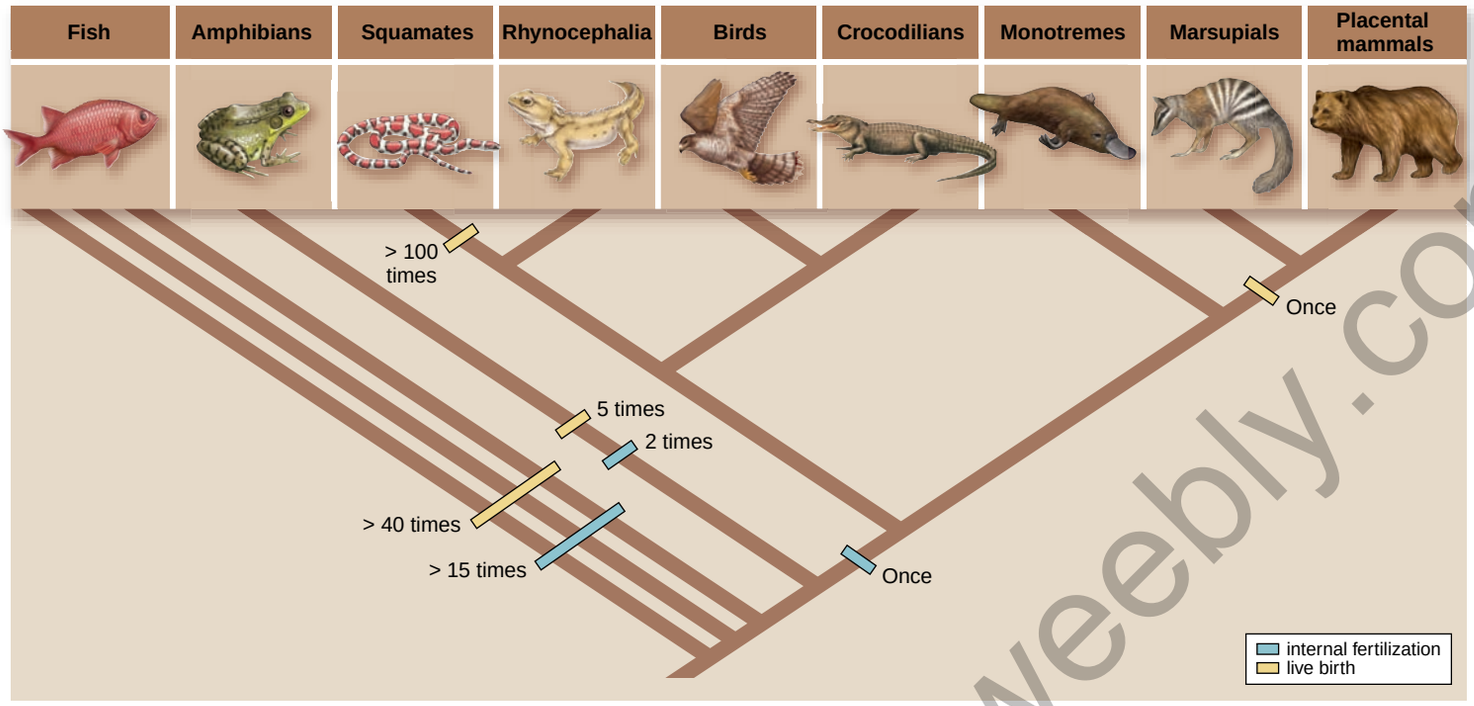


Figure 53.5 Evolution of internal fertilization and live birth in vertebrates. Although live birth has evolved many times in fishes and squamate reptiles, most species in both groups lay eggs. Evolutionary reversal from live birth to egg-laying has occurred very rarely, if at all. Estimates of the number of origins in fishes and squamates is based on detailed phylogenetic analyses within each group; uncertainty in numbers is a result of incomplete information in some groups.

Inquiry question

Why do you think that egg-laying rarely evolves from live-bearing?

each side—in snakes and lizards. Moreover, intromittent organs have been lost entirely in birds and rhynchocephalians; to achieve internal fertilization, males and females of these species simply align their cloacae and pass the sperm from male to female.

Most fishes and amphibians have external fertilization

Most fishes and amphibians, unlike other vertebrates, reproduce by means of external fertilization, although internal fertilization has arisen many times.

Fishes

Fertilization in most species of bony fish (teleosts) is external, and the eggs contain only enough yolk to sustain the developing embryo for a short time. After the initial supply of yolk has been exhausted, the young fish must seek its food from the waters around it. Development is speedy, and the young that survive mature rapidly. Although thousands or even millions of eggs are fertilized in a single mating, many of the resulting individuals succumb to microbial infection or predation, and few grow to maturity.

In marked contrast to the bony fish, fertilization in most cartilaginous fish is internal. Development of the young is generally viviparous, and the female usually gives birth to few, well-developed offspring.

Amphibians

The life cycle of amphibians is still tied to the water. Fertilization is external in most amphibians. Gametes from both males and females are released through the cloaca. Among the frogs and toads, the male grasps the female and discharges fluid containing the sperm onto the eggs as the female releases them into the water (figure 53.6).

Although the eggs of most amphibians develop in the water, there are some interesting exceptions (figure 53.7). In some frogs, for example, the eggs develop in the back of the parents; in others, males carry around the tadpoles in their vocal sacs, and the young frogs leave through their parents' mouths.

Reptiles and birds have internal fertilization

All birds and about 80% of reptile species are oviparous. After the eggs are fertilized internally, they are deposited outside the mother's body to complete their development.

Figure 53.6 The eggs of frogs are fertilized externally. When frogs mate, the clasp of the male induces the female to release a large mass of mature eggs, over which the male discharges his sperm.

Figure 53.8 Crested penguins incubating their egg. This nesting pair is changing the parental guard in a stylized ritual.

Reptiles

Most oviparous reptiles lay eggs and then abandon them. These eggs are surrounded by a leathery shell that is deposited as the egg passes through the oviduct, the part of the female reproductive tract leading from the ovary. Other species of reptiles are ovoviviparous, forming eggs that develop into embryos within the body of the mother, and some species are viviparous.

Birds

All birds practice internal fertilization, though most male birds lack a penis (some, including swans, geese, and ostriches, have modified the wall of the cloaca wall to serve as an intromittent organ).

As the egg passes along the oviduct, glands secrete albumin proteins (the egg white) and the hard, calcareous shell that distinguishes bird eggs from reptilian eggs. Although modern reptiles are ectotherms, birds are endotherms (see chapter 43); therefore, most birds incubate their eggs after laying them to keep them warm (figure 53.8). The young that hatch from the eggs of most bird species are unable to survive unaided because their development is still incomplete. These young birds are fed and nurtured by their parents, and they grow to maturity gradually.

The shelled eggs of reptiles and birds constitute one of the most important adaptations of these vertebrates to life on land. As described in chapter 35, these eggs are known as *amniotic eggs* because the embryo develops within a fluid-filled cavity surrounded by a membrane called the *amnion*. Other extraembryonic membranes in amniotic eggs include the *chorion*, which lines the inside of the eggshell, the *yolk sac*, and the *allantois*. Together, these extraembryonic membranes in combination with the external calcareous shell help form a desiccation-resistant egg that can be laid in dry places. In

a. *b.* *c.* *d.*

Figure 53.7 Different ways young develop in frogs. ***a.*** In poison arrow frogs (family Dendrobatidae), the male carries the tadpoles on his back. ***b.*** In the female Surinam toad *(Pipa pipa)*, froglets develop from eggs in special brooding pouches on the back. ***c.*** In the South American pygmy marsupial frog *(Flectonotus pygmaeus)*, the female carries the developing larvae in a pouch on her back. ***d.*** Tadpoles of the Darwin's frog *(Rhinoderma darwinii)* develop into froglets in the vocal pouch of the male and emerge from the mouth.

contrast, the eggs of fish and amphibians contain only one extraembryonic membrane, the yolk sac, and must be deposited in an aquatic habitat to keep from drying out.

The viviparous mammals, including humans, also have extraembryonic membranes, as described in the following chapter.

Mammals generally do not lay eggs, but give birth to their young

Some mammals are seasonal breeders, reproducing only once a year, while others have more frequent reproductive cycles. Among the latter, the females generally undergo the reproductive cycles, and the males are more constant in their reproductive capability.

Female reproductive cycles

Cycling in females involves the periodic release of a mature ovum from the ovary in a process known as *ovulation*. Most female mammals are "in heat," or sexually receptive to males, only around the time of ovulation. This period of sexual receptivity is called **estrus,** and the reproductive cycle is therefore called an estrous cycle. Reproductive cycles continue in females until they become pregnant.

In the estrous cycle of most mammals, changes in the secretion by the anterior pituitary gland of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) cause changes in egg cell development and hormone secretion in the ovaries (see chapter 46). Humans and apes have menstrual cycles that are similar to the estrous cycles of other mammals in their pattern of hormone secretion and ovulation. Unlike mammals with estrous cycles, however, human and ape females bleed when they shed the inner lining of their uterus, a process called **menstruation,** and they may engage in copulation at any time during the cycle.

Rabbits and cats differ from most other mammals in that they are induced ovulators. Instead of ovulating in a cyclic fashion regardless of sexual activity, the females ovulate only after copulation, as a result of a reflex stimulation of LH secretion.

Monotremes, marsupials, and placental mammals

The most primitive mammals, the **monotremes** (consisting solely of the duck-billed platypus and the echidna), are oviparous, like the reptiles from which they evolved. They incubate their eggs in a nest (figure 53.9*a*) or specialized pouch, and the young hatchlings obtain milk from their mother's mammary glands by licking her skin (because monotremes lack nipples).

All other mammals are viviparous and are divided into two subcategories based on how they nourish their young. The **marsupials,** a group that includes opossums and kangaroos, give birth to small, fetuslike offspring that are incompletely developed. The young complete their development in a pouch of their mother's skin, where they can obtain nourishment from nipples of the mammary glands (figure 53.9*b*).

The placental mammals (figure 53.9*c*) retain their young for a much longer period of development within the mother's uterus. The fetuses are nourished by a structure known as the placenta, which is derived from both an extraembryonic membrane (the chorion) and the mother's uterine lining. Because the fetal and maternal blood vessels are in very close proximity in the placenta, the fetus can obtain nutrients by diffusion from the mother's blood. The functioning of the placenta is discussed in more detail in chapter 54.

Learning Outcomes Review 53.2

Oviparous species lay eggs; the amniotic eggs of reptiles and birds protect the embryo from dessication. Females of ovoviviparous species retain fertilized eggs inside their bodies and release fully developed young when eggs hatch. Most mammals are viviparous, giving birth to young that have been nourished by the mother's body. Internal fertilization allows embryos to develop inside the female's body, leading to greater reproductive success.

- ***Under what circumstances would an estrous cycle be advantageous?***

a.

b.

c.

Figure 53.9 Reproduction in mammals. ***a.*** Monotremes lay eggs in a nest, such as the duck-billed platypus *(Ornithorhynchus anatinus)* shown here with newly hatched offspring. ***b.*** Marsupials, such as this red kangaroo *(Macropus rufus)*, give birth to small offspring that complete their development in a pouch. ***c.*** In placental mammals, such as this spotted deer doe *(Axis axis)* nursing her fawn, the young remain inside the mother's uterus for a longer period of time and are born relatively more developed.

53.3 Structure and Function of the Human Male Reproductive System

Learning Outcomes

1. *Describe the sequence of events in spermatogenesis.*
2. *Describe semen and explain how it is released during mating.*
3. *Explain how hormones regulate male reproductive function.*

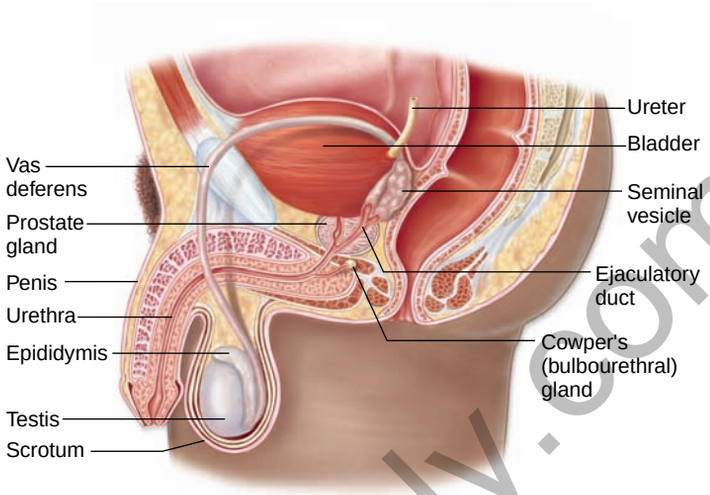


Figure 53.10 Organization of the human male reproductive system. The penis and scrotum are the external genitalia, the testes are the gonads, and the other organs are accessory sex organs, aiding the production and ejaculation of semen.

The structures of the human male reproductive system, typical of male mammals, are illustrated in figure 53.10. When testes form in the human embryo, they develop seminiferous tubules, the sites of sperm production, beginning around 43 to 50 days after conception. At about 9 to 10 weeks, the Leydig cells, located in the interstitial tissue between the seminiferous tubules, begin to secrete testosterone (the major male sex hormone, or androgen). Testosterone secretion during embryonic development converts indifferent structures into the male external genitalia, the *penis* and the *scrotum*, the latter being a sac that contains the testes. In the absence of testosterone, these structures develop into the female external genitalia. Testosterone is also responsible at puberty for male secondary sex characteristics, such as development of the beard, a deeper voice, and body hair.

In an adult, each testis is composed primarily of the highly convoluted seminiferous tubules (figure 53.11, left). Although the testes are actually formed within the abdominal cavity, shortly before birth they descend through an opening called the inguinal canal into the scrotum, which suspends them outside the abdominal cavity. The scrotum maintains the testes at around 34°C, slightly lower than the core body temperature (37°C). This lower temperature is required for normal sperm development in humans.

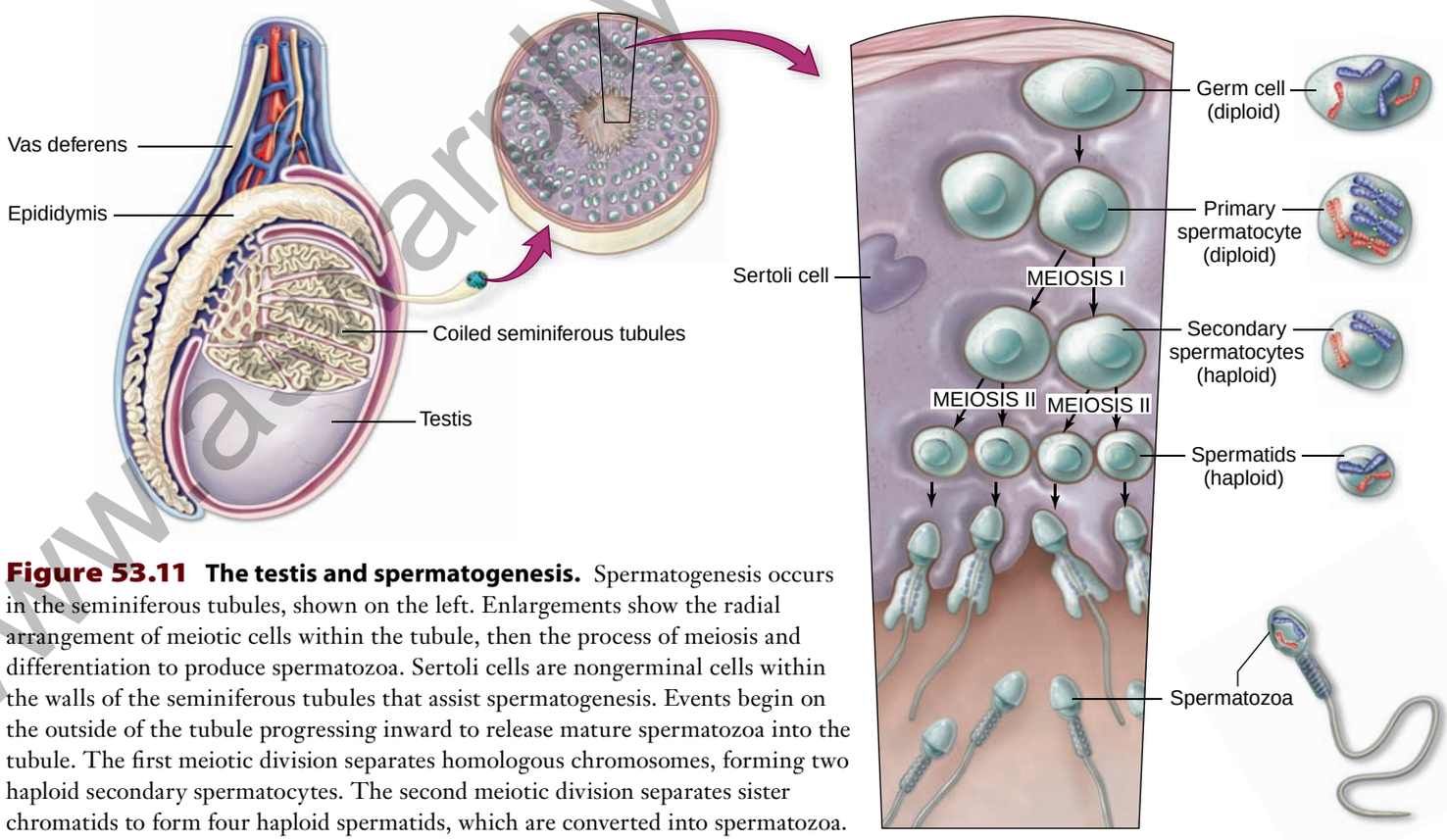


Figure 53.11 The testis and spermatogenesis. Spermatogenesis occurs in the seminiferous tubules, shown on the left. Enlargements show the radial arrangement of meiotic cells within the tubule, then the process of meiosis and differentiation to produce spermatozoa. Sertoli cells are nongerminal cells within the walls of the seminiferous tubules that assist spermatogenesis. Events begin on the outside of the tubule progressing inward to release mature spermatozoa into the tubule. The first meiotic division separates homologous chromosomes, forming two haploid secondary spermatocytes. The second meiotic division separates sister chromatids to form four haploid spermatids, which are converted into spermatozoa.

