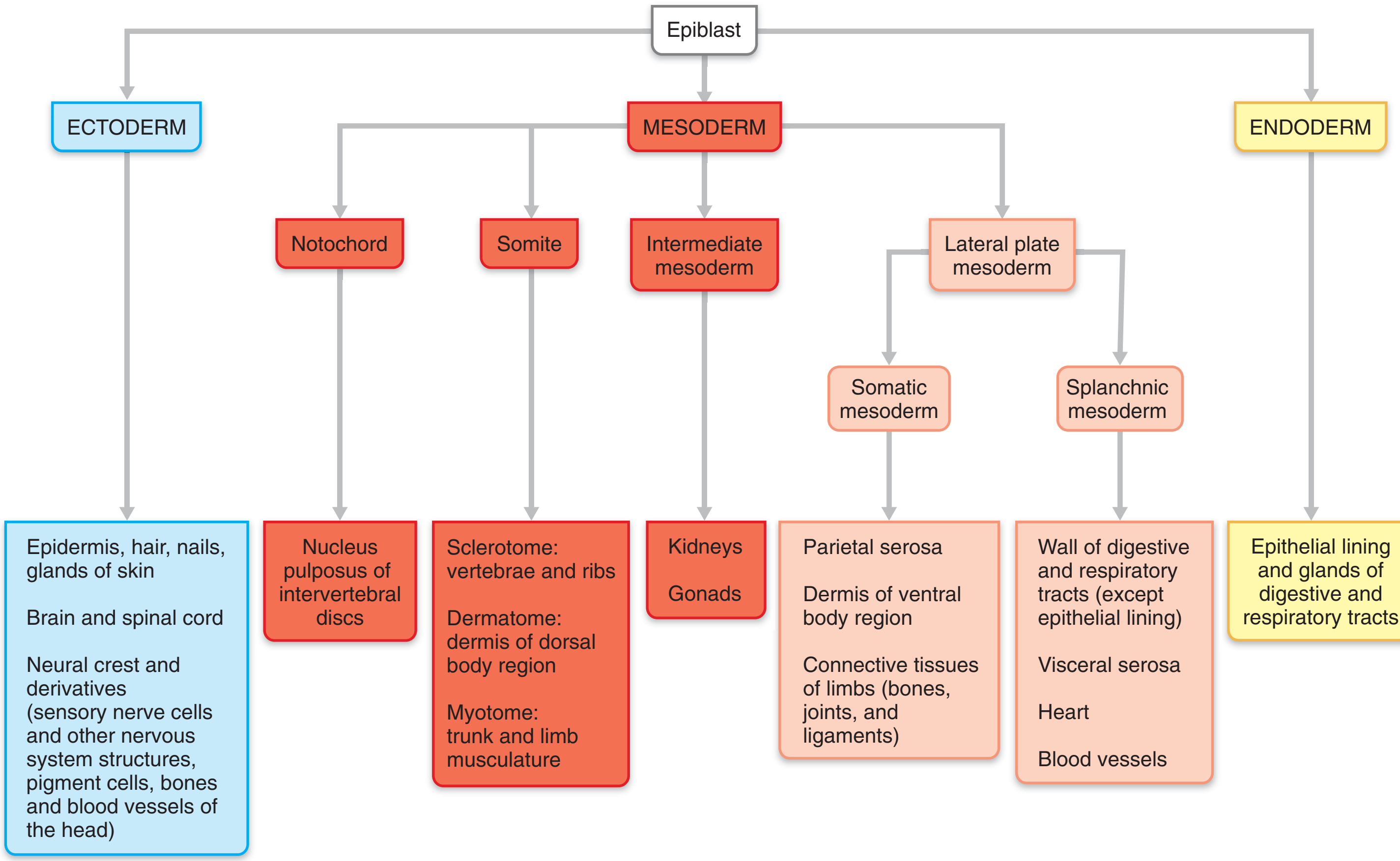


FIGURE 3.10 Flowchart showing major derivatives of embryonic germ layers.