Sperm cells are produced by the millions

The wall of the seminiferous tubule consists of spermatogonia, or *germ cells*, and supporting Sertoli cells. The germ cells near the outer surface of the seminiferous tubule are diploid and are the only cells that will undergo meiosis to produce gametes (see chapter 11). The developing gamete cells, located closer to the lumen of the tubule, are haploid.

Cell divisions leading to sperm

A spermatogonium cell divides by mitosis to produce two diploid cells. One of these two cells then undergoes meiotic division to produce four haploid cells that will become sperm while the other remains as a spermatogonium. In that way, the male never runs out of spermatogonia to produce sperm. Adult males produce an average of 100 to 200 million sperm each day and can continue to do so throughout most of the rest of their lives.

The diploid daughter cell that begins meiosis is called a primary spermatocyte. In humans it has 23 pairs of chromosomes (46 chromosomes total), and each chromosome is duplicated, with two chromatids. The first meiotic division separates the homologous chromosome pairs, producing two haploid secondary spermatocytes. However, each chromosome still consists of two duplicate chromatids.

Each of these cells then undergoes the second meiotic division to separate the chromatids and produce two haploid cells, the **spermatids.** Therefore, a total of four haploid spermatids are produced from each primary spermatocyte (see figure 53.11, right). All of these cells constitute the germinal epithelium of the seminiferous tubules because they "germinate" the gametes.

Supporting tissues

In addition to the germinal epithelium, the walls of the seminiferous tubules contain nongerminal cells such as the Sertoli cells mentioned earlier. These cells nurse the developing sperm and secrete products required for spermatogenesis. They also help convert the spermatids into **spermatozoa (sperm)** by engulfing their extra cytoplasm.

Sperm structure

Spermatozoa are relatively simple cells, consisting of a head, body, and flagellum (tail) (figure 53.12). The head encloses a compact nucleus and is capped by a vesicle called an acrosome, which is derived from the Golgi complex. The acrosome contains enzymes that aid in the penetration of the protective layers surrounding the egg. The body and tail provide a propulsive mechanism: Within the tail is a flagellum, and inside the body are a centriole, which acts as a basal body for the flagellum, and mitochondria, which generate the energy needed for flagellar movement.

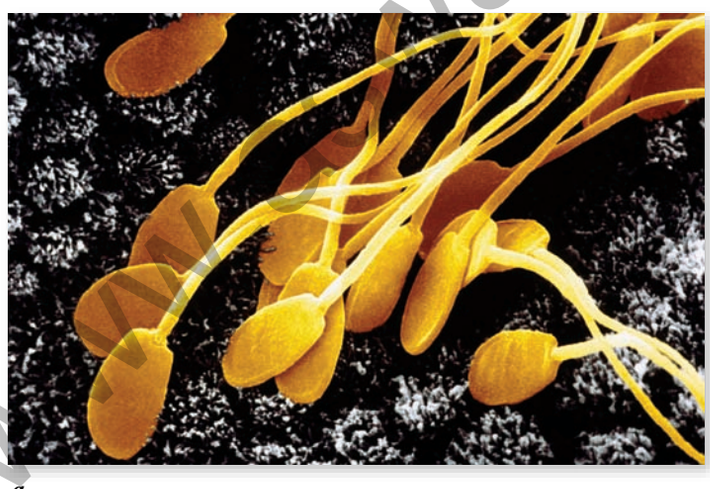
Male accessory sex organs aid in sperm delivery

After the sperm are produced within the seminiferous tubules, they are delivered into a long, coiled tube called the **epididymis**. The sperm are not motile when they arrive in the epididymis, and they must remain there for at least 18 hours before their motility develops. From the epididymis, the sperm enter another long tube, the **vas deferens,** which passes into the abdominal cavity via the inguinal canal.

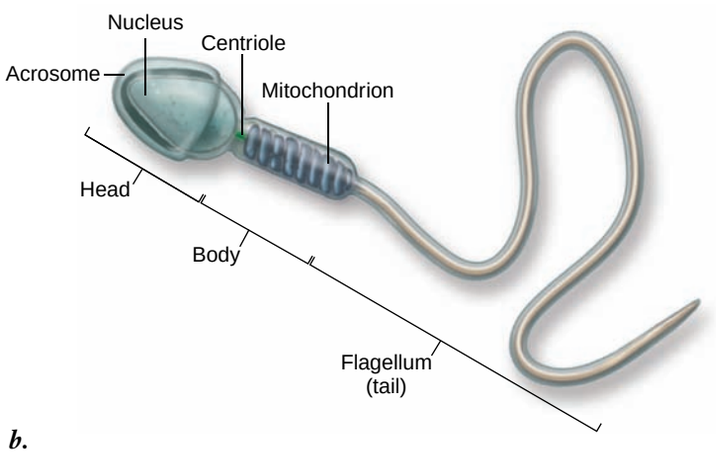
Semen production

Semen is a complex mixture of fluids and sperm. The vas deferens from each testis joins with one of the ducts from a pair of glands called the seminal vesicles (see figure 53.10), which produce a fructose-rich fluid constituting about 60% of semen volume. From this point, the vas deferens continues as the ejaculatory duct and enters the prostate gland at the base of the urinary bladder.

In humans, the **prostate gland** is about the size of a golf ball and is spongy in texture. It contributes up to 30% of the bulk of the semen. Within the prostate gland, the ejaculatory duct merges with the urethra from the urinary bladder. The urethra carries the semen out of the body through the tip of the penis. A pair of pea-sized bulbourethral glands add secretions to make up the last 10% of semen, also secreting a fluid that lines the urethra and lubricates the tip of the penis prior to coitus (sexual intercourse).



a.



b.

Figure 53.12 Human sperm. ***a.*** A scanning electron micrograph with sperm digitally colored yellow. ***b.*** A diagram of the main components of a sperm cell.

Structure of the penis and erection

In addition to the urethra, the penis has two columns of erectile tissue, the corpora cavernosa, along its dorsal side and one column, the corpus spongiosum, along the ventral side (figure 53.13). Penile erection is produced by neurons in the parasympathetic division of the autonomic nervous system, which release nitric oxide (NO), causing arterioles in the penis to dilate. The erectile tissue becomes turgid as it engorges with blood. This increased pressure in the erectile tissue compresses the veins, so blood flows into the penis but cannot flow out.

Most mammals have a bone in the penis, called a *"baculum,"* that contributes to its stiffness during erection, but humans do not.

Ejaculation

The result of erection and continued sexual stimulation is ejaculation, the ejection from the penis of about 2 to 5 mL of semen containing an average of 300 million sperm. Successful fertilization requires such a high sperm count because the odds against any one sperm cell completing the journey to the egg and fertilizing it are extraordinarily high, and the acrosomes of many sperm need to interact with the egg before a single sperm can penetrate the egg (fertilization is described in chapter 54). Males with fewer than 20 million sperm per milliliter are generally considered sterile. Despite their large numbers, sperm constitute only about 1% of the volume of the semen ejaculated.

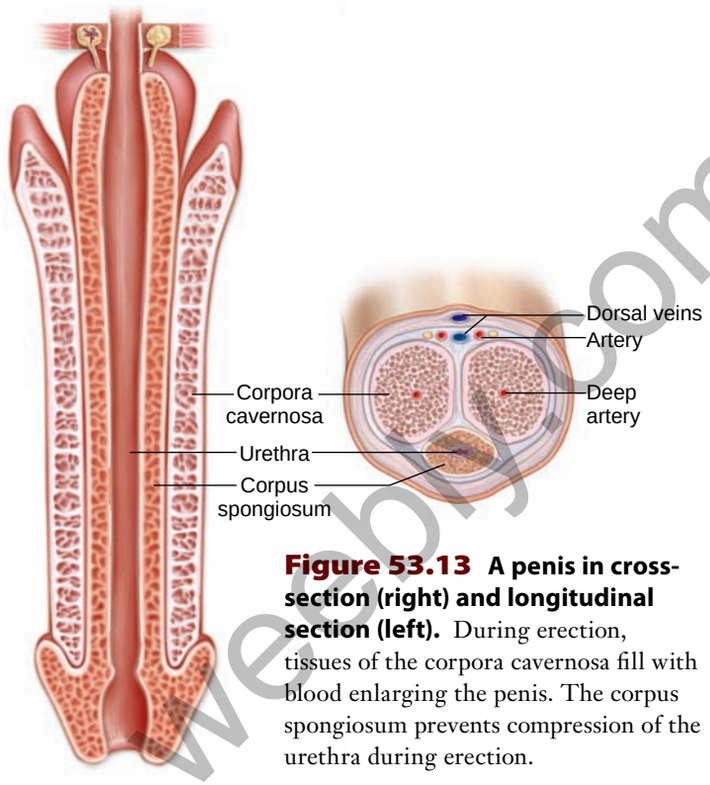


Figure 53.13 A penis in cross-section (right) and longitudinal section (left). During erection, tissues of the corpora cavernosa fill with blood enlarging the penis. The corpus spongiosum prevents compression of the urethra during erection.

Hormones regulate male reproductive function

As you saw in chapter 46, the anterior pituitary gland secretes two gonadotropic hormones: follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Although these hormones are named for their actions in the female, they are also involved in regulating male reproductive function (table 53.1). In males, FSH stimulates the Sertoli cells to facilitate sperm development, and LH stimulates the Leydig cells to secrete testosterone.

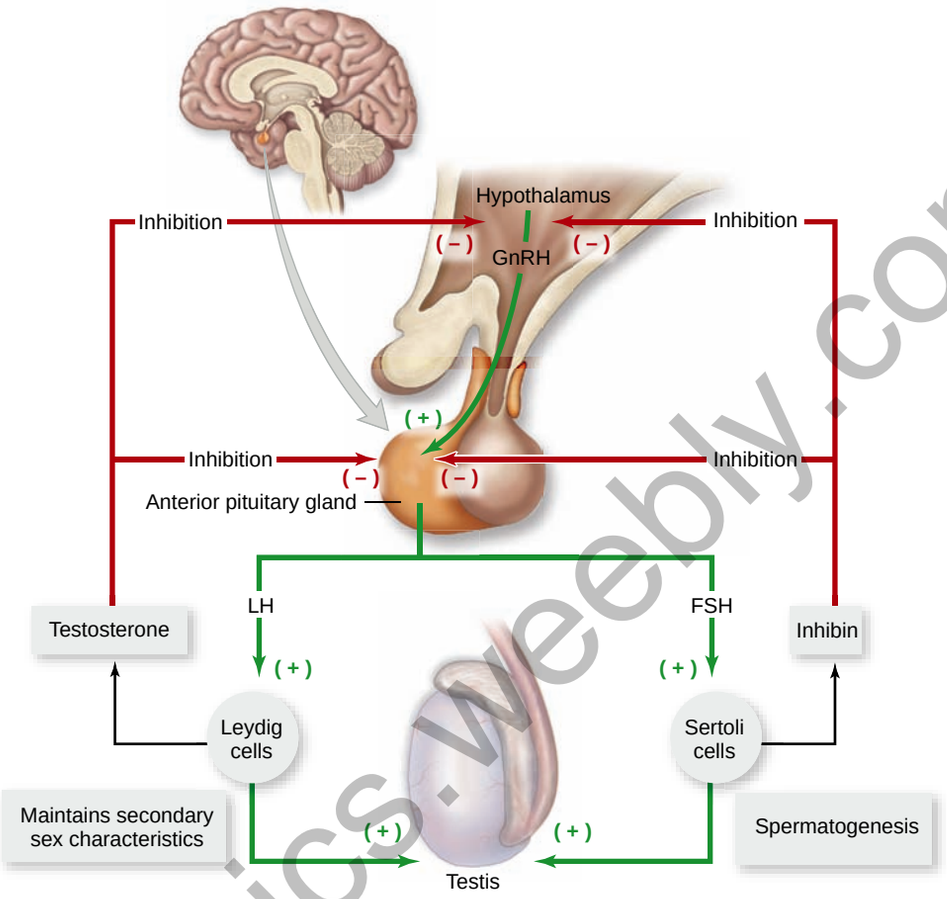
The principle of negative feedback inhibition applies to the control of FSH and LH secretion (figure 53.14). The hypothalamic hormone gonadotropin-releasing hormone (GnRH) stimulates the anterior pituitary gland to secrete both FSH and LH. FSH causes the Sertoli cells to release a peptide hormone called inhibin, which specifically inhibits FSH secretion. Similarly, LH stimulates testosterone secretion, and testosterone feeds back to inhibit the release of LH, both directly at the anterior pituitary gland and indirectly by reducing GnRH release from the hypothalamus.

The importance of negative feedback inhibition can be demonstrated by removing the testes; in the absence of testosterone and inhibin, the secretion of FSH and LH from the anterior pituitary is greatly increased.

TABLE 53.1 Mammalian Reproductive Hormones

MALE	
Follicle-stimulating hormone (FSH)	Stimulates spermatogenesis via Sertoli cells
Luteinizing hormone (LH)	Stimulates secretion of testosterone by Leydig cells
Testosterone	Stimulates development and maintenance of male secondary sexual characteristics, accessory sex organs, and spermatogenesis
FEMALE	
Follicle-stimulating hormone (FSH)	Stimulates growth of ovarian follicles and secretion of estradiol
Luteinizing hormone (LH)	Stimulates ovulation, conversion of ovarian follicles into corpus luteum, and secretion of estradiol and progesterone by corpus luteum
Estradiol (estrogen)	Stimulates development and maintenance of female secondary sexual characteristics; prompts monthly preparation of uterus for pregnancy
Progesterone	Completes preparation of uterus for pregnancy; helps maintain female secondary sexual characteristics
Oxytocin	Stimulates contraction of uterus and milk-ejection reflex
Prolactin	Stimulates milk production

Figure 53.14 Hormonal interactions between the testes and anterior pituitary. The hypothalamus secretes GnRH, which stimulates the anterior pituitary to produce LH and FSH. LH stimulates the Leydig cells to secrete testosterone, which is involved in development and maintenance of secondary sexual characteristics, and stimulates spermatogenesis. FSH stimulates the Sertoli cells of the seminiferous tubules, which facilitate spermatogenesis. FSH also stimulates Sertoli cells to secrete inhibin. Testosterone and inhibin exert negative feedback inhibition on the secretion of LH and FSH, respectively.



Inquiry question

Why do you think the brain is affected when the testes are surgically removed (termed *castration*)?

Learning Outcomes Review 53.3

Each of the spermatogonia lining the seminiferous tubules of the testes undergoes mitosis; one of the two daughter cells then undergoes meiosis to produce four haploid sperm cells. Semen consists of sperm from the testes and fluid from the seminal vesicles and prostate gland. Sexual stimulation causes erection of the penis, and continued stimulation leads to ejaculation of semen. Production of sperm and secretion of testosterone from the testes are controlled by FSH and LH from the anterior pituitary.

- ***Would natural selection favor those males that produce more sperm? Explain your answer.***

53.4 *Structure and Function of the Human Female Reproductive System*

Learning Outcomes

1. ***Describe the sequence of events in production of an oocyte.***
2. ***Explain ovulation and the female reproductive cycle.***
3. ***Explain how hormones regulate female reproductive function.***

The structures of the reproductive system in a human female are shown in figure 53.15. In contrast to the testes, the ovaries develop much more slowly. In the absence of testosterone, the female embryo develops a **clitoris** and labia majora from the same embryonic structures that produce a penis and a scrotum in males. Thus, the clitoris and penis, and the labia majora and scrotum, are said to be homologous structures.

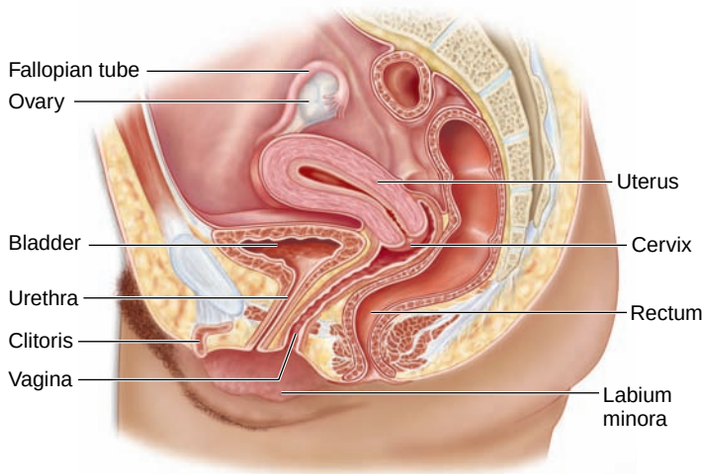


Figure 53.15 Organization of the human female reproductive system. The ovaries are the gonads, the Fallopian tubes receive the ovulated ova, and the uterus is the womb, the site of development of an embryo if the egg cell becomes fertilized.

The clitoris, like the penis, contains corpora cavernosa and is therefore erectile.

The ovaries contain microscopic structures called ovarian follicles, which each contain a potential egg cell called a primary oocyte and smaller **granulosa cells.**

At puberty, the granulosa cells begin to secrete the major female sex hormone, estradiol (also called estrogen), triggering *menarche*, the onset of menstrual cycling. Estradiol also stimulates the formation of the female secondary sexual characteristics, including breast development and the production of pubic hair. In addition, estradiol and another steroid hormone, progesterone, help maintain the female accessory sex organs: the fallopian tubes, uterus, and vagina.

Usually only one egg is produced per menstrual cycle

At birth, a female's ovaries contain about 1 million follicles, each containing a **primary oocyte** that has begun meiosis but is arrested in prophase of the first meiotic division. Some of these primary oocyte-containing follicles are stimulated to develop during each cycle. The human menstrual cycle lasts approximately one month (28 days on the average) and can be divided in terms of ovarian activity into a follicular phase and luteal phase, with the two phases separated by the event of ovulation (figure 53.16).

Follicular phase

During each *follicular phase*, several follicles in the ovaries are stimulated to grow under FSH stimulation, but only one achieves full maturity as a **tertiary,** or **Graafian, follicle** by ovulation. This follicle forms a thin-walled blister on the surface of the ovary. The uterus is lined with a simple columnar epithelial membrane called the endometrium, and during the follicular phase estradiol causes growth of the endometrium. This phase is therefore also known as the **proliferative phase** of the endometrium (see figure 53.16).

The primary oocyte within the Graafian follicle completes the first meiotic division during the follicular phase. Instead of forming two equally large daughter cells,

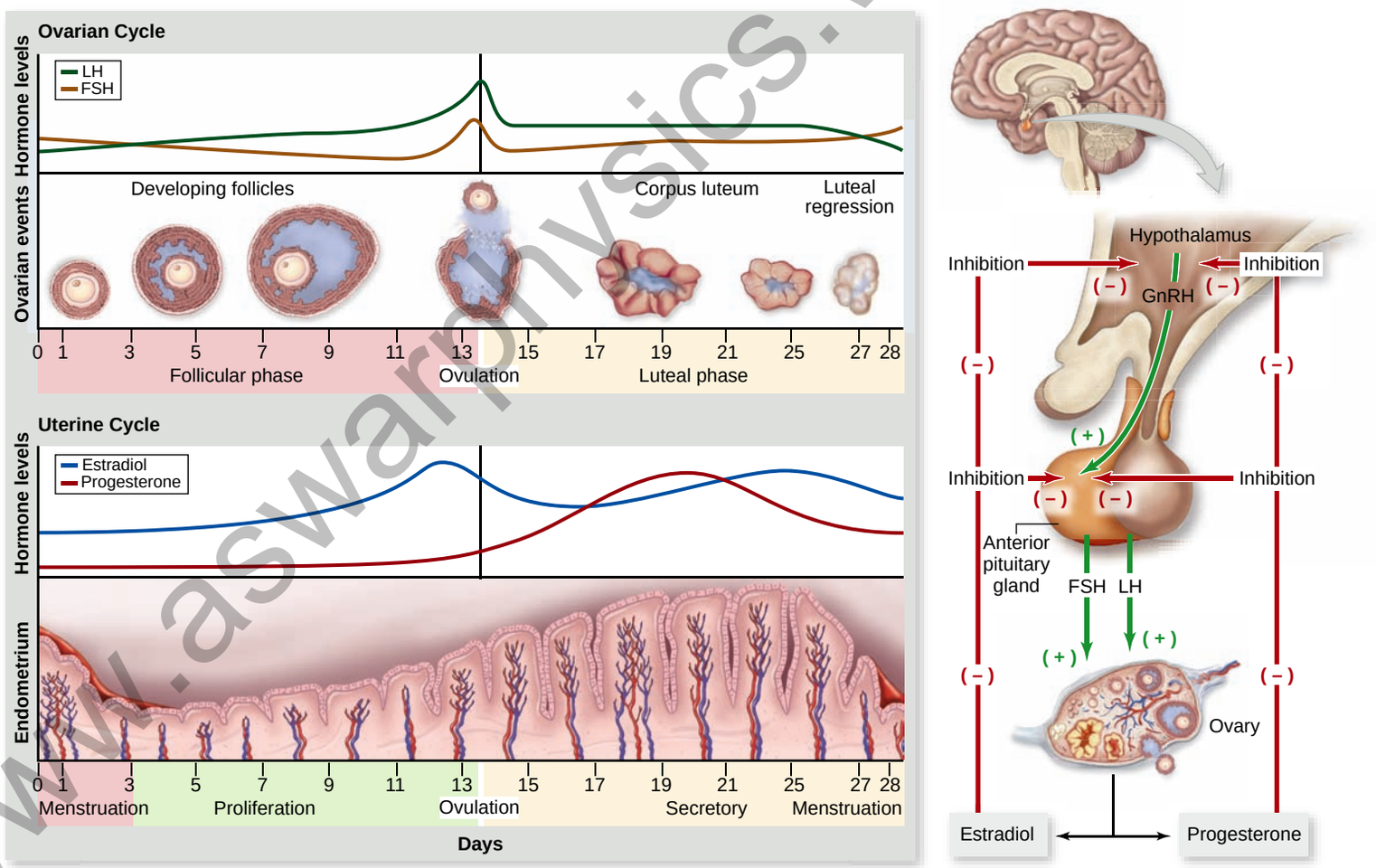


Figure 53.16 The human menstrual cycle. Left: Hormone levels during the cycle are correlated with ovulation and the growth of the endometrial lining of the uterus. Growth and thickening of the endometrium is stimulated by estradiol during the proliferative phase. Estradiol and progesterone maintain and regulate the endometrium during the secretory phase. Decline in the levels of these two hormones triggers menstruation. Right: Production of estradiol and progesterone by the anterior pituitary is controlled by negative feedback.

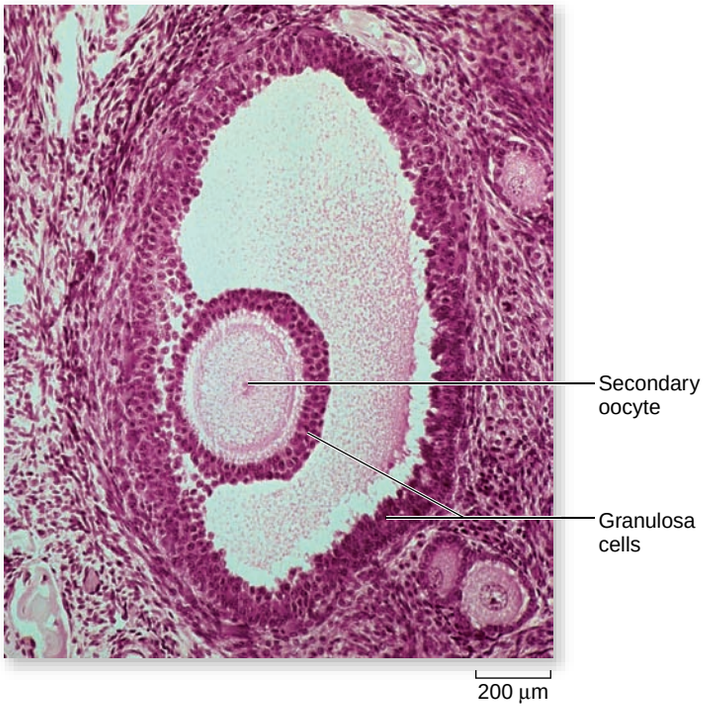


Figure 53.17 A mature Graafian follicle in a cat ovary. Note the ring of granulosa cells that surrounds the secondary oocyte. This ring will remain around the egg cell when it is ovulated, and sperm must tunnel through the ring in order to reach the plasma membrane of the secondary oocyte.

however, it produces one large daughter cell, the secondary oocyte (figure 53.17), and one tiny daughter cell, called a **polar body.** Thus, the secondary oocyte acquires almost all of the cytoplasm from the primary oocyte (unequal cytokinesis), increasing its chances of sustaining the early embryo should the oocyte be fertilized. The polar body, on the other hand, disintegrates.

The secondary oocyte then begins the second meiotic division, but its progress is arrested at metaphase II. It is in this form that the potential egg cell is discharged from the ovary at ovulation, and it does not complete the second meiotic division unless it becomes fertilized in the Fallopian tube.

Ovulation

The increasing level of estradiol in the blood during the follicular phase stimulates the anterior pituitary gland to secrete LH about midcycle. This sudden secretion of LH causes the fully developed Graafian follicle to burst in the process of ovulation, releasing its secondary oocyte.

The released oocyte enters the abdominal cavity near the fimbriae, the feathery projections surrounding the opening to the Fallopian tube. The ciliated epithelial cells lining the Fallopian tube draw in the oocyte and propel it through the Fallopian tube toward the uterus.

If it is not fertilized, the oocyte disintegrates within a day following ovulation. If it is fertilized, the stimulus of fertilization allows it to complete the second meiotic division, forming a fully mature ovum and a second polar body (figure 53.18). Fusion of the nuclei from the ovum and the sperm produces a diploid zygote. Fertilization normally occurs in the upper one-third of the Fallopian tube, and in humans the zygote takes

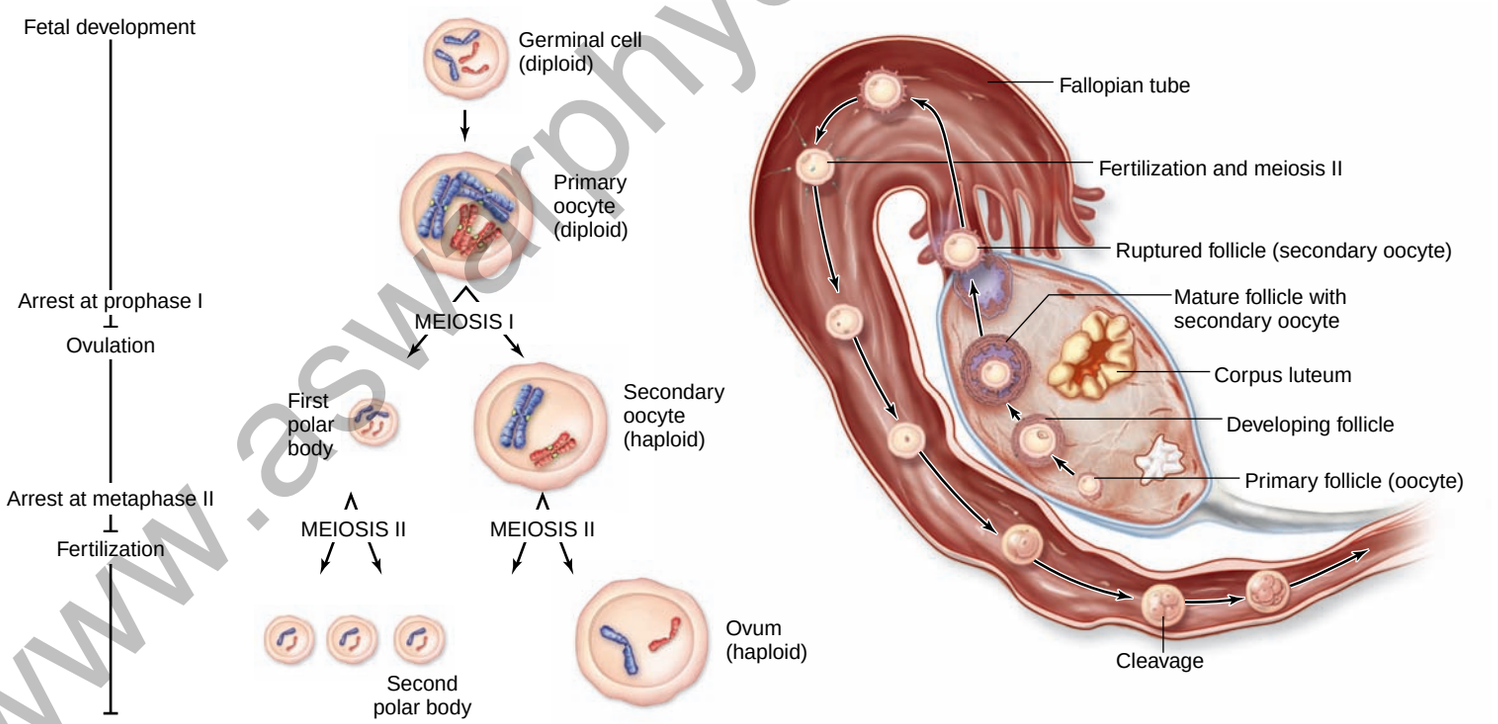


Figure 53.18 The meiotic events of oogenesis in humans. A primary oocyte is diploid. At the completion of the first meiotic division, one division product is eliminated as a polar body, and the other, the secondary oocyte, is released during ovulation. The secondary oocyte does not complete the second meiotic division until after fertilization; that division yields a second polar body and a single haploid egg, or ovum. Fusion of the haploid egg nucleus with a haploid sperm nucleus produces a diploid zygote.

approximately 3 days to reach the uterus and then another 2 to 3 days to implant in the endometrium (figure 53.19).

Luteal phase

After ovulation, LH stimulation completes the development of the Graafian follicle into a structure called the **corpus luteum.** For this reason, the second half of the menstrual cycle is referred to as the **luteal phase.** The corpus luteum secretes both estradiol and another steroid hormone, progesterone. The high blood levels of estradiol and progesterone during the luteal phase now exert negative feedback inhibition of FSH and LH secretion by the anterior pituitary gland (see figure 53.16). This inhibition during the luteal phase is in contrast to the stimulation exerted by estradiol on LH secretion at midcycle, which caused ovulation. The inhibitory effect of estradiol and progesterone after ovulation acts as a natural contraceptive mechanism, preventing both the development of additional follicles and continued ovulation.

During the luteal phase of the cycle, the combination of estradiol and progesterone cause the endometrium to become more vascular, glandular, and enriched with glycogen deposits. Because of the endometrium's glandular appearance and function, this portion of the cycle is known as the **secretory phase** of the endometrium. These changes prepare the uterine lining for embryo implantation.

In the absence of fertilization, the corpus luteum degenerates due to the decreasing levels of LH and FSH near the end of the luteal phase. Estradiol and progesterone, which the corpus luteum produces, inhibit the secretion of LH, the hormone needed for its survival. The disappearance of the corpus luteum results in an abrupt decline in the blood concentration of estradiol and progesterone at the end of the luteal phase, causing the built-up endometrium to be sloughed off with accompanying bleeding. This is menstruation; the portion of the cycle in which it occurs is known as the *menstrual phase* of the endometrium.

If the ovulated oocyte is fertilized, however, the tiny embryo prevents regression of the corpus luteum and subsequent menstruation by secreting *human chorionic gonadotropin (hCG)*, an LH-like hormone produced by the chorionic membrane of the embryo. By maintaining the corpus luteum, hCG keeps the levels of estradiol and progesterone high and thereby prevents menstruation, which would terminate the pregnancy. Because hCG comes from the embryonic chorion and not from the mother, it is the hormone tested for in all pregnancy tests.

Mammals with estrous cycles

Menstruation is absent in mammals with an estrous cycle. Although such mammals do cyclically shed cells from the endometrium, they don't bleed in the process. The estrous cycle is divided into four phases: proestrus, estrus, metestrus, and diestrus, which correspond to the proliferative, midcycle, secretory, and menstrual phases of the endometrium in the menstrual cycle.

Female accessory sex organs receive sperm and provide nourishment and protection to the embryo

The Fallopian tubes (also called uterine tubes or oviducts) transport ova from the ovaries to the uterus. In humans, the

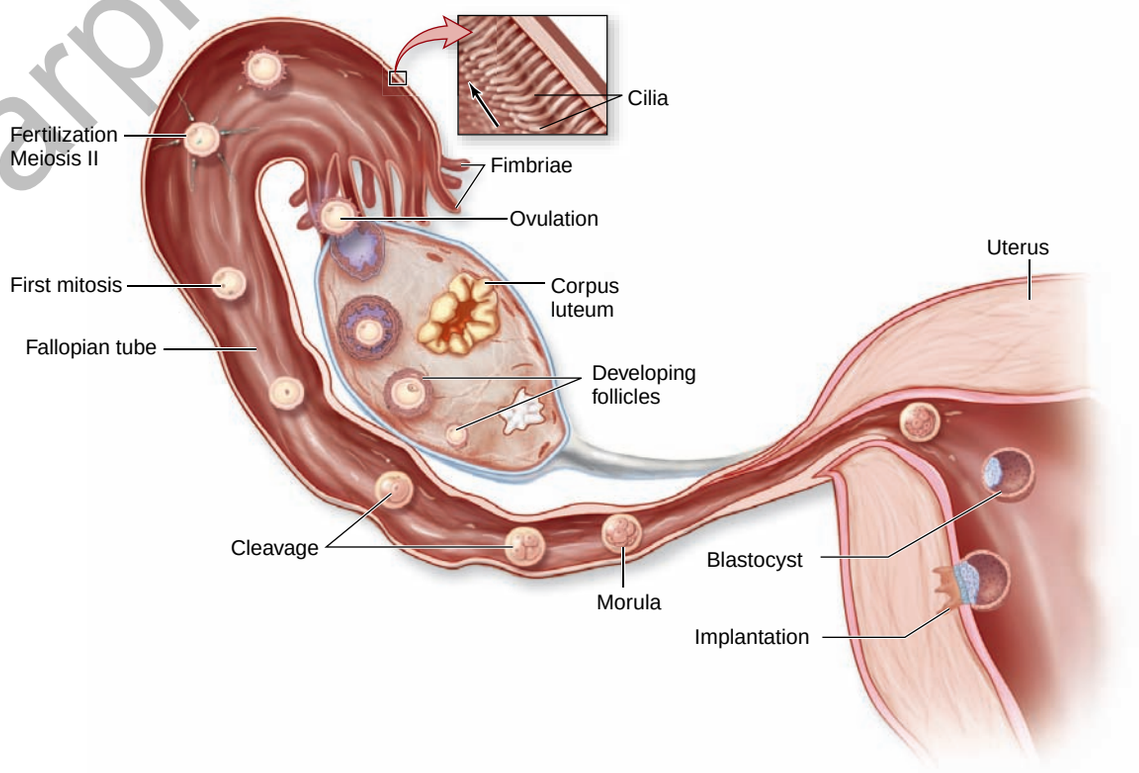


Figure 53.19 The journey of an egg. Produced within a follicle and released at ovulation, the secondary oocyte is swept into a Fallopian tube and carried along by waves of ciliary motion in the tube walls. Sperm journeying upward from the vagina penetrate the secondary oocyte, meiosis is completed and fertilization of the resulting ovum occurs within the Fallopian tube. The resulting zygote undergoes several mitotic divisions while still in the tube. By the time it enters the uterus, it is a hollow sphere of cells called a blastocyst. The blastocyst implants within the wall of the uterus, where it continues its development. (The egg and its subsequent stages have been enlarged for clarification.)