3.9c, you can see that the intermediate mesoderm lies in the same relative location as the adult kidneys, outside the peritoneal cavity, or **retroperitoneal.**

The splanchnic and somatic lateral plate mesoderm are separated by the coelom body cavity. By now, the *splanchnic mesoderm* surrounds the endodermally derived gut tube lining (Figure 3.9b). The splanchnic mesoderm gives rise to the entire wall of the digestive and respiratory tubes, except the inner epithelial lining; that is, it forms the musculature, connective tissues, and the slippery visceral serosae of the digestive and respiratory structures. Splanchnic mesoderm also gives rise to the heart and most blood vessels.

Somatic mesoderm (Figure 3.9b), just external to the coelom, produces the parietal serosa and the dermal layer of the skin in the ventral body region. Its cells migrate into the forming limbs and produce the bone, ligaments, and dermis of each limb.

check your understanding

7. After folding takes place, what embryonic germ layer forms the outer covering of the embryo?
8. Does endoderm form the inner lining of the inner tube or the outer tube?
9. What part of the somite forms the vertebrae and ribs?
10. What does the splanchnic lateral plate mesoderm form?

For answers, see Appendix B.

Weeks 5–8: The Second Month of Embryonic Development

➤ Describe the main events of the second month of development.

Figure 3.11 shows an embryo at the start of the second month. At this time, the embryo is only about a half centimeter long. Around day 28, the first rudiments of the limbs appear as **limb buds.** The upper limb buds appear slightly earlier than the lower limb buds.

You can think of month 2 as the time when the body becomes less tadpole-like and starts to become recognizably human (see Figure 3.1). The limbs grow from rudimentary buds to fully formed extremities with fingers and toes. The head enlarges quickly and occupies almost half the volume of the entire body. The eyes, ears, and nose appear, and the face gains a human appearance as the embryonic period draws to a close. The protruding tail of the 1-month-old embryo disappears at the end of week 8. All major organs are in place by the end of month 2, at least in rudimentary form. Successive chapters discuss the development of each organ system, so you will often return to the events of month 2.

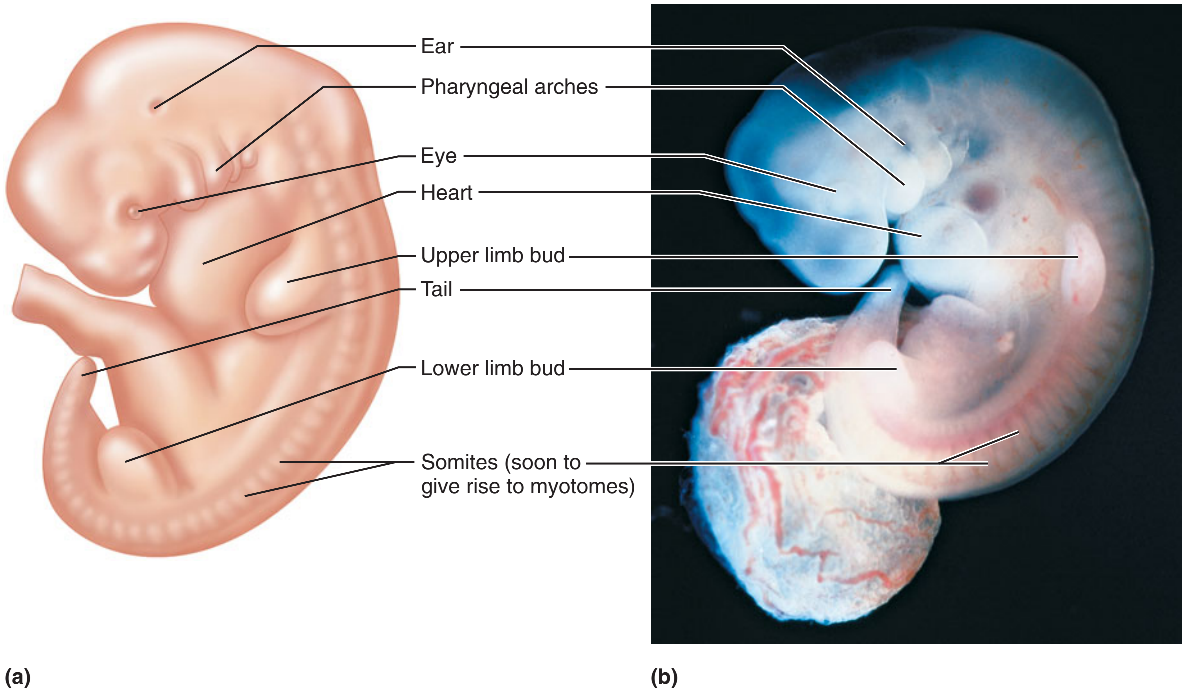
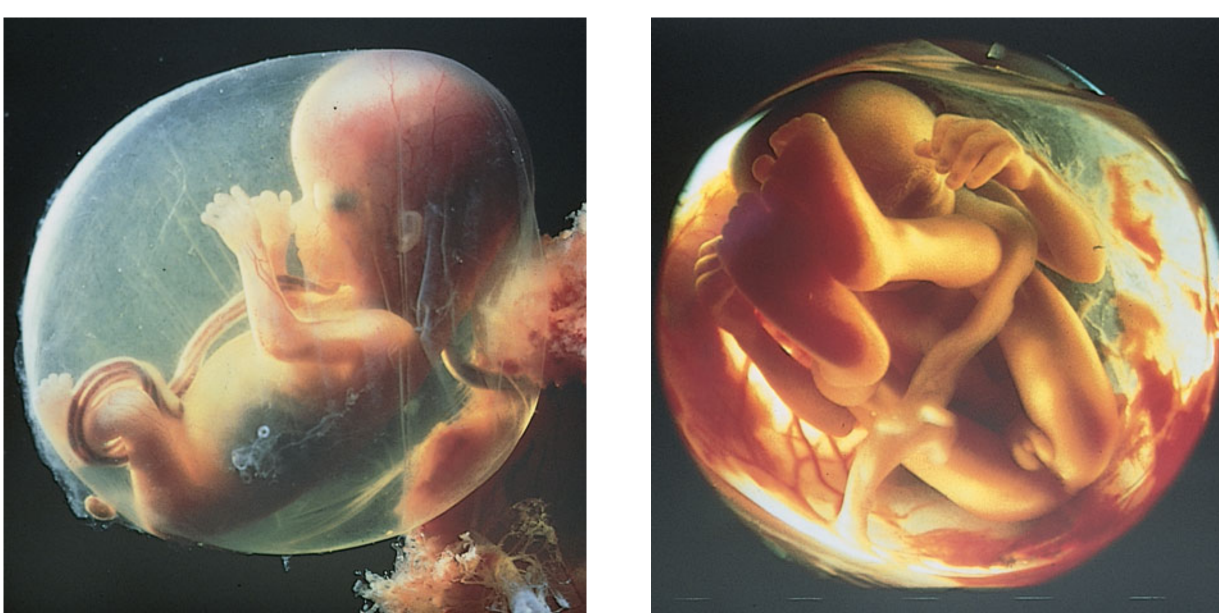


FIGURE 3.11 A 29-day embryo. (a) Diagram. **(b)** Fiber-optic photograph. Note the limb buds. Also note the segmented somites, which soon give rise to segmented myotomes.

THE FETAL PERIOD

➤ List the major events of fetal development.

The main events of the fetal period—weeks 9 through 38—are listed chronologically in **Table 3.1**. The fetal period is a time of maturation and rapid growth of the body structures that were established in the embryo. The fetal period is more than just a time of growth, however. During the first half of this period, cells are still differentiating into specific cell types to form the body's distinctive tissues and complete the fine details of body structure. The fetus at 3 months and 5 months is shown in **Figure 3.12**.