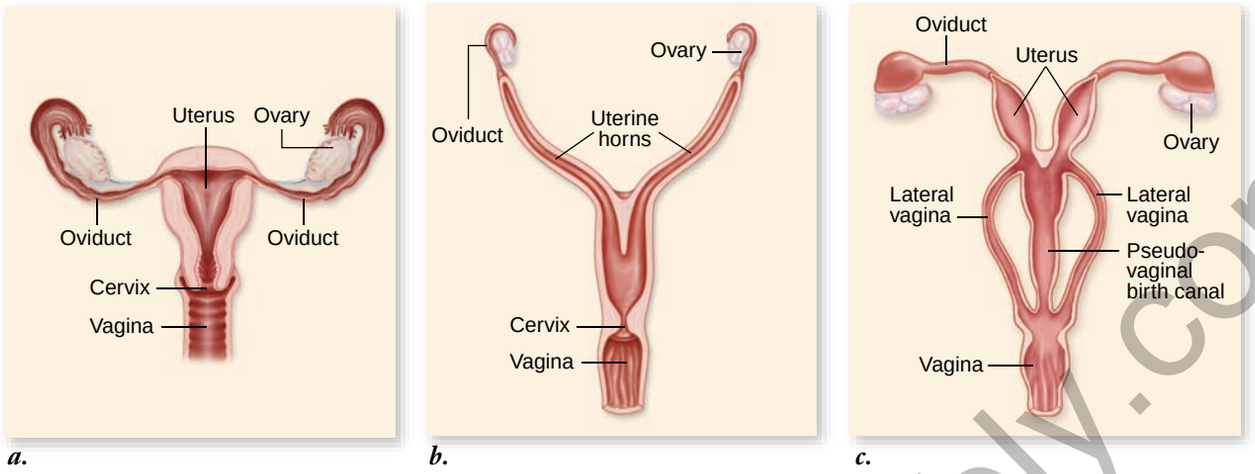


Figure 53.20
A comparison of mammalian uteruses.
a. Humans and other primates; *(b)* cats, dogs, and cows; and *(c)* marsupials.

uterus is a muscular, pear-shaped organ that narrows to form a neck, the cervix, which leads to the vagina (figure 53.20*a*).

The entrance to the vagina is initially covered by a membrane called the *hymen*. This will eventually be disrupted by vigorous activity or actual sexual intercourse. In the latter case, this can make the first experience painful when the hymen is ruptured.

During sexual arousal, the labia minora, clitoris, and vagina all become engorged with blood, much like the male erectile tissues. The clitoris has many sensory nerve endings and is one of the most sensitive and responsive areas for female arousal. During sexual arousal, glands located near the vaginal opening called Bartholin's glands, secrete a lubricating fluid that facilitates penetration by the penis. Ejaculation by the male introduces sperm cells that must then make the long swim out of the vagina and up the Fallopian tubes to encounter a secondary oocyte for fertilization to occur.

Mammals other than primates have more complex female reproductive tracts, in which part of the uterus divides to form uterine "horns," each of which leads to an oviduct (figure 53.20*b*, *c*). Cats, dogs, and cows, for example, have one cervix but two uterine horns separated by a septum, or wall. Marsupials, such as opossums, carry the split even further, with two unconnected uterine horns, two cervices, and two vaginas. A male marsupial has a forked penis that can enter both vaginas simultaneously.

Learning Outcomes Review 53.4

Primary oocytes reside in follicles in the ovaries. At puberty, some oocytes are triggered by FSH to develop with every menstrual cycle. Unequal cytokinesis produces a single egg and three polar bodies from each primary oocyte. During the follicular phase, one follicle matures; ovulation is the release of this follicle's secondary oocyte triggered by LH. This oocyte completes division only if fertilization occurs. During the luteal phase, development of additional oocytes is inhibited. If fertilization does not occur, the endometrium is sloughed off as menstrual bleeding.

- ***Would more than one offspring per pregnancy be favored by natural selection? Under what conditions?***

53.5 *Contraception and Infertility Treatments*

Learning Outcomes

1. ***Compare the different types of birth control.***
2. ***Describe causes of infertility.***

In most vertebrates, copulation is associated solely with reproduction. Reflexive behavior that is deeply ingrained in the female limits sexual receptivity to those periods of the sexual cycle when she is fertile. In humans and a few species of apes, the female can be sexually receptive throughout her reproductive cycle, and this extended receptivity to sexual intercourse serves a second important function—it reinforces pair-bonding, the emotional relationship between two individuals.

Sexual intercourse may be a necessary and important part of humans' emotional lives—and yet not all couples desire to initiate a pregnancy every time they engage in sex. Throughout history, people and cultures have attempted to control reproduction while still being able to engage in sexual intercourse. The prevention of pregnancy or giving birth is known as birth control. Physiologically, pregnancy begins not at fertilization but approximately a week later with successful implantation. Methods of birth control that act prior to implantation are usually termed contraception.

In contrast, some couples desire to have children, but find for a variety of reasons that pregnancy is not occurring—a condition termed infertility. Technologies have also been developed to assist these couples in having children.

Contraception is aimed at preventing fertilization or implantation

A variety of approaches, differing in effectiveness and in their acceptability to different couples, religions, and cultures, are commonly taken to prevent pregnancy (figure 53.21 and table 53.2).

a.

b.

c.

d.

Figure 53.21 Four common methods of birth control. *a.* Condom; *(b)* diaphragm and spermicidal jelly; *(c)* oral contraceptives; *(d)* medroxyprogesterone acetate (Depo-Provera).

TABLE 53.2 Methods of Birth Control

Device	Action	Failure Rate*	Advantages	Disadvantages
Oral contraceptive	Hormones (progesterone analogue alone or in combination with other hormones) primarily prevent ovulation	1–5, depending on type	Convenient; highly effective; provides significant noncontraceptive health benefits such as protection against ovarian and endometrial cancers	Must be taken regularly; possible minor side effects, which new formulations have reduced; not for women with cardiovascular risks (mostly smokers over age 35)
Condom	Thin sheath for penis collects semen; "female condoms" sheath vaginal walls	3–15	Easy to use, effective, inexpensive, protects against some sexually transmitted diseases	Requires male cooperation, may diminish spontaneity, may deteriorate on the shelf
Diaphragm	Soft rubber cup covers entrance to uterus; prevents sperm from reaching egg, holds spermicide	4–25	No dangerous side effects; reliable if used properly; provides some protection against sexually transmitted diseases and cervical cancer	Requires careful fitting, some inconvenience associated with insertion and removal; may be dislodged during intercourse
Intrauterine device (IUD)	Small plastic or metal device placed in the uterus, prevents implantation; some contain copper, others release hormones	1–5	Convenient, highly effective; infrequent replacement	Can cause excess menstrual bleeding and pain; risk of perforation, infection, expulsion, pelvic inflammatory disease, and infertility; not recommended for those who eventually intend to conceive or are not monogamous; dangerous in pregnancy
Cervical cap	Miniature diaphragm covers cervix closely, prevents sperm from reaching egg, holds spermicide	Probably similar to that of diaphragm	No dangerous side effects; fairly effective; can remain in place longer than diaphragm	Problems with fitting and insertion; comes in limited number of sizes
Foams, creams, jellies, vaginal suppositories	Chemical spermicides inserted in vagina before intercourse prevent sperm from entering uterus	10–25	Can be used by anyone who is not allergic; protect against some sexually transmitted diseases; no known side effects	Relatively unreliable; sometimes messy; must be used 5–10 minutes before each act of intercourse
Implant (levonorgestrel; Norplant)	Capsules surgically implanted under skin slowly release hormone that blocks ovulation	0.03	Very safe, convenient, and effective; very long-lasting (5 years); may have nonreproductive health benefits like those of oral contraceptives	Irregular or absent periods; minor surgical procedure needed for insertion and removal; some scarring may occur
Injectable contraceptive (medroxyprogesterone; Depo-Provera)	Injection every 3 months of a hormone that is slowly released and prevents ovulation	1	Convenient and highly effective; no serious side effects other than occasional heavy menstrual bleeding	Animal studies suggest it may cause cancer, though new studies in humans are mostly encouraging; occasional heavy menstrual bleeding

*Failure rate is expressed as pregnancies per 100 actual users per year.

Source: Data from American College of Obstetricians and Gynecologists: Contraception, Patient Education Pamphlet No. AP005. ACOG, Washington, D.C., 1990.

Abstinence

The most reliable way to avoid pregnancy is to not have sexual intercourse at all, which is called *abstinence*. Of all the methods of contraception, this is the most certain. It is also the most limiting and the most difficult method to sustain. The drive to engage in sexual intercourse is compelling, and many unwanted pregnancies result when a couple who desire each other and are attempting to adhere to abstinence fail in the attempt.

Sperm blockage

If sperm cannot reach the uterus, fertilization cannot occur. One way to prevent the delivery of sperm is to encase the penis within a thin sheath, or condom. Some males do not favor the use of condoms, which tend to decrease males' sensory pleasure during intercourse. In principle, this method is easy to apply and foolproof, but in practice it has a failure rate of 3 to 15% per year because of incorrect or inconsistent use or condom failure. Nevertheless, condom use is the most commonly employed form of contraception in the United States. Condoms are also widely used to prevent the transmission of AIDS and other sexually transmitted diseases (STDs). Over a billion condoms are sold in the United States each year.

A second way to prevent the entry of sperm into the uterus is to place a cover over the cervix. The cover may be a relatively tight-fitting cervical cap, which is worn for days at a time, or a rubber dome called a diaphragm, which is inserted before intercourse. Because the dimensions of individual cervices vary, a cervical cap or diaphragm must be initially fitted by a physician. Pregnancy rates average 4 to 25% per year for women using diaphragms. Failure rates for cervical caps are somewhat lower.

Sperm destruction

A third general approach to pregnancy prevention is to eliminate the sperm after ejaculation. This can be achieved in principle by washing out the vagina immediately after intercourse, before the sperm have a chance to enter the uterus. Such a procedure is called a douche. The douche method is difficult to apply well, because it involves a rapid dash to the bathroom immediately after ejaculation and a very thorough washing. Douching can, in fact, increase the possibility of conception by forcing sperm farther up into the vagina and uterus, thereby accounting for its high failure rate (40%).

Alternatively, sperm delivered to the vagina can be destroyed there with spermicidal agents, jellies, or foams. These treatments generally require application immediately before intercourse. Their failure rates vary from 10 to 25%. The use of a spermicide with a condom or diaphragm increases the effectiveness over each method used independently.

Prevention of ovulation

Since about 1960, a widespread form of contraception in the United States has been the daily ingestion of birth control pills, or oral contraceptives, by women. These pills contain analogues of progesterone, sometimes in combination with estrogens. As described earlier, progesterone and estradiol act by negative feedback to inhibit the secretion of FSH and LH during the luteal phase of the ovarian cycle, thereby preventing follicle development and ovulation. They also cause a buildup of the endometrium. The hormones in birth control pills have the same effects. Because the pills block ovulation, no ovum is available to be fertilized.

A woman generally takes the hormone-containing pills for 3 weeks; during the fourth week, she takes pills without hormones, allowing the levels of those hormones in her blood to fall, which causes menstruation.

Oral contraceptives provide a very effective means of birth control, with a failure rate of only 1 to 5% per year. In a variation of the oral contraceptive, hormone-containing capsules are implanted beneath the skin. These implanted capsules have failure rates below 1%.

A small number of women using birth control pills or implants experience undesirable side effects, such as blood clotting and nausea. These side effects have been reduced in newer generations of birth control pills, which contain less estrogen and different analogues of progesterone. Moreover, these new oral contraceptives provide a number of benefits, including reduced risks of endometrial and ovarian cancer, cardiovascular disease, and osteoporosis (for older women). However, they may increase the risk of developing breast cancer and cervical cancer.

The risks involved with birth control pills increase in women who smoke and increase greatly in women over 35 who smoke. The current consensus is that, for many women, the health benefits of oral contraceptives outweigh their risks, although a physician must help each woman determine the relative risks and benefits.

Prevention of embryo implantation

The insertion of an intrauterine device (IUD), such as a coil or other irregularly shaped object, is an effective means of contraception because the irritation it produces prevents the implantation of an embryo. IUDs have a failure rate of only 1 to 5%. Their high degree of effectiveness probably reflects their convenience; once they are inserted, they can be forgotten. The great disadvantage of this method is that almost a third of the women who attempt to use IUDs experience cramps, pain, and sometimes bleeding and therefore must discontinue using them. There is also a risk of uterine infection with insertion of the IUD.

Another method of preventing embryo implantation is the "morning-after pill," or Plan B, which contains 50 times the dose of estrogen present in birth control pills. The pill works by temporarily stopping ovum development, by preventing fertilization, or by stopping the implantation of a fertilized ovum. Its failure rate is 1 to 10% per use.

Many women are uneasy about taking such high hormone doses because side effects can be severe. This pill is not designed as a regular method of pregnancy prevention, but rather as a method of emergency contraception.

Sterilization

Sterilization is usually accomplished by the surgical removal of portions of the tubes that transport the gametes from the gonads (figure 53.22). It is an almost 100% effective means of contraception. Sterilization may be performed on either males or females, preventing sperm from entering the semen in males and preventing an ovulated oocyte from reaching the uterus in females.

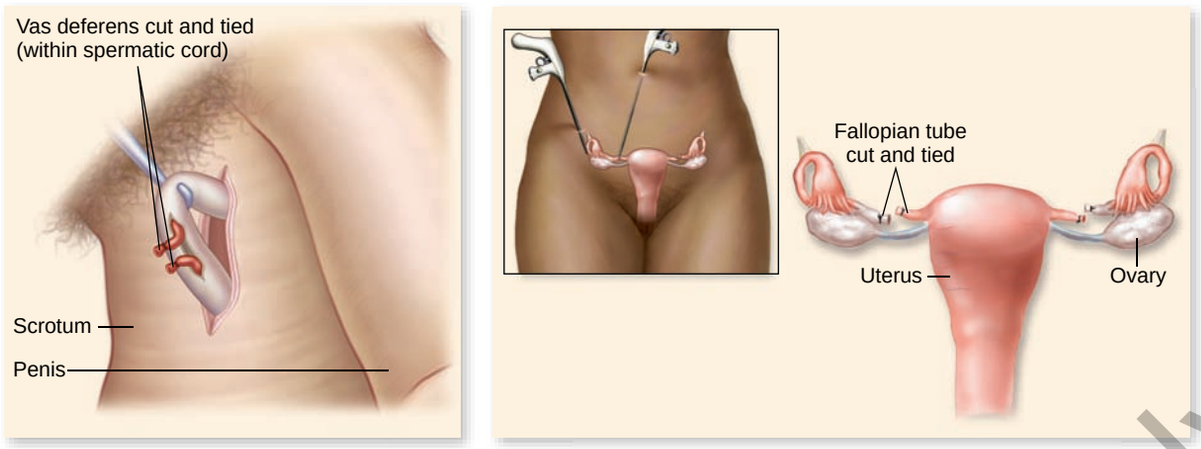


Figure 53.22 Birth control through sterilization. ***a.*** Vasectomy; ***(b)*** tubal ligation.

In males, sterilization involves a vasectomy, the removal and tying off of a portion of the vas deferens from each testis. In females, the comparable operation, called tubal ligation, involves the removal of a section of each Fallopian tube and tying off the tube. In very rare cases, it is possible for the tubes to grow back together, restoring fertility. This is more common in vasectomy but does occur in both at a very low level. This accounts for the less than 100% effectiveness statistically. Both methods can also be reversed surgically, though for vasectomy the surgery is both expensive and frequently unsuccessful.

Infertility occurs in both males and females

Infertility is defined as the inability to conceive after 12 months of contraception-free sexual intercourse. In about 40% of cases, the failure to conceive is due to problems on the male side with about 45% due to problems on the female side, leaving another 15% unexplained (idiopathic infertility). Given these background statistics, it is clear that we still have a lot to learn about human fertility, despite a significant amount of study.

Female infertility

Infertility in females can occur due to a failure at any stage from the production of an oocyte, to the implantation of the zygote. The most common problems arise from failure to ovulate, and from some kind of mechanical blockage preventing either fertilization or implantation.

The leading cause of infertility worldwide is pelvic inflammatory disease (PID). This can be caused by infection with a number of different bacteria that all lead to blockage of the Fallopian tubes. This blockage then causes problems in sperm passage, and of transfer of fertilized eggs to the uterus.

Endometriosis, the presence of ectopic endometrial tissue, can lead to infertility by a mechanism similar to PID. The body responds to the ectopic tissue by trying to wall it off with scar tissue. The buildup of scar tissue can then prevent the transfer of eggs to the uterus.

Another common cause of infertility in females is age, or premature ovarian failure (POF). Fertility declines significantly in females with age, and the incidence of some genetic abnormalities caused by nondisjunction of chromosomes increases (see chapter 13). If a women younger than 40 has a diminished supply of eggs, this is considered diagnostic of POF.

Disruption of the normal hormonal control of ovulation discussed earlier is also a common cause of infertility in females. Decreased levels of GnRH will disrupt ovulation, a condition referred to as hypogonadotropic hypogonadism. This can arise from damage to the hypothalamus or pituitary, or by any disorder that affects normal levels of hypothalamic hormones. For example, diabetes, thyroid disease, and excessive adrenal androgen production all affect hormonal feedback to the hypothalamus and can disrupt its normal function, leading to decreased levels of GnRH and infertility. Excessive exercise and anorexia can also lead to reduced GnRH levels and produce infertility.

Hormonal imbalances can occur during the luteal phase as well. Inadequate levels of progesterone during the luteal phase reduce the thickening of the uterine wall. If the uterine wall is inadequately prepared, implantation may not occur or can lead to an increased likelihood of spontaneous abortion.

Male infertility

Infertility in males can be due to a reduced number, viability, or motility of sperm in the ejaculate. These can be due to a variety of factors from infection to hormonal imbalances. Analysis on the male side is easier since sperm collection is noninvasive. Sperm can be easily analyzed for number, viability, morphology, and motility.

Infertility can arise from autoimmunity to sperm, leading to sperm loss, as well as due to abnormalities of all of the glands that contribute to the production of semen. Damage to the vas deferens or to the seminiferous tubules can also result in infertility. Anything that disrupts the maturation process of sperm can result in possible infertility.

After all possible causes have been ruled out, up to 5% of infertile men suffer from idiopathic, or unexplained, infertility. This may be due to genetic causes as the numbers seem to be similar worldwide despite different environments. It has been estimated in studies of *Drosophila* that up to 1500 recessive genes contribute to male fertility. Work is ongoing to examine the human genome for evidence of similar genes.