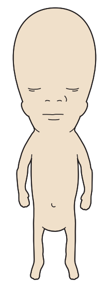
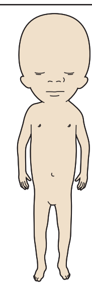
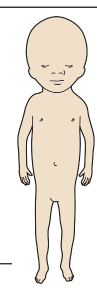
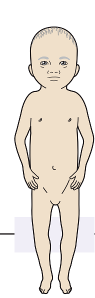


(a) Fetus in month 3, about 6 cm long

(b) Fetus late in month 5, about 19 cm long

FIGURE 3.12 Photographs of a developing fetus.

TABLE 3.1 Developmental Events of the Fetal Period

Time After Fertilization		Events
8 weeks (end of embryonic period)	 8 weeks	Eyes and ears first look human; neck region first becomes evident. All major divisions of the brain are present; first brain waves occur in brain stem. Liver is disproportionately large. Bone formation has just begun; weak muscle contractions occur. Limbs are complete; digits are initially webbed, but fingers and toes are free by end of week 8. The cardiovascular system is fully functional; the heart has been pumping blood since week 4. Approximate crown-to-rump length: 3 cm (1.2 inches); weight: 2 g (0.06 ounce).
9–12 weeks (month 3)	 12 weeks	Body is elongating; brain continues to enlarge; retina of eye is present. Skin epidermis and dermis are differentiated. Right and left halves of palate (roof of mouth) are fusing; walls of hollow visceral organs are gaining smooth muscle; intestines move into body cavity. Blood cell formation begins in bone marrow (also occurs in liver and spleen). Notochord is degenerating and bone formation is accelerating. Sex can be determined from the genitals. Approximate crown-to-rump length at end of 12 weeks: 6 cm.
13–16 weeks (month 4)	 16 weeks	Sucking motions of the lips occur, and eyes can flinch if stimulated. Body begins to outgrow head; limbs are no longer so disproportionately small. Hard palate is fused. Kidneys attain their typical structure. Most bones are now distinct, and joint cavities are apparent. Approximate crown-to-rump length at end of 16 weeks: 11 cm.
17–20 weeks (month 5)		Eyelashes and eyebrows are present; a fatty skin secretion covers the body; silklike hair, called lanugo, covers the skin. Quickening occurs (mother feels fetus moving). Body first bends forward into the fetal position because of space restrictions in the uterus. Limbs achieve near-final proportions. Rapid brain growth begins; hearing is functioning. Approximate crown-to-rump length at end of 20 weeks: 16 cm.
21–30 weeks (months 6 and 7)		Body size and weight substantially increase; eyes open. Fingernails and toenails are complete. Skin is wrinkled and red; the fatty layer under the skin (hypodermis) is just starting to gain fat, so body is lean. Bone marrow becomes the only site of blood cell formation. Cerebrum grows; convolutions develop on brain surface. Testes reach the scrotum in month 7 (males). Lungs develop. Approximate crown-to-rump length at end of 30 weeks: 38 cm.
30–38 weeks (months 8 and 9)	At birth	Fat accumulates in hypodermis below skin. Approximate crown-to-rump length at end of 38 weeks: 47 cm; weight 2.7–4.5 kg (6–10 pounds).

a closer look

Focus on Birth Defects

About 3% of all newborns exhibit a significant birth defect, or **congenital abnormality** (*congenital* = present at birth). This figure increases to 6% by 1 year of age, when initially unrecognized conditions become evident.