Treatment of infertility often involves assisted reproductive technologies

There are two basic possibilities for treating infertility: hormonal treatment and **assisted reproductive technologies (ART).** The number and variety of assisted technologies available today is large and growing.

Hormone treatment

In the case of female infertility due to ovulatory defects, treatment is designed to produce high levels of FSH and LH at a single point during the normal menstrual cycle. Given the complexity of the hormonal control of the cycle, it is not surprising that this can be achieved in a number of ways. The most common drug currently used is clomiphine (Clomid), which is a competitive inhibitor of the estrogen receptor. This interferes with the negative feedback loop controlling estradiol production by the ovaries and consequently increases FSH and LH levels. If this is not successful, gonadatropins can be injected to stimulate ovulation.

Assistive reproductive technology

The simplest method to assist reproduction is to use artificial insemination, a process by which sperm are introduced into the female reproductive tract artificially. This is widely used in reproduction of domestic animals and is also used in humans. This has also been extended in cases of infertility in which both sperm and egg are introduced artificially by a technique called *gametic intrafallopian transfer*, or *GIFT.*

The birth of the first "test tube baby" in 1978 was heralded as the beginning of a new age of reproductive technology. Even the early pioneers may not have envisioned how far this technology would proceed. The basic technique of external fertilization is called *in vitro fertilization* (*IVF*), and transfer of the developing embryo is called simply *embryo transfer* (*ET*). When the sperm are unable to successfully fertilize an egg in vitro, they can be directly injected into an egg by *intracytoplasmic sperm injection* (*ICSI*).

One of the downsides of much of this assisted technology is multiple births. This is due to the common practice of transferring more than one embryo to ensure that at least one implants and develops normally. With advances in understanding of human development, it is possible to monitor early embryo growth to select the "best" embryos for transfer and to therefore transfer fewer embryos to reduce multiple births.

It is also possible to freeze sperm, eggs, and even human embryos to reduce the number of invasive techniques such as harvesting oocytes. Live births have been achieved using all combinations of frozen eggs, sperm, and embryos. This allows the transfer of a single embryo while freezing others produced by in vitro fertilization. If the first embryo transferred does not implant, then the others can be thawed and transferred later.

Learning Outcomes Review 53.5

Pregnancy can be prevented by a variety of contraception methods, including abstinence, barrier contraceptives, hormonal inhibition, and sterilization surgery. Some methods are more susceptible to human error than others and thus have a lower success rate. Infertility can be treated by hormonal manipulation to induce ovulation or by the use of assisted reproductive technologies. These assisted technologies include in vitro fertilization and intracytoplasmic sperm injection.

- ***Why isn't there a male birth control pill?***

Chapter Review

53.1 Animal Reproductive Strategies

Some species have developed novel reproductive methods.

Sexual reproduction involves production by meiosis of haploid gametes (eggs and sperm). These join at fertilization to produce a diploid zygote.

Asexual reproduction produces offspring with the same genes as the parent organism.

In budding, a part of an individual becomes separated and develops into a new, identical individual. In parthenogenesis, females produce offspring from unfertilized eggs. In hermaphroditism, an individual has both testes and ovaries (simultaneous) or may change sex (sequential).

Sex can be determined genetically or by environmental conditions.

In some animals, the temperature an individual experiences as an embryo determines its sex. In mammals, sex is genetically determined by the presence of a Y chromosome (see figure 53.3).

53.2 Vertebrate Fertilization and Development

Internal fertilization has led to three strategies for development of offspring.

Vertebrates with internal fertilization exhibit three strategies for development: oviparity, ovoviviparity, and viviparity. Both internal fertilization and live birth have evolved many times.

Most fishes and amphibians have external fertilization.

Most fish and amphibians release eggs and sperm into the water, where the gametes unite by chance. Few fertilized eggs grow to maturity.

Reptiles and birds have internal fertilization.

The embryos of reptiles and birds develop in a fluid-filled cavity surrounded by the amnion and extraembryonic membranes and a shell to help prevent desiccation.

Mammals generally do not lay eggs, but give birth to their young.

Mammals are also amniotic, but most species are viviparous. Most mammals have an estrus cycle, but primates have a menstrual cycle.

53.3 Structure and Function of the Human Male Reproductive System

Sperm cells are produced by the millions.

Haploid sperm are produced by meiosis of spermatogonia with the aid of Sertoli cells (see figure 53.11). Each spermatogonium produces four sperm cells. A sperm cell has three parts: a head with an acrosome, a body containing mitochondria, and a flagellar tail.

Male accessory sex organs aid in sperm delivery.

Semen is a complex mixture of sperm and fluids from the seminal vesicles, prostate gland, and bulbourethral glands.

The urethra of the penis transports both sperm and urine and contains two columns of erectile tissue, blood vessels, and nerves (see figure 53.13). Ejaculation is the ejection of semen from the penis by smooth muscle contraction.

Hormones regulate male reproductive function.

Male reproductive function is controlled by the hormones FSH and LH and negative feedback loops (see figure 53.14, table 53.1).

53.4 Structure and Function of the Human Female Reproductive System

Usually only one egg is produced per menstrual cycle.

The female clitoris and labial lips have the same embryonic origin as the penis and scrotum. They develop in the absence of testosterone.

In adult females, FSH stimulates follicular development, which in turn produces estrogen. LH stimulates ovulation and corpus luteum development, which produces progesterone and more estrogen. Estrogen and progesterone are necessary to develop and maintain the uterine lining (see figure 53.16).

The ovarian cycle has three phases: follicular phase, ovulation, and luteal phase. The uterine cycle has three stages that mirror the ovarian cycle: menstruation, proliferation, and secretion.

At birth, all primary oocytes are arrested in the first meiotic division. Each oocyte is capable of producing one ovum and three polar bodies. Each month, one oocyte completes meiosis I. This secondary oocyte begins the second meiotic division and arrests until the egg is fertilized (see figure 53.18).

A fertilized egg, or zygote, develops into a blastocyst and implants in the wall of the uterus. Here it produces hCG, which maintains the corpus luteum and prevents menstruation.

If fertilization and implantation do not occur, the production of hormones declines, causing the built-up endometrium in the uterus to be sloughed off during menstruation.

Female accessory organs receive sperm and provide nourishment and protection to the embryo.

The Fallopian tubes transport ova from the ovaries to the uterus. The vagina receives sperm, which enters the uterus via the cervix (see figure 53.20). Other female organs are involved in sexual response.

53.5 Contraception and Infertility Treatments

Contraception is aimed at preventing fertilization or implantation.

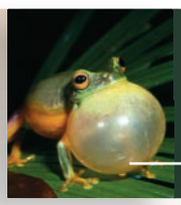
Pregnancy can be avoided by abstinence, by blocking sperm from reaching the ovum, by destroying sperm after ejaculation, by preventing ovulation or embryo implantation, or by sterilization. Some methods are more successful in practice than others.

Infertility occurs in both males and females.

Female infertility ranges from failure of oocyte production to failure of zygote implantation. Male infertility is usually due to reduction in sperm number, viability, or motility; hormonal imbalance; or damage to the sperm delivery system.

Treatment of infertility often involves assisted reproductive technologies.

Hormonal treatment may be used to correct ovulatory defects or sperm production defects. Assistive reproduction technologies involve artificial insemination, in vitro fertilization and embryo transfer, or intracytoplasmic sperm injection.



Review Questions

UNDERSTAND

1. You have discovered a new organism living in tide pools at your favorite beach. Every so often, one of the creature's appendages will break off and gradually grow into a whole new organism, identical to the first. This is an example of
   a. sexual reproduction.
   b. fission.
   c. budding.
   d. parthenogenesis.
2. If you decided that the organism you discovered in question 1 used parthenogenesis, what would you also know about this species?
   a. It is asexual.
   b. All the individuals are female.
   c. Each individual develops from an unfertilized egg.
   d. All of these would be true.
3. Which of the following terms describes your first stage as a diploid organism?
   a. Sperm
   b. Egg
   c. Gamete
   d. Zygote
4. Which of the following structures is the site of spermatogenesis?
   a. Prostate
   b. Bulbourethral gland
   c. Urethra
   d. Seminiferous tubule
5. FSH and LH are produced by the
   a. ovaries.
   b. testes.
   c. anterior pituitary.
   d. adrenal glands.
6. Gametogenesis requires the conclusion of meiosis II. When does this occur in females?
   a. During fetal development
   b. At the onset of puberty
   c. After fertilization
   d. After implantation
7. Mutations that affect proteins in the acrosome would impede which of the following functions?
   a. Fertilization
   b. Locomotion
   c. Meiosis
   d. Semen production

8. In humans, fertilization occurs in the____, and implantation of the zygote occurs in the____.
   a. seminiferous tubules; uterus
   b. vagina; oviduct
   c. oviduct; uterus
   d. urethra; uterus
9. The testicles of male mammals are suspended in the scrotum because
   a. the optimum temperature for sperm production is less than the normal core body temperature of the organism.
   b. the optimum temperature for sperm production is higher than the normal core body temperature of the organism.
   c. there is not enough room in the pelvic area for the testicles to be housed internally.
   d. it is easier for the body to expel sperm during ejaculation.

APPLY

1. The major difference between an estrous cycle and a menstrual cycle is that
   a. sexual receptivity occurs only around ovulation in the estrous cycle, but it can occur during any time of the menstrual cycle.
   b. estrous cycles occur in reptiles, but menstrual cycles occur in mammals.
   c. estrous cycles are determined by FSH, but menstrual cycles are determined by LH.
   d. estrous cycles occur monthly, but menstrual cycles occur sporadically.
2. Which of the following is a major difference between spermatogenesis and oogenesis?
   a. Spermatogenesis involves meiosis, and oogenesis involves mitosis.
   b. Spermatogenesis is continuous, but oogenesis is variable.
   c. Spermatogenesis produces fewer gametes per precursor cell than oogenesis.
   d. All of these are significant differences between oogenesis and spermatogenesis.
3. In species with environmental sex determination
   a. sex is determined during development as an embryo.
   b. environmental conditions determine the sex of an individual.
   c. hermaphroditism always occurs.
   d. a and b are correct.
4. Internal and external fertilization differ in that all species that
   a. produce an amniotic egg have internal fertilization.
   b. do not produce an amniotic egg have external fertilization.
   c. produce live young have a penis or other intromittent organ.
   d. lay eggs are external fertilizers.

SYNTHESIZE

1. Suppose that the *SRY* gene mutated such that a male embryo could not produce functional protein. What kinds of changes would you expect to see in the embryo?
2. Why do you think that amphibians and many fish have external fertilization, whereas lizards, birds, and mammals rely on internal fertilization?
3. How are the functions of FSH and LH similar in male and female mammals? How do they differ?
4. You are interested in developing a contraceptive that blocks hCG receptors. Will it work? Why or why not?
5. Why are all parthenogenic parents female?

ONLINE RESOURCE

www.ravenbiology.com

Understand, Apply, and Synthesize—enhance your study with animations that bring concepts to life and practice tests to assess your understanding. Your instructor may also recommend the interactive eBook, individualized learning tools, and more.

Chapter 54

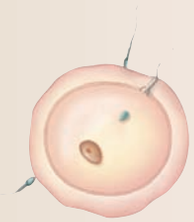
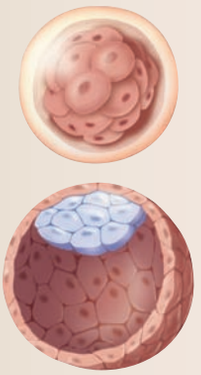
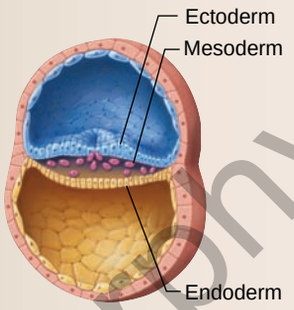
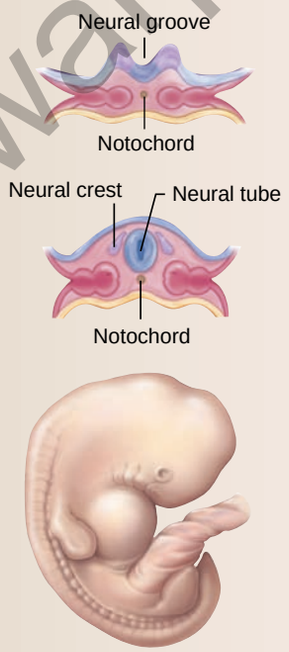
Animal Development

Chapter Outline

Introduction

Sexual reproduction in all but a few animals unites two haploid gametes to form a single diploid cell called a zygote. *The zygote develops by a process of cell division and differentiation into a complex multicellular organism, composed of many different tissues and organs, as the picture illustrates. At the same time, a group of cells that constitute the* germ line *are set aside to enable the developing organism to engage in sexual reproduction as an adult. In this chapter, we focus on the stages that all coelomate animals pass through during embryogenesis: fertilization, cleavage, gastrulation, and organogenesis (table 54.1). Development is a dynamic process, and so the boundaries between these stages are somewhat artificial. Although differences can be found in the details, developmental genes and cellular pathways have been greatly conserved, and they create similar structures in different organisms.*

TABLE 54.1 Stages of Animal Development (Using a Mammal as an Example)

Fertilization	The haploid male and female gametes fuse to form a diploid zygote.	
Cleavage	The zygote rapidly divides into many cells, with no overall increase in size. In many animals, these divisions affect future development because different cells receive different portions of the egg cytoplasm and, hence, different cytoplasmic determinants. Cleavage ends with formation of a blastula (called a blastocyst in mammals), which varies in structure among animal embryos.	 Blastocyst
Gastrulation	The cells of the embryo move, forming the three primary germ layers: ectoderm, mesoderm, and endoderm.	 Ectoderm Mesoderm Endoderm
Organogenesis	Cells from the three primary germ layers interact in various ways to produce the organs of the body. In chordates, organogenesis begins with formation of the notochord and the hollow dorsal nerve cord in the process of neurulation.	 Neural groove Notochord Neural crest Neural tube Notochord

54.1 Fertilization

Learning Outcomes

1. *Describe the events necessary for fertilization to occur.*
2. *List different ways that polyspermy is blocked.*

In all sexually reproducing animals, the first step in development is the union of male and female gametes, a process called *fertilization*. As you learned in the preceding chapter, fertilization is typically external in aquatic animals. In contrast, internal fertilization is used by most terrestrial animals to provide a nondessicating environment for the gametes.

One physical challenge of sexual reproduction is for gametes to get together. Many elaborate strategies have evolved to enhance the likelihood of such encounters. For example, most marine invertebrates release hundreds of millions of eggs and sperm into the surrounding sea water on spawning; others use lunar cycles to time gamete release. Elaborate courtship behaviors are typical of many animals that utilize internal fertilization (see chapter 53). Fertilization itself consists of three events: sperm penetration and membrane fusion, egg activation, and fusion of nuclei.

A sperm must penetrate to the plasma membrane of the egg for membrane fusion to occur

Embryonic development begins with the fusion of the sperm and egg plasma membranes. But the unfertilized egg presents a challenge to this process, since it is enveloped by one or more protective coats. These protective coats include the *chorion* of insect eggs, the *jelly layer* and *vitelline envelope* of sea urchin and frog eggs, and the *zona pellucida* of mammalian eggs. Mammalian oocytes are also surrounded by a layer of supporting granulosa cells (figure 54.1). Thus, the first challenge of fertilization is that sperm have to penetrate these external layers to reach the plasma membrane of the egg.

A saclike organelle named the **acrosome** is positioned between the plasma membrane and the nucleus of the sperm head. The acrosome contains digestive enzymes, which are released by the process of exocytosis when a sperm reaches the outer layers of the egg. These enzymes create a hole in the protective layers, enabling the sperm to tunnel its way through to the egg's plasma membrane.

In sea urchin sperm, actin monomers assemble into cytoskeletal filaments just under the plasma membrane to create a long narrow offshoot—the *acrosomal process*. The acrosomal process extends through the vitelline envelope to the egg's plasma membrane, and the sperm nucleus then passes through the acrosomal process to enter the egg.

In mice, an acrosomal process is not formed, and the entire sperm head burrows through the zona pellucida to the egg. Membrane fusion of the sperm and egg then allows the sperm nucleus to pass directly into the egg cytoplasm. In many species, egg cytoplasm bulges out at membrane fusion to engulf the head of the sperm (figure 54.2).

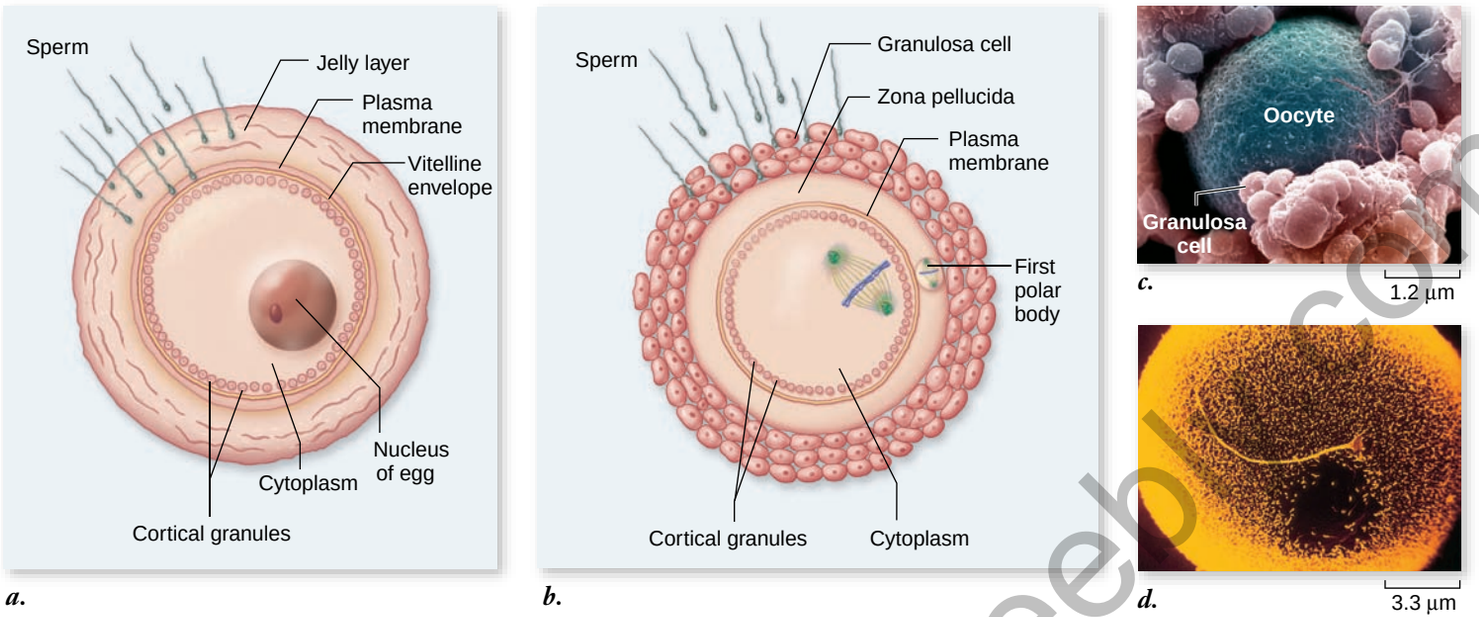


Figure 54.1 Animal reproductive cells. ***a.*** The structure of a sea urchin egg at fertilization. This diagram also shows the relative sizes of the sperm and egg. ***b.*** A mammalian sperm must penetrate a layer of granulosa cells and then a glycoprotein layer called the zona pellucida before it reaches the oocyte membrane. The scanning electron micrographs show ***(c)*** a human oocyte surrounded by numerous granulosa cells and ***(d)*** a human sperm on an egg.

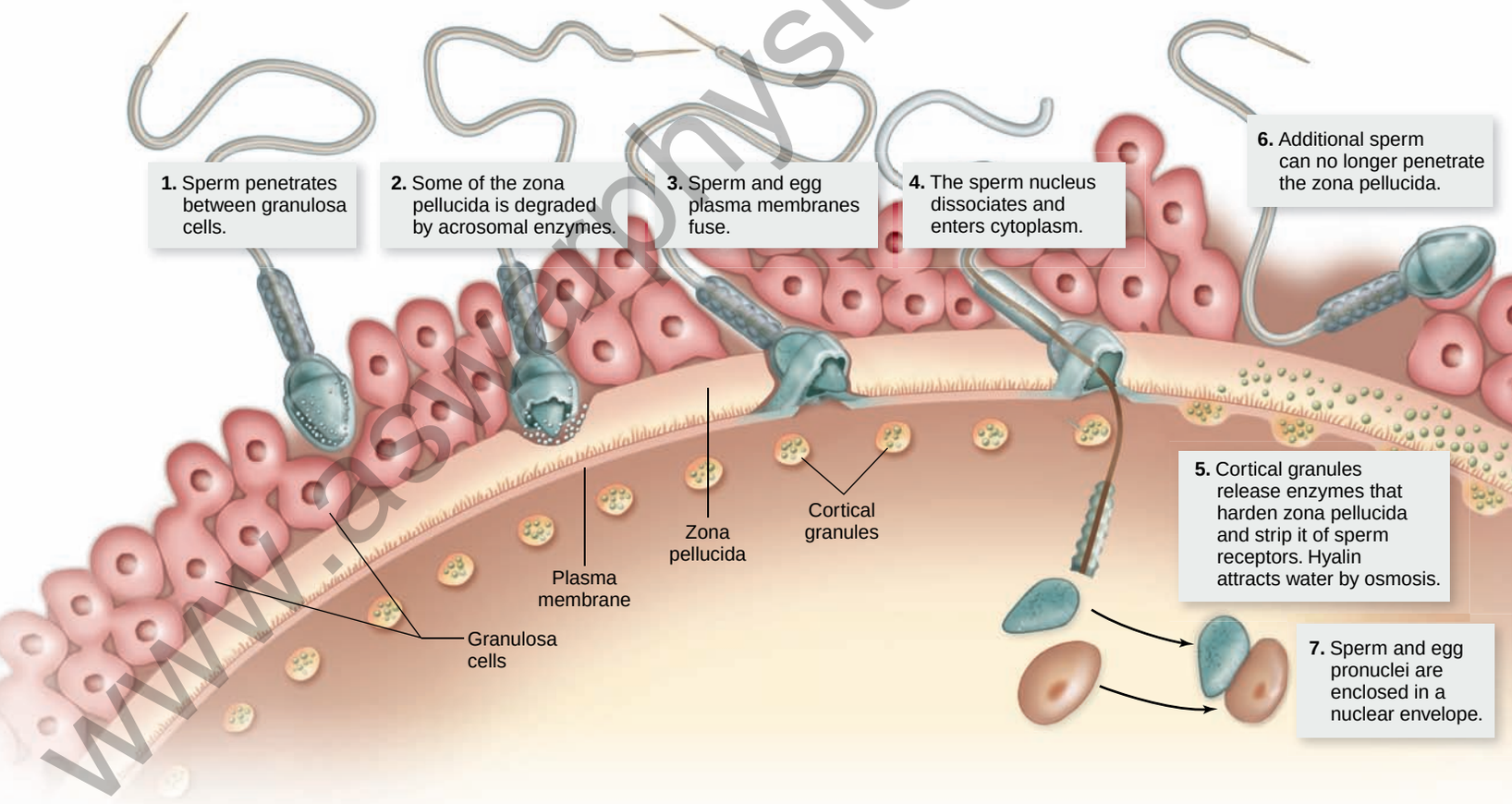


Figure 54.2 Sperm penetration and fusion. The sperm must penetrate the outer layers around the egg before fusion of sperm and egg plasma membranes can occur. Fusion activates the egg and leads to a series of events that prevent polyspermy.

Membrane fusion activates the egg

After ovulation, the egg remains in a quiescent state until fusion of the sperm and egg membranes triggers reactivation of the egg's metabolism. In most species, there is a dramatic increase in the levels of free intracellular Ca^{2+} ions in the egg shortly after the sperm makes contact with the egg's plasma membrane. This increase is due to release of Ca^{2+} from internal, membrane-bounded organelles, starting at the point of sperm entry and traversing across the egg.

Scientists have been able to watch this wave of Ca^{2+} release by preloading unfertilized eggs with a dye that fluoresces when bound to free Ca^{2+}, and then fertilizing the eggs (figure 54.3). The released Ca^{2+} act as second messengers in the cytoplasm of the egg, to initiate a host of changes in protein activity. These many events initiated by membrane fusion are collectively called *egg activation*.

Blocking of additional fertilization events

Because large numbers of sperm are released during spawning or ejaculation, many more than one sperm is likely to reach, and try to fertilize, a single egg. Multiple fertilization would result in a zygote that has three or more sets of chromosomes, a condition known as *polyploidy*. Polyploidy is incompatible with animal development, although it is frequently found in plants. As a result, an early response to sperm fusion in many animal eggs is to prevent fusion of additional sperm—in other words, to initiate a block to *polyspermy*.

In sea urchins, membrane contact by the first sperm results in a rapid, transient change in membrane potential of the egg, which prevents other sperm from fusing to the egg's plasma membrane. The importance of this event was shown by experiments where sea urchin eggs are fertilized in low-sodium, artificial seawater. The change in membrane potential is mostly due to an influx of Na^+, so fertilization in low-sodium water prevents this. Under these conditions polyspermy is much more frequent than in normal seawater.

Many animals use additional mechanisms to permanently alter the composition of the exterior egg coats, preventing any further sperm from penetrating through these layers. In sea urchins and mammals, specialized vesicles called **cortical granules,** located just beneath the plasma membrane of the egg, release their contents by exocytosis into the space between the plasma membrane and the vitelline envelope or zona pellucida, respectively. In each case, cortical granule enzymes remove critical sperm receptors from the outer coat of the egg.

Finally, the vitelline envelopes in many sea urchin species "lift off" the surfaces of the eggs via the combined action of different cortical granule enzymes and hyalin release. The enzymes digest connections between the vitelline envelope and the plasma membrane to allow separation. *Hyalin* is a sugar-rich macromolecule that attracts water by osmosis into the space between the vitelline envelope and the egg surface, thus separating the two. Additional sperm cannot penetrate through the hardened, elevated vitelline envelope, which is now called a *fertilization envelope*.

Many animals do not utilize any specific mechanisms to prevent multiple sperm from entering an egg. In these species, all but one of the sperm nuclei is degraded or subsequently extruded from the egg to prevent polyploidy.

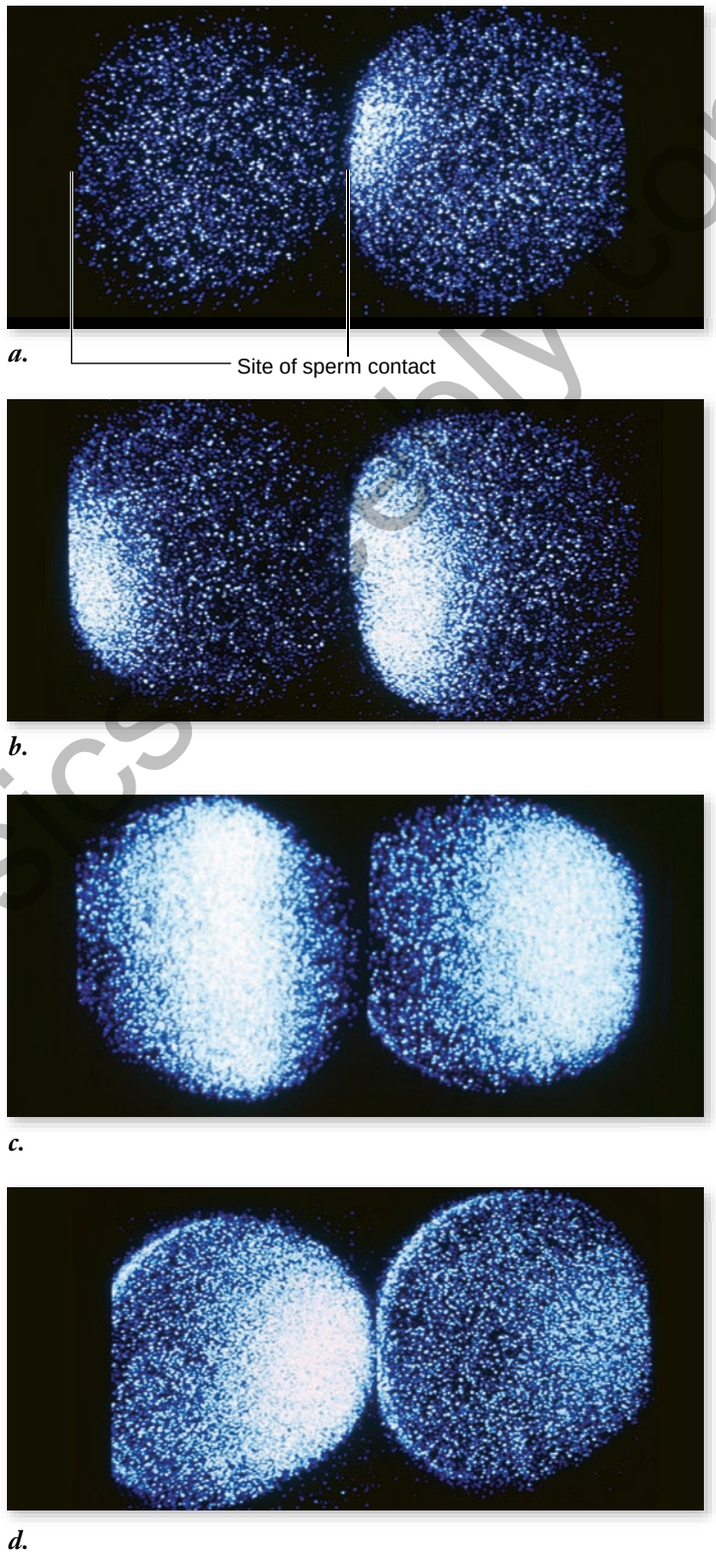


Figure 54.3 Calcium ions are released in a wave across two sea urchin eggs following sperm contact. The bright white dots are dye molecules that fluoresce when they are bound to Ca^{2+}. The Ca^{2+} wave moves from left to right in these two eggs ***(a–d)***. The egg on the right was fertilized a few seconds before the egg on the left. The wave takes about 30 sec to cross the entire egg.

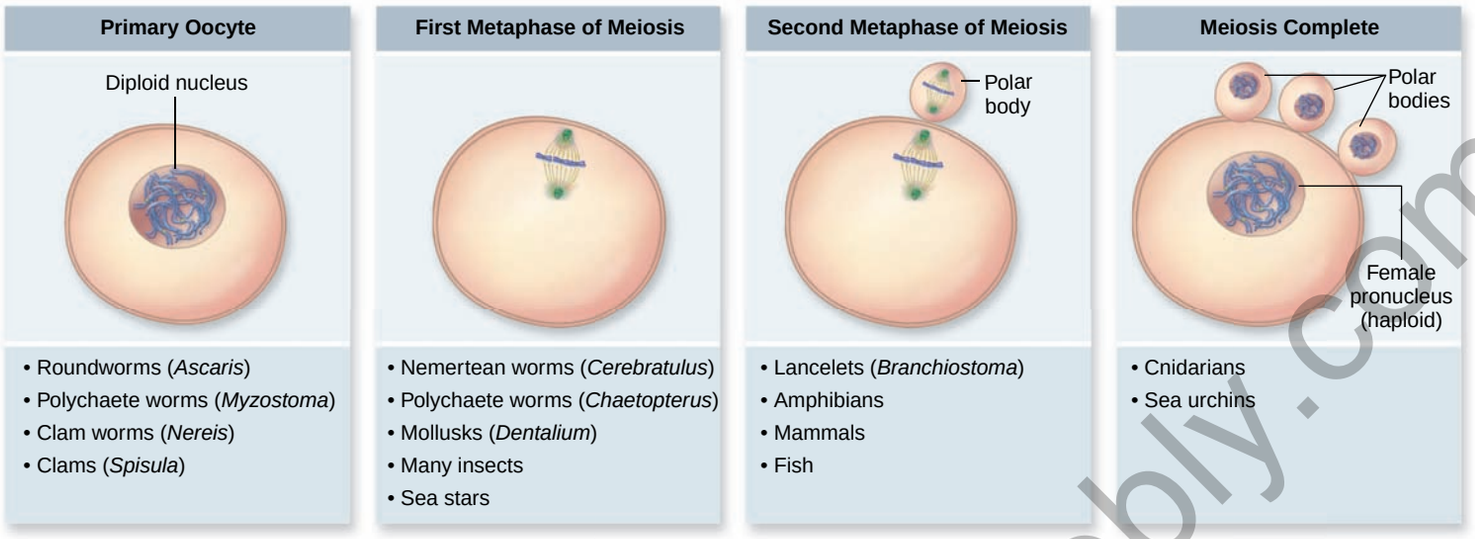


Figure 54.4 **Stage of egg maturation at time of sperm binding in representative animals.**

Other effects of sperm penetration

In addition to the previously mentioned surface changes, sperm penetration can have three other effects on the egg. First, in many animals, the nucleus of the unfertilized egg is not yet haploid because it had not entered or completed meiosis prior to ovulation (figure 54.4). Fusion of the sperm plasma membrane then triggers the eggs of these animals to complete meiosis. In mammals, a single large egg with a haploid nucleus and one or more small polar bodies, which contain the other nuclei, are produced (see chapter 53).

Second, sperm penetration in many animals triggers movements of the egg cytoplasm. In chapter 19, we discussed the cytoplasmic rearrangements of newly fertilized tunicate eggs, which result in the asymmetrical localization of pigment granules that determine muscle development. In amphibian embryos, the point of sperm entry is the focal point of cytoplasmic movements in the egg, and these movements ultimately establish the bilateral symmetry of the developing animal.

In some frogs, for example, sperm penetration causes an outer pigmented cap of egg cytoplasm to rotate toward the point of entry, uncovering a gray crescent of interior cytoplasm opposite the point of penetration (figure 54.5). The position of this gray crescent determines the orientation of the first cell division.

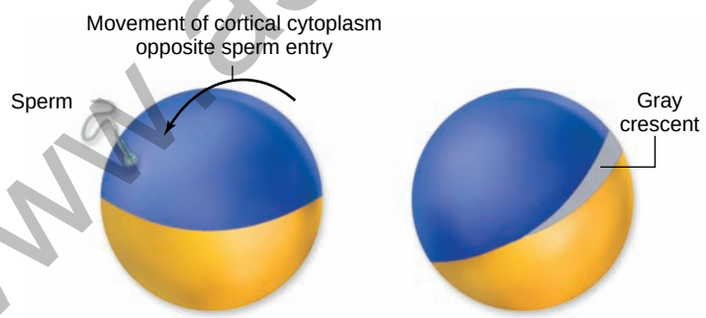


Figure 54.5 **Gray crescent formation in frog eggs.**
The gray crescent forms on the side of the egg opposite the point of penetration by the sperm.

A line drawn between the point of sperm entry and the gray crescent would bisect the right and left halves of the future adult.

Third, activation is characterized by a sharp increase in protein synthesis and an increase in metabolic activity in general. Experiments demonstrate that the burst of protein synthesis in an activated egg uses mRNAs that were deposited into the cytoplasm of the egg during oogenesis.

In some animals, it is possible to artificially activate an egg without the entry of a sperm, simply by pricking the egg membrane. An egg that is activated in this way may go on to develop parthenogenetically. A few kinds of amphibians, fish, and reptiles rely entirely on parthenogenetic reproduction in nature, as we mentioned in chapter 53.

The fusion of nuclei restores the diploid state

In the third and final stage of fertilization, the haploid sperm nucleus fuses with the haploid egg nucleus to form the diploid nucleus of the zygote. The process involves migration of the two nuclei toward each other along a microtubule-based aster. A centriole that enters the egg cell with the sperm nucleus organizes the microtubule array, which is made from stored tubulin proteins in the egg's cytoplasm.