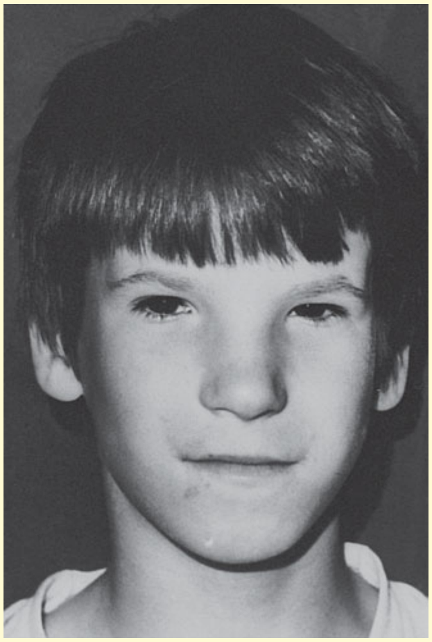
Birth defects have many causes, including defective chromosomes or genes, exposure to chemicals and harmful radiation, and viruses passed from the mother to the embryo. Chemical, physical, and biological factors that disrupt development and cause birth defects are called **teratogens** (ter′ah-to-jenz; "monster formers"). Teratogens include many drugs, some organic solvents and pollutants, toxic metals, various forms of radiation such as X rays, and infectious agents, particularly rubella (German measles). Although many teratogens have been identified, it must be emphasized that most birth defects cannot be traced to any known teratogen or genetic disorder. Most are caused by several factors.

When a pregnant woman drinks alcohol, she increases the likelihood of birth defects. Excessive alcohol consumption produces **fetal alcohol syndrome (FAS),** typified by microcephaly (small head and jaw), growth deficiencies, and distinctive facial features (see photo). FAS is the most common nonhereditary cause of mental retardation in the United States. Among the children of women who drink heavily, the incidence of severe FAS is 6%, and a milder form called *fetal alcohol effect* is even more common. There is now evidence that even moderate drinking, one to three drinks per day, adversely affects the development of the brain, lessening the child's ability to learn and remember. Therefore, physicians advise pregnant women to avoid alcohol entirely.

Some prescription drugs can cause catastrophic birth defects. Thalidomide, for example, was used as a sedative and to relieve morning sickness by many pregnant women in Europe from 1958 to 1962. When taken during the period of limb differentiation (days 24–36), it sometimes resulted in tragically deformed infants with short, flipper-like limbs. Similarly, a drug called diethylstilbestrol (DES) was commonly given to pregnant women from the 1940s to 1970, because it was wrongly thought to prevent miscarriages. Instead, it caused cancer of the vagina and uterus in daughters exposed to DES in the womb.

An expectant mother must be particularly careful of her health and chemical intake during the third to eighth weeks after conception. It is easy to understand why weeks 3–8 are the "danger period": Insults delivered *before* week 3 tend to destroy critical early cell lines so that development cannot proceed, and a natural abortion occurs. After week 8, almost all organs are already in place, so teratogens may produce only minor malformations. However, this does not mean that the subsequent fetal period is risk-free; exposure of the fetus to teratogens can still impair body growth and organ functions, produce abnormalities of the eyes, and lead to mental retardation.

Surprisingly, most human embryos die in the womb. About 15% to 30% of all fertilized zygotes are never implanted in the uterus, either because they have lethal chromosomal defects or the uterine wall is unprepared to receive them. Among implanted embryos, about one-third are so malformed that they die, most often during week 2 or 3. Smaller numbers are miscarried later in development. Overall, at least half of all fertilized ova fail to produce living infants—some studies say 75%. We fail to realize how many embryos die because those lost in the first 2 weeks are shed without notice in the next menstrual flow. Perhaps this great loss of embryos is a biological screening process that promotes the birth of healthy offspring.



A child with fetal alcohol syndrome, the most common preventable cause of mental retardation in the United States. Typical features are unusually shaped eyes and lips (including a thin upper lip), short nose, receding chin, problems with vision and hearing, and possible heart defects. Behavioral traits include difficulties with learning, attention, problem solving, and memory, as well as problems with mental health and social interaction.

Normal births typically occur 38 weeks after conception. A **premature birth** is one that occurs before that time. Infants born as early as week 30 (7 months) usually survive without requiring life-saving measures. Medical technology can save many fetuses born prematurely, sometimes as early as 22 weeks (in month 6). However, the lungs of premature infants are not fully functional, and death may result from respiratory distress (see Chapter 22, the section "Respiratory Distress Syndrome," for more details). Among those that survive, rates of visual problems and mental retardation are elevated.

check your understanding

11. Why is respiratory distress common in babies born in their sixth or seventh month of gestation?

For the answer, see Appendix B.