In mammals, including humans, the nuclei do not actually fuse. Instead sperm and egg nuclear membranes each break down prior to the formation of a new diploid nucleus. A new nuclear membrane forms around the two sets of chromosomes.

Learning Outcomes Review 54.1

Following penetration, fusion of sperm with the egg membrane initiates a series of events including egg activation, blocks to polyspermy, and major rearrangements of cytoplasm. Polyspermy is blocked by changes in membrane polarity, release of enzymes that remove sperm receptors, and release of hyalin that lifts the vitelline envelope from the cell membrane. Egg and sperm nuclei then fuse to create a diploid zygote.

- ***What is the role of Ca^{2+} in egg activation?***

54.2 Cleavage and the Blastula Stage

Learning Outcomes

1. *Define the terms cleavage and blastula.*
2. *Describe the different patterns of cleavage.*
3. *Explain what is meant by regulative development.*

Following fertilization, the second major event in animal development is the rapid division of the zygote into a larger and larger number of smaller and smaller cells (see table 54.1). This period of division, called *cleavage*, is not accompanied by an increase in the overall size of the embryo. Each individual cell in the resulting tightly packed mass of cells is referred to as a *blastomere*. In many animals, the two ends of the egg and subsequent embryo are traditionally referred to as the **animal pole** and the **vegetal pole.** In general, the blastomeres of the animal pole go on to form the external tissues of the body, and those of the vegetal pole form the internal tissues.

The blastula is a hollow mass of cells

In many animal embryos, the outermost blastomeres in the ball of cells produced during cleavage become joined to one another by tight junctions, belts of protein that encircle a cell and weld it to its neighbors (see chapter 4). These tight junctions create a seal that isolates the interior of the cell mass from the surrounding medium.

Subsequently, cells in the interior of the mass begin to pump Na^+ from their cytoplasm into the spaces between cells. The resulting osmotic gradient causes water to be drawn into the center of the embryo, enlarging the intercellular spaces. Eventually, the spaces coalesce to form a single large cavity within the embryo. The resulting hollow ball of cells is called a *blastula* (or *blastocyst* in mammals), and the fluid-filled cavity within the blastula is known as the **blastocoel** (see table 54.1).

Cleavage patterns are highly diverse and distinctive

Cleavage divisions are quite rapid in most species, and chapter 19 provides an overview of the conserved set of proteins that control the cell cycle in animal embryos. Cleavage patterns are quite diverse, and there are about as many ways to divide up the cytoplasm of an animal egg during cleavage as there are phyla of animals! Nonetheless, we can make some generalizations.

First, the relative amount of nutritive yolk in the egg is the characteristic that most affects the cleavage pattern of an animal embryo (figure 54.6). Vertebrates exhibit a variety of developmental strategies involving different patterns of yolk utilization.

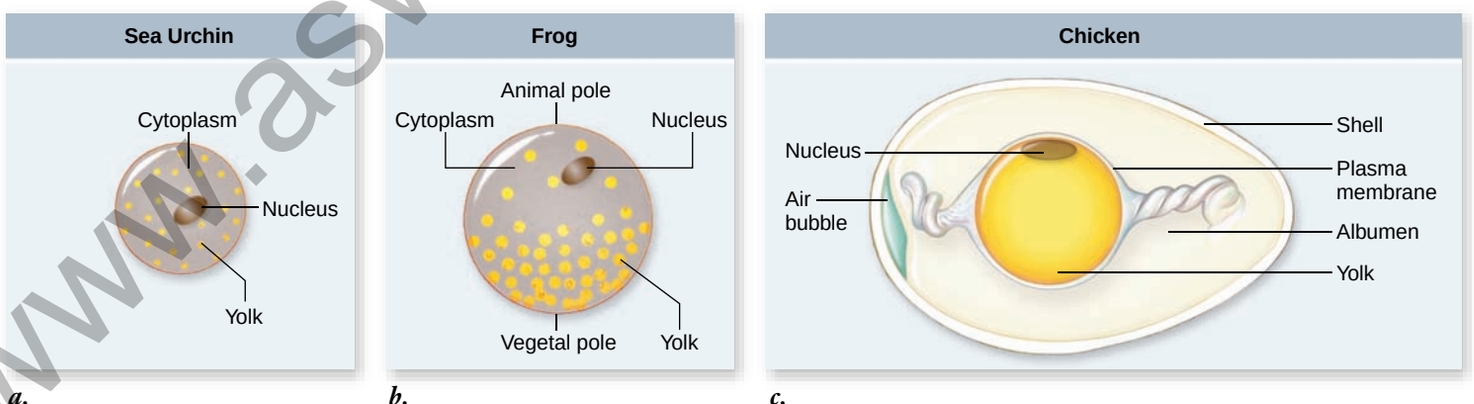
Cleavage in insects

Insects have yolk-rich eggs, and in chapter 19 we discussed the *syncytial blastoderm* of insects, in which multiple mitotic divisions of the nucleus occur in the absence of cytokinesis. Because there are no membranes separating the early embryonic nuclei of insects, gradients of diffusible proteins termed *morphogens* within the egg's cytoplasm can directly and differentially affect the activity of these embryonic nuclei, and thus the pattern of the early embryo. The nuclei eventually migrate to the periphery of the egg, where cell membranes form around each nucleus. The resulting *cellular blastoderm* of an insect has a single layer of cells surrounding a central mass of yolk (see figure 19.12 and table 54.2) .

Cleavage of eggs with moderate or little yolk

In eggs that contain moderate to little yolk, cleavage occurs throughout the whole egg, a pattern called **holoblastic cleavage** (figure 54.7). This pattern of cleavage is characteristic of invertebrates such as mollusks, annelids, echinoderms, and tunicates, and also of amphibians and mammals (described shortly).

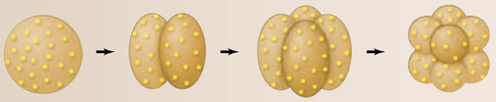
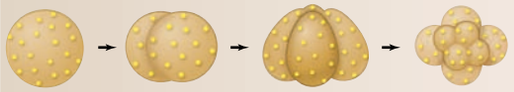
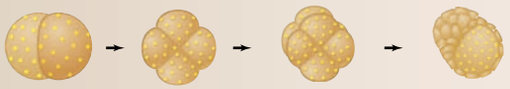
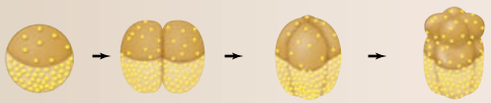
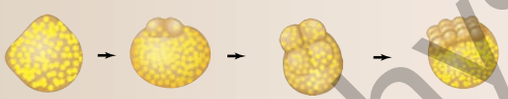
In sea urchins, holoblastic cleavage results in the formation of a symmetrical blastula composed of a single layer of cells of approximately equal size surrounding a spherical blastocoel. In contrast, amphibian eggs contain much more cytoplasmic yolk in the vegetal hemisphere than in the animal hemisphere. Because yolk-rich regions divide much more



a. *b.* *c.*

Figure 54.6 Yolk distribution in three kinds of eggs. ***a.*** In a sea urchin egg, the cytoplasm contains a small amount of evenly distributed yolk and a centrally located nucleus. ***b.*** In a frog egg, there is much more yolk, and the nucleus is displaced toward one pole. ***c.*** Bird eggs are complex, with the nucleus contained in a small disc of cytoplasm that sits on top of a large, central yolk mass.

TABLE 54.2 The Major Cleavage Patterns of Animal Embryos

HOLOBLASTIC (COMPLETE) CLEAVAGE	
Isolecithal (Sparse, evenly distributed yolk)	
Radial cleavage Echinoderms	
Spiral cleavage Annelids Mollusks Flatworms	
Rotational cleavage Mammals Nematodes	
Mesolecithal (Moderate vegetal yolk disposition)	
Displaced radial cleavage Amphibians	
MEROBLASTIC (INCOMPLETE) CLEAVAGE	
Telolecithal (Dense yolk throughout most of cell)	
Discoidal cleavage Fish Reptiles Birds	
Centrolecithal (Yolk in center of egg)	
Syncytial cleavage Most insects	

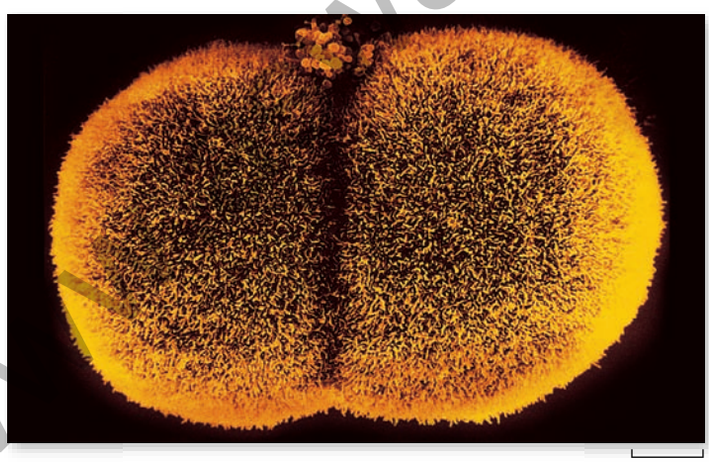
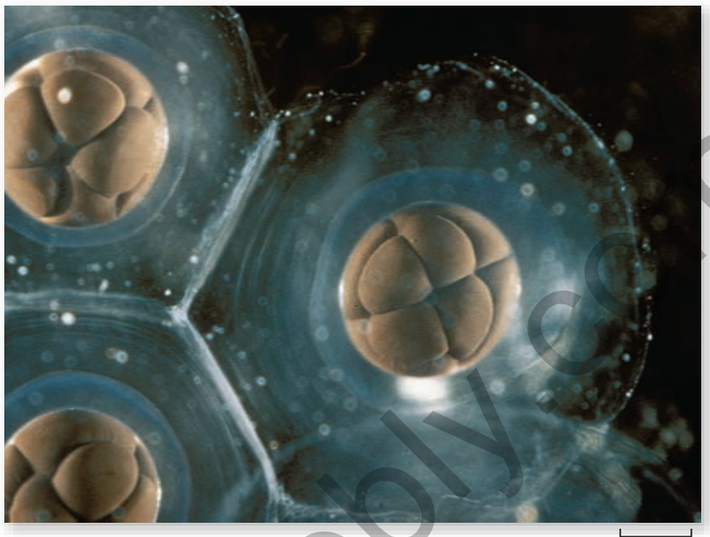
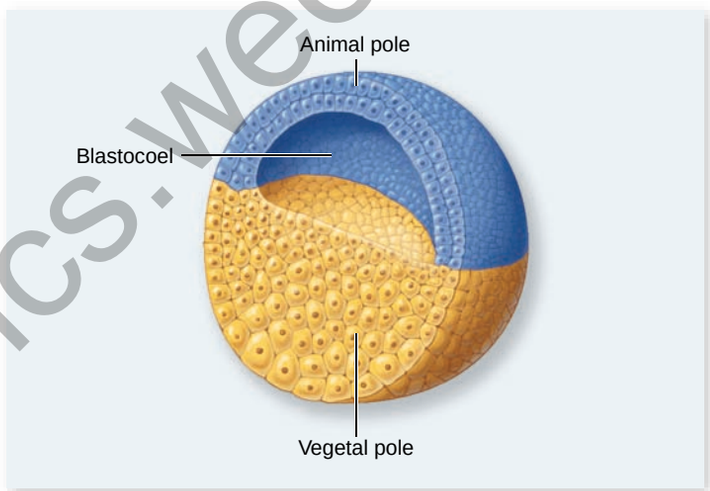


Figure 54.7 Holoblastic cleavage. In this type of cleavage, which is characteristic of eggs with relatively small amounts of yolk, cell division occurs throughout the entire egg.



a.



b.

Figure 54.8 Frog cleavage and blastula formation. ***a.*** The closest cells in this photo (those near the animal pole) divide faster and are smaller than those near the vegetal pole (below cells of the animal pole). ***b.*** A cross-section of a frog blastula, showing an eccentric blastocoel, larger yolk-filled cells at the vegetal pole, and smaller cells with little yolk at the animal pole.

slowly than areas with little yolk, horizontal cleavage furrows are displaced toward the animal pole (figure 54.8*a*). Thus, holoblastic cleavage in frog eggs results in an asymmetrical blastula, with a displaced blastocoel. The blastula consists of large cells containing a lot of yolk at the vegetal pole, and smaller, more numerous cells containing little yolk at the animal pole (figure 54.8*b*).

Cleavage of eggs with large amounts of yolk

The eggs of reptiles, birds, and some fishes are composed almost entirely of yolk, with a small amount of clear cytoplasm concentrated at one pole called the **blastodisc.** Cleavage in these eggs is restricted to the blastodisc. The yolk is essentially an inert mass. This type of cleavage pattern is called **meroblastic**

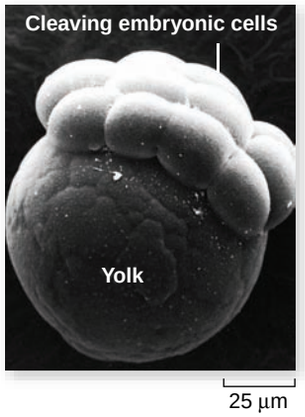


Figure 54.9 Meroblastic cleavage. Only a portion of the egg actively divides to form a mass of cells in this type of cleavage, which occurs in eggs with relatively large amounts of yolk.

cleavage (figure 54.9). The resulting embryo is not spherical, but rather has the form of a thin cap perched on the yolk.

Cleavage in mammals

Mammalian eggs contain very little yolk; however, mammalian embryogenesis has many similarities to development of their reptilian and avian relatives.

Because cleavage is not impeded by yolk in mammalian eggs, it is holoblastic, forming a structure called a *blastocyst*, in which a single layer of cells surrounds a central fluid-filled blastocoel. In addition, an **inner cell mass (ICM)** is located at one pole of the blastocoel cavity (figure 54.10). The ICM is similar to the blastodisc of reptiles and birds, and it goes on to form the developing embryo.

The outer layer of cells, called the **trophoblast,** is similar to the cells that form the membranes underlying the tough outer shell of the reptilian egg. These cells have changed during the course of mammalian evolution to carry out a very different function: Part of the trophoblast enters the maternal endometrium (the epithelial lining of the uterus) and contributes to the *placenta*, the organ that permits exchanges between the fetal and maternal blood supplies. The placenta will be discussed in more detail in a later section.

The major cleavage patterns of animal embryos are summarized in table 54.2.

Blastomeres may or may not be committed to developmental paths

Viewed from the outside, cleavage-stage embryos often look like a simple ball or disc of similar cells. In many animals, this appearance is misleading; for example, the unequal segregation of cytoplasmic determinants into specific blastomeres of tunicate embryos (described in chapter 19) commits those cells to different developmental paths. The experimental destruction or removal of these committed cells results in embryos deficient in the tissues that would have developed from those cells.

In contrast, mammals exhibit highly *regulative development*, in which early blastomeres do not appear to be committed to a particular fate. For example, if a blastomere is removed from an early eight-cell stage human embryo (as is done in the process of preimplantation genetic diagnosis), the remaining seven cells of the embryo will "regulate" and develop into a complete individual if implanted into the uterus of a woman. Similarly, embryos that are split into two (either naturally or experimentally) form identical twins. It therefore appears that inheritance of maternally encoded determinants is not an important mechanism in mammalian development, and body form is determined primarily by cell–cell interactions.

The earliest patterning events in mammalian embryos occur during the preimplantation stages that lead to formation of the blastocyst. At the eight-cell stage, the outer surfaces of many mammalian blastomeres flatten against each other in a process called *compaction*, which serves to polarize the blastomeres. The polarized blastomeres then undergo asymmetrical cell divisions. Cell lineage studies have shown that cells that are in the interior of the embryo most often become ICM cells of the mammalian blastocyst, whereas cells on the exterior of the embryo usually become trophoblast cells.

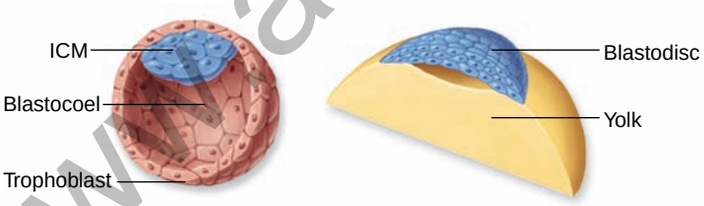


Figure 54.10 The embryos of mammals and birds are more similar than they seem. A mammalian blastula *(left)*, called a blastocyst, is composed of a sphere of cells, the trophoblast, surrounding a cavity, the blastocoel, and an inner cell mass (ICM). An avian (bird) blastula consists of a cap of cells, the blastodisc, resting atop a large yolk mass *(right)*. The blastodisc will form an upper and a lower layer with a compressed blastocoel in between.

Learning Outcomes Review 54.2

Cleavage is a series of rapid cell divisions that transforms the zygote into the blastula—a hollow ball of cells. The amount of yolk is the major determinant of cleavage pattern. Eggs with little yolk cleave completely (holoblastic cleavage); eggs with a large yolk cannot cleave completely (meroblastic cleavage). In many animals, each blastomere is committed to a developmental path; in mammals, blastomeres are not committed but can regulate as needed to produce a complete individual.

- ***If the cells of a mammalian embryo were separated at the four-cell stage, would they develop normally? What about a frog embryo at the four-cell stage?***

54.3 Gastrulation

Learning Outcomes

1. *Define gastrulation.*
2. *Compare gastrulation in different animals.*
3. *Name the extraembryonic membranes in amniotes.*

In a complex series of cell shape changes and cell movements, the cells of the blastula rearrange themselves to form the basic body plan of the embryo. This process, called *gastrulation*, forms the three primary germ layers and converts the blastula

TABLE 54.3	Developmental Fates of the Primary Germ Layers in Vertebrates
Ectoderm	Epidermis of skin, nervous system, sense organs
Mesoderm	Skeleton, muscles, blood vessels, heart, blood, gonads, kidneys, dermis of skin
Endoderm	Lining of digestive and respiratory tracts, liver, pancreas, thymus, thyroid

into a bilaterally symmetrical embryo with a central progenitor gut and visible anterior–posterior and dorsal–ventral axes.

Gastrulation produces the three germ layers

Gastrulation creates the three primary *germ layers:* endoderm, ectoderm, and mesoderm. The cells in each germ layer have very different developmental fates. The cells that move into the embryo to form the tube of the primitive gut are *endoderm;* they give rise to the lining of the gut and its derivatives (pancreas, lungs, liver, etc.). The cells that remain on the exterior are *ectoderm*, and their derivatives include the epidermis on the outside of the body and the nervous system. The cells that move into the space between the endoderm and ectoderm are *mesoderm;* they eventually form the notochord, bones, blood vessels, connective tissues, muscles and internal organs such as the kidneys and gonads (table 54.3).

Cells move during gastrulation using a variety of cell shape changes. Some cells use broad, actin-filled extensions called *lamellipodia* to crawl over neighboring cells. Other cells send out narrow extensions called *filopodia*, which are used to "feel out" the surfaces of other cells or the extracellular matrix. Once a satisfactory attachment is made, the filopodia retract to pull the cell forward. Contractions of actin filament bundles are responsible for many of these cell shape changes. Cells that are tightly attached to one another via desmosomes or adherens junctions will move as cell sheets.

In embryos with little yolk and a hollow blastula, the cell sheet at the vegetal pole of the blastula **invaginates** (dents inward) to form the primitive gut tube. In embryos with large yolky cells that are hard to move, sheets of smaller cells **involute** (roll inward) from the surface of the blastula and move over the basal surfaces of the outer cells. Other cells break away from cell sheets and migrate as individual cells during **ingression.**

Avian and mammalian gastrulation begins with **delamination,** in which one sheet of cells splits into two sheets. Each migrating cell possesses particular cell-surface glycoproteins, which adhere to specific molecules on the surfaces of other cells or in the extracellular matrix. Changes in cell adhesiveness, as described in chapter 19, are key events in gastrulation. The extracellular matrix protein fibronectin and the corresponding integrin receptors of cells are essential molecules of gastrulation in many animals.

Gastrulation patterns also vary according to the amount of yolk

Just as in cleavage patterns, yolk quantity also affects the types of cell movements that occur during gastrulation. Here, we examine gastrulation in four representative classes of embryos with differing quantities of yolk.

Gastrulation in sea urchins

Echinoderms such as sea urchins develop from relatively yolk-poor eggs and form hollow, symmetrical blastulas. Gastrulation begins when cells at the vegetal surface of the blastula change their shape to form a flattened **vegetal plate.** In an example of ingression, a subset of cells in the vegetal plate breaks away from the blastula wall and moves into the blastocoel cavity. These **primary mesenchyme cells** are future mesoderm cells, and they use *filopodia* to migrate through the blastocoel cavity (figure 54.11).

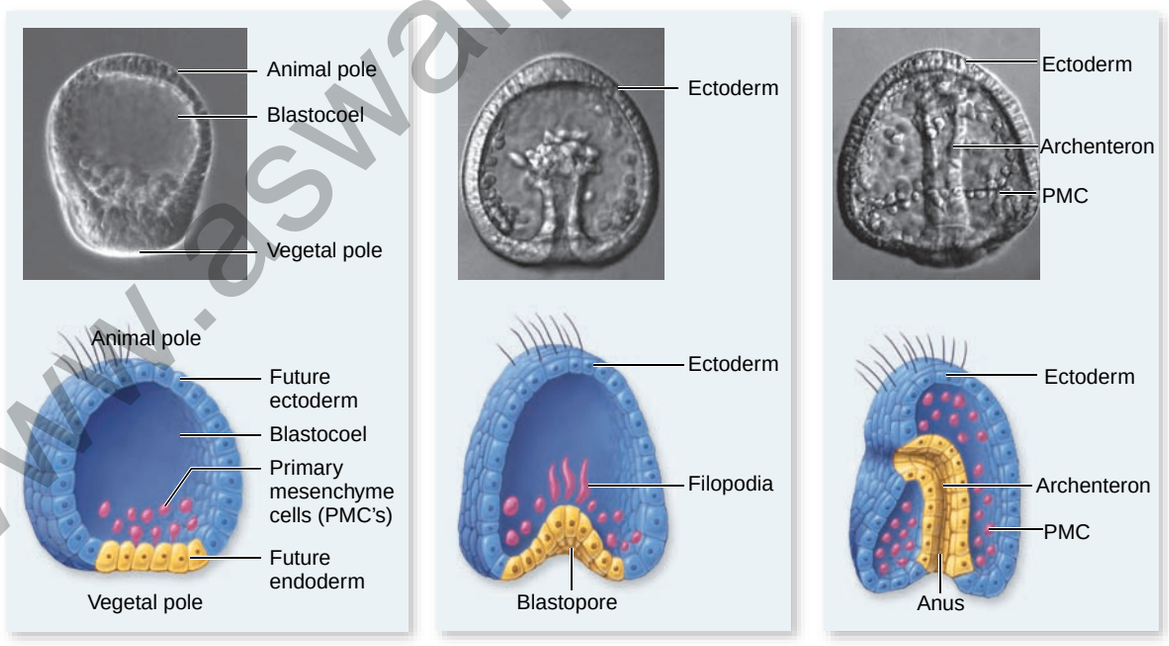


Figure 54.11
Gastrulation in a sea urchin. ***a.*** Gastrulation begins with formation of the vegetal plate and ingression of primary mesenchyme cells (prospective mesoderm cells) into the blastocoel cavity. ***b.*** The endoderm is then formed by invagination of the remaining vegetal plate cells and extension of a cellular tube to produce the primitive gut, or archenteron. ***c.*** Cells that remain on the surface form the ectoderm.

Eventually, they become localized in the ventrolateral corners of the blastocoel, where they form the larval skeleton.

The remaining cells of the vegetal plate then invaginate into the blastocoel to form the endoderm layer, creating a structure that looks something like an indented tennis ball. Eventually, the inward-moving tube of cells contacts the opposite side of the gastrula and stops moving. The hollow structure resulting from the invagination is called the *archenteron*, and it is the progenitor of the digestive tube. The opening of the archenteron, the future anus, is known as the *blastopore*. A secondary opening develops at the point where the archenteron contacts the opposite side of the gastrula, forming the mouth (see figure 54.11). Animals in which the anus develops first and the mouth second are termed *deuterostomes*, as was discussed in chapter 32.

Gastrulation in frogs

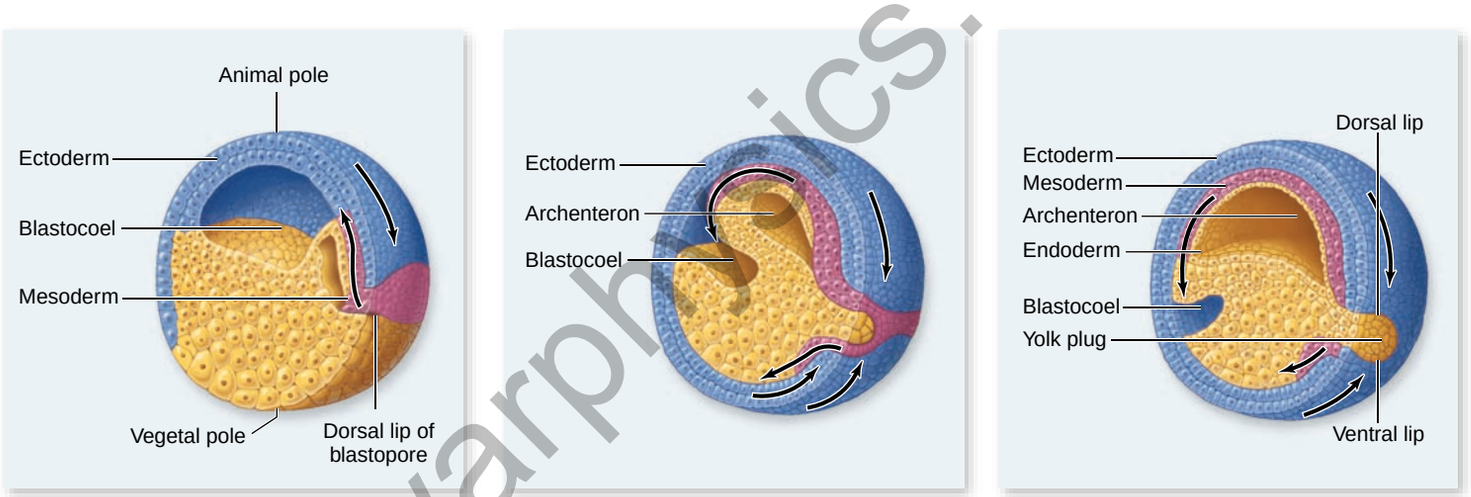
The blastula of an amphibian has an asymmetrical yolk distribution, and the yolk-laden cells of the vegetal pole are less numerous but much larger than the yolk-free cells of the animal pole. Consequently, gastrulation is more complex than it is in sea urchins. In frogs, a layer of surface cells first invaginates to form a small, crescent-shaped slit, which initiates formation of the blastopore. Next, cells from the animal pole involute over the dorsal lip of the blastopore (see figure 54.12*a*), which forms at the same location as the gray crescent of the fertilized egg (see figure 54.5).

The involuting cell layer eventually presses against the inner surface of the opposite side of the embryo, eliminating the blastocoel and producing an archenteron with a blastopore. In this case, however, the blastopore is filled with yolk-rich cells, forming the **yolk plug** (figure 54.12*b*, *c*). The outer layer of cells resulting from these movements is the ectoderm, and the inner layer is the endoderm. Other cells that involute over the dorsal lip and ventral lip (the two lips of the blastopore that are separated by the yolk plug) migrate between the ectoderm and endoderm to form the third germ layer—the mesoderm (figure 54.12*c*–*e*).

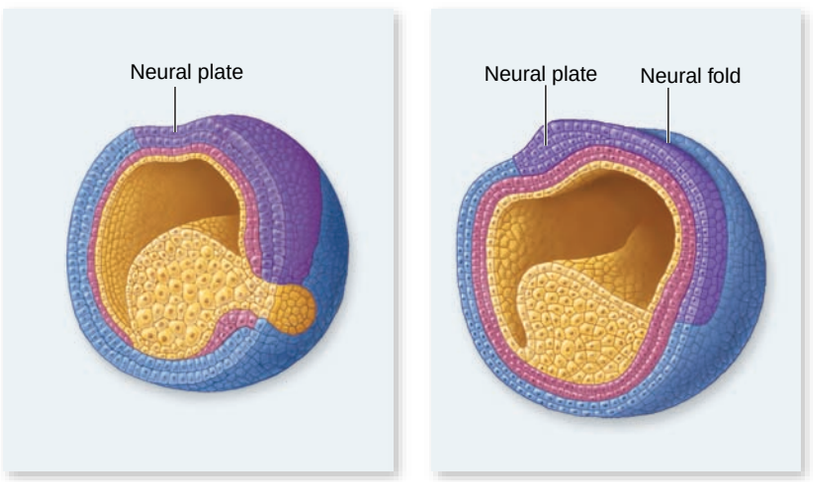
Gastrulation in birds

At the end of cleavage in a bird or reptile, the developing embryo is a small cap of cells called the **blastoderm,** which sits on top of the large ball of yolk (figure 54.13*a*). As a result, gastrulation proceeds somewhat differently.

In birds, the blastoderm first separates into two layers, and a blastocoel cavity forms between them (figure 54.13*b*).



a. *b.* *c.*



d. *e.*

Figure 54.12 Frog gastrulation. ***a.*** A layer of cells from the animal pole moves toward the vegetal pole, ultimately involuting through the dorsal lip of the blastopore. ***b.*** Cells in the dorsal lip zone then involute into the hollow interior, or blastocoel, eventually pressing against the far wall. The three primary germ tissues (ectoderm, mesoderm, and endoderm) become distinguished. Ectoderm is shown in blue, mesoderm in red, and endoderm in yellow. ***c.*** The movement of cells through the blastopore creates a new internal cavity, the archenteron, which displaces the blastocoel. ***d.*** Organogenesis begins when the neural plate forms from dorsal ectoderm to begin the process of neurulation. ***e.*** The neural plate next forms a neural groove and then a neural tube. The cells of the neural ectoderm are shown in purple.

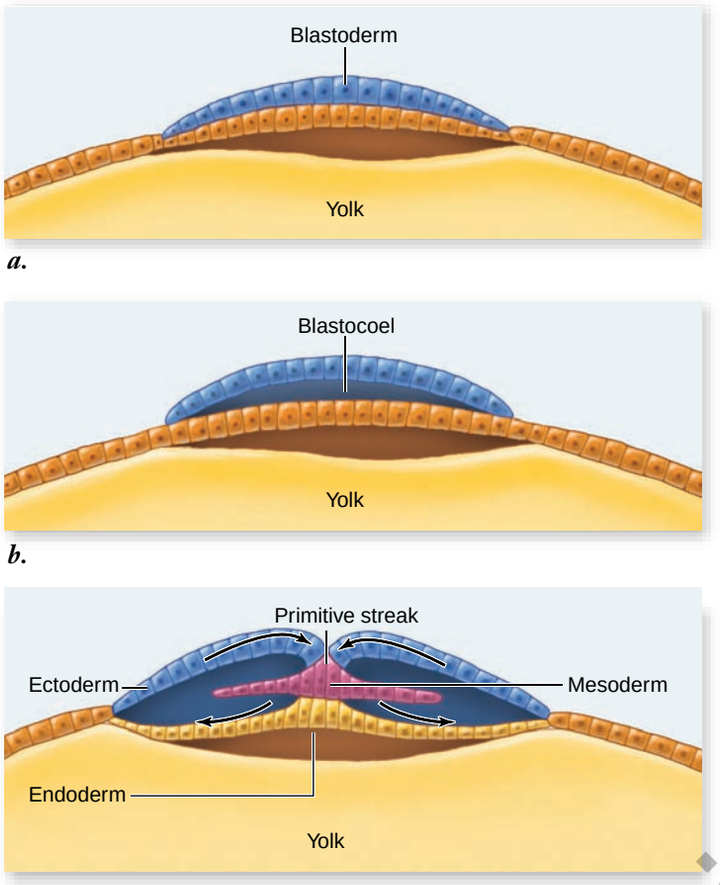


Figure 54.13 Gastrulation in birds. ***a.*** The avian blastula is made up of a disc of cells sitting atop the large yolk mass. ***b.*** Gastrulation commences with the delamination of the blastoderm into two layers. All three germ layers are derived from the upper layer of the blastoderm. ***c.*** Cells that migrate through the primitive streak into the interior of the embryo are future endoderm or mesoderm cells. Cells that remain in the upper layer form the ectoderm.

The deep, internal layer of the bilayered blastoderm gives rise to extraembryonic tissues only (described later on), whereas all cells of the embryo proper are derived from the upper layer of cells. Thus, the upper layer of the blastoderm gives rise to all three germ layers.

Some of the surface cells begin moving to the midline, where they break away from the surface sheet of cells and ingress into the blastocoel cavity. A furrow along the longitudinal midline marks the site of this ingression (figure 54.13*c*). This furrow, analogous to an elongated blastopore, is called the **primitive streak.** Some cells migrate through the primitive streak and across the blastocoel cavity to displace cells in the lower layer. These deep-migrating cells form the endoderm. Other cells that move through the primitive streak migrate laterally into intermediate regions and form a new layer—the mesoderm. Cells that remain on the surface and do not enter the primitive streak form the ectoderm.

Gastrulation in mammals

Mammalian gastrulation proceeds much the same as it does in birds. In both types of animals, the embryo develops from a flattened collection of cells—the blastoderm in birds or the inner cell mass in mammals. Although the blastoderm of a bird is flattened because it is pressed against a mass of yolk, the inner cell mass of a mammal is flat despite the absence of a yolk mass.

In mammals, the placenta has made yolk dispensable; the embryo obtains nutrients from its mother following implantation into the uterine wall. However, the embryo still gastrulates as though it were sitting on top of a ball of yolk.

In mammals, a primitive streak forms, and cell movements through the primitive streak give rise to the three primary germ layers, much the same as in birds (figure 54.14). Similarly, mammalian embryos envelop their "missing" yolk by forming a yolk sac from extraembryonic cells that migrate away from the lower layer of the blastoderm and line the blastocoel cavity.

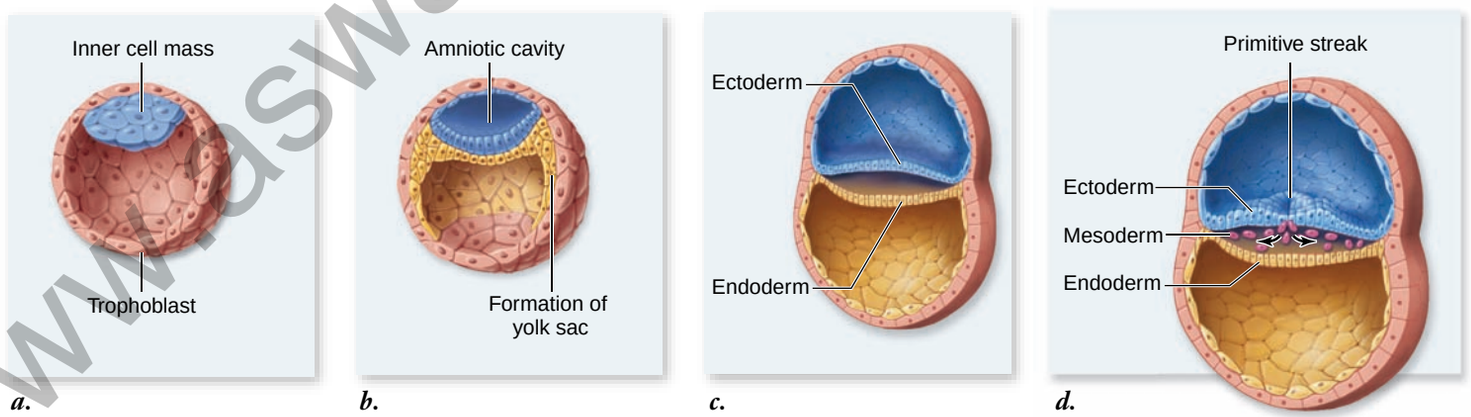