RELATED CLINICAL TERMS

ABORTION (*abort* = born prematurely) Premature removal of the embryo or fetus from the uterus. Abortions can be spontaneous (resulting from fetal death) or induced.

AMNIOCENTESIS (am″ne-o-sen-te′sis; "puncture of the amnion") A procedure for obtaining a sample of amniotic fluid. A needle is inserted through the abdominal and uterine walls, and a small amount of amniotic fluid is obtained. Shed cells from the fetus can be studied for chromosomal and genetic abnormalities, and chemicals in the fluid can reveal other disorders. Conditions such as Down syndrome and spina bifida can be diagnosed. The procedure can be performed as early as week 11 of pregnancy.

CONJOINED (SIAMESE) TWINS Identical twins that are born joined together. This phenomenon is caused by incomplete division of the inner cell mass or embryonic disc during the twinning process. The twins may be joined at any body region and often share organs. Some can be separated successfully by surgery.

ECTOPIC PREGNANCY (ek-top′ik) (*ecto* = outside) A pregnancy in which the embryo implants itself in any site other than in the uterus. Ectopic pregnancy can occur in the body wall or on the outside of the uterus, but it usually occurs in a uterine tube, a condition known as a tubal pregnancy. Because the uterine tube is unable to establish a placenta or accommodate growth, it ruptures unless the condition is diagnosed early. If rupture occurs, internal bleeding may threaten the woman's life. For obvious reasons, ectopic pregnancies almost never result in live births.

TERATOLOGY (ter″ah-tol′o-je) (*terato* = a monster; *logos* = study of) The study of birth defects and of fetuses with congenital deformities.

CHAPTER SUMMARY

1. The study of the 38-week prenatal period is called embryology. Embryology helps one understand the basic organization of the human body, as well as the origin of birth defects. (Congenital abnormalities are considered in the box on p. 60).

Stages of Prenatal Development (p. 48)

2. The embryonic period, during which the basic body plan is established, is the first 8 weeks of prenatal development. The fetal period, primarily a time of growth and maturation, is the remaining 30 weeks.

The Basic Body Plan (pp. 48–49)

3. Basic features of the adult body that are established in the embryonic period include the skin, trunk muscles, vertebral column, spinal cord and brain, digestive and respiratory tubes, serous cavities (peritoneal, pleural, and pericardial cavities), heart, kidneys, gonads, and limbs (see Figure 3.2).

The Embryonic Period (pp. 49–57)

Week 1: From Zygote to Blastocyst (pp. 49–50)

4. After fertilization occurs in the uterine tube, the zygote undergoes cleavage (early cell division without growth) to produce a solid ball of cells called the morula. Around day 4, the morula enters the uterus.

5. The morula gains an internal blastocyst cavity and becomes a blastocyst, which consists of an inner cell mass and a trophoblast. The inner cell mass becomes the embryo, and the trophoblast forms part of the placenta. The blastocyst is implanted in the uterine wall from about day 6 to day 13.

Week 2: The Two-Layered Embryo (pp. 50–51)

6. By day 7, the inner cell mass has formed two touching sheets of cells, the epiblast and hypoblast. These layers form the bilaminar embryonic disc.

7. The amniotic sac, whose wall is an extension of the epiblast, contains amniotic fluid that buffers the growing embryo from physical trauma. The yolk sac, whose wall is an extension of the hypoblast, later contributes to the digestive tube. The earliest blood cells and blood vessels form from tissue around the yolk sac.

Week 3: The Three-Layered Embryo (pp. 51–55)

8. At the start of week 3, gastrulation occurs. The primitive streak appears on the posterior part of the epiblast layer. Epiblast cells migrate through the primitive streak to form the endoderm and mesoderm. The embryonic disc now has three layers—ectoderm, mesoderm, and endoderm—all derived from epiblast.

9. Ectoderm and endoderm are epithelial tissues (sheets of closely attached cells). Mesoderm, by contrast, is a mesenchyme tissue (embryonic tissue with star-shaped, migrating cells that remain unattached to one another).

10. The primitive node, at the anterior end of the primitive streak, is the site where the notochord originates. The notochord defines the longitudinal body axis and later forms each nucleus pulposus of the vertebral column.

11. The notochord signals the overlying ectoderm to fold into a neural tube, the future spinal cord and brain. This infolding carries other ectoderm cells, neural crest cells, into the body.

12. By the end of week 3, the mesoderm on both sides of the notochord has condensed into three parts. These are, from medial to lateral, somites (segmented blocks that derive from nonsegmented paraxial mesoderm), intermediate mesoderm (segmented balls), and the lateral plate (an unsegmented layer). The coelom divides the lateral plate into somatic and splanchnic mesoderm layers.

Week 4: The Body Takes Shape (pp. 55–57)

13. The flat embryo folds inward at its sides and at its head and tail, taking on a tadpole shape. As this occurs, a tubular part of the yolk sac becomes enclosed in the body as the primitive gut.

14. The basic body plan is attained as the body achieves this tadpole shape, as you can see by comparing Figure 3.9b and c. The major adult structures derived from ectoderm, endoderm, and mesoderm are summarized in Figure 3.10.

15. The limb buds appear at the end of week 4.

Weeks 5–8: The Second Month of Embryonic Development (p. 57)

16. All major organs are present by the end of month 2. During this month, the embryo becomes less tadpole-like and recognizably human as the eyes, ears, nose, and limbs form.

The Fetal Period (pp. 58–61)

17. Most cell and tissue differentiation is completed in the first months of the fetal period. The fetal period is a time of growth and maturation of the body.

18. The main events of the fetal period are summarized in Table 3.1.

REVIEW QUESTIONS

Multiple Choice/Matching Questions

For answers, see Appendix B.

1. Indicate whether each of the following relates to (a) cleavage or (b) events at the primitive streak.

____ **(1)** period when a morula forms

____ **(2)** period when the notochord forms

____ **(3)** period when the three embryonic germ layers appear

____ **(4)** period when individual cells become markedly smaller

2. The outer layer of the blastocyst, which attaches to the uterine wall, is the (a) yolk sac, (b) trophoblast, (c) amnion, (d) inner cell mass.

3. Most birth defects can be traced to disruption of the developmental events during this part of the prenatal period: (a) first 2 weeks, (b) second half of month 1 and all of month 2, (c) month 3, (d) end of month 4, (e) months 8 and 9.

4. The primary germ layer that forms the trunk muscles, heart, and skeleton is (a) ectoderm, (b) endoderm, (c) mesoderm.

5. Match each embryonic structure in column B with its adult derivative in column A.

Column A	Column B
____ **(1)** kidney	**(a)** notochord
____ **(2)** peritoneal cavity	**(b)** ectoderm (not neural tube)
____ **(3)** pancreas secretory cells	**(c)** intermediate mesoderm
____ **(4)** parietal serosa	**(d)** splanchnic mesoderm
____ **(5)** nucleus pulposus	**(e)** sclerotome
____ **(6)** visceral serosa	**(f)** coelom
____ **(7)** hair and epidermis	**(g)** neural tube
____ **(8)** brain	**(h)** somatic mesoderm
____ **(9)** ribs	**(i)** endoderm

6. Match each date in column B (approximate time after conception) with a developmental event or stage in column A.

Column A	Column B
____ **(1)** blastocyst	**(a)** 38 weeks
____ **(2)** implantation occurs	**(b)** 15 days
____ **(3)** first few somites appear	**(c)** 4–7 days
____ **(4)** flat embryo becomes cylindrical	**(d)** about 21 days
____ **(5)** embryo/fetus boundary	**(e)** about 21–24 days
____ **(6)** birth	**(f)** about 60 days
____ **(7)** primitive streak appears	**(g)** days 6–13

7. It is currently possible to save some premature babies born as early as week (a) 8, (b) 16, (c) 22, (d) 38, (e) 2.

8. Somites are evidence of (a) a structure from ectoderm, (b) a structure from endoderm, (c) a structure from lateral plate mesoderm, (d) segmentation in the human body.

9. Which of the following embryonic structures are segmented? (More than one is correct.) (a) intermediate mesoderm, (b) lateral plate, (c) endoderm, (d) myotomes.

10. Endoderm gives rise to (a) the entire digestive tube, (b) the skin, (c) the neural tube, (d) the kidney, (e) none of these.

11. When it is 1.5 months old, an average embryo is the size of (a) the figure of Lincoln on a penny, (b) an adult fist, (c) its mother's nose, (d) the head of a common pin.

12. Gastrulation is the (a) formation of three germ layers by the epiblast at the primitive streak, (b) formation of the placenta, (c) same as cleavage, (d) folding of the gut into a tube during week 4.

13. The epiblast forms (a) only the ectoderm, (b) the yolk sac, (c) only the mesoderm and ectoderm, (d) all three primary germ layers.

14. The limbs develop during the (a) start of the second month, (b) start of the second trimester, (c) start of the second week, (d) start of the fetal period.

15. The notochord develops from (a) ectoderm, (b) neural crest, (c) mesoderm, (d) endoderm.

16. The fetal period is (a) from weeks 9–38, (b) the time of rapid growth of body organs, (c) a time of cell differentiation, (d) all of the above, (e) none of the above.

Short Answer Essay Questions

17. What important event occurs at the primitive streak? At the primitive node?

18. What is the function of the amniotic sac and the fluid it contains?

19. (a) What is mesenchyme? (b) How does it differ from epithelium?

20. Explain how the flat embryonic disc takes on the cylindrical shape of a tadpole.

21. In anatomy lab, Thaya pointed to the vertebrae of a cadaver and said "sclerotome." He pointed to a kidney and said, "intermediate mesoderm," to the biceps muscle in the arm and said, "splanchnic mesoderm," to the inner lining of the stomach and said, "endoderm," and to the brain and said, "ectoderm." Point out Thaya's *one* mistake.

22. Recently, the neural crest has generated much scientific interest because it is the one embryonic tissue that is unique to vertebrate animals. List some adult structures that develop from the neural crest.

23. Many embryonic events first occur cranially, then proceed caudally. Give three examples of structures that develop craniocaudally.

24. Define induction, and give one example of an inductive interaction.

25. Differentiate the outer tube from the inner tube. Identify three structures that are located in the outer tube and three that are located in the inner tube.

26. Before Delta studied embryology in her anatomy course, she imagined a developing human as a shapeless mass of indistinct tissues until about halfway through pregnancy. Was Delta correct? At what stage does the embryo or fetus really start to look like a developing human?

CRITICAL REASONING & CLINICAL APPLICATION QUESTIONS

1. A friend in your dormitory, a freshman, tells you that she just discovered she is 3 months pregnant. You know that since she came to college she has been experimenting with recreational drugs. Circle the best advice you could give her, and explain your choice. (a) She must stop taking the drugs, but they could not have affected her fetus during these first few months of her pregnancy. (b) Harmful substances usually cannot pass from mother to embryo, so she can keep using drugs. (c) There could be defects in the fetus, so she should stop using drugs and visit a doctor as soon as possible. (d) If she has not taken any drugs in the last week, she is OK.

2. Insufficient folic acid in the early weeks of pregnancy can result in neural tube deficits in the developing embryo. Why is it important that a woman take folic acid supplements prior to becoming pregnant?

3. Your cat finds a large ball of string and starts eating it unbeknownst to you. When you discover him, he has string extending from both his mouth and his anus. What primary germ layer(s) is the string in contact with as it passes through the cat?

4. When is the earliest time the sex of a fetus can be determined using ultrasound examination?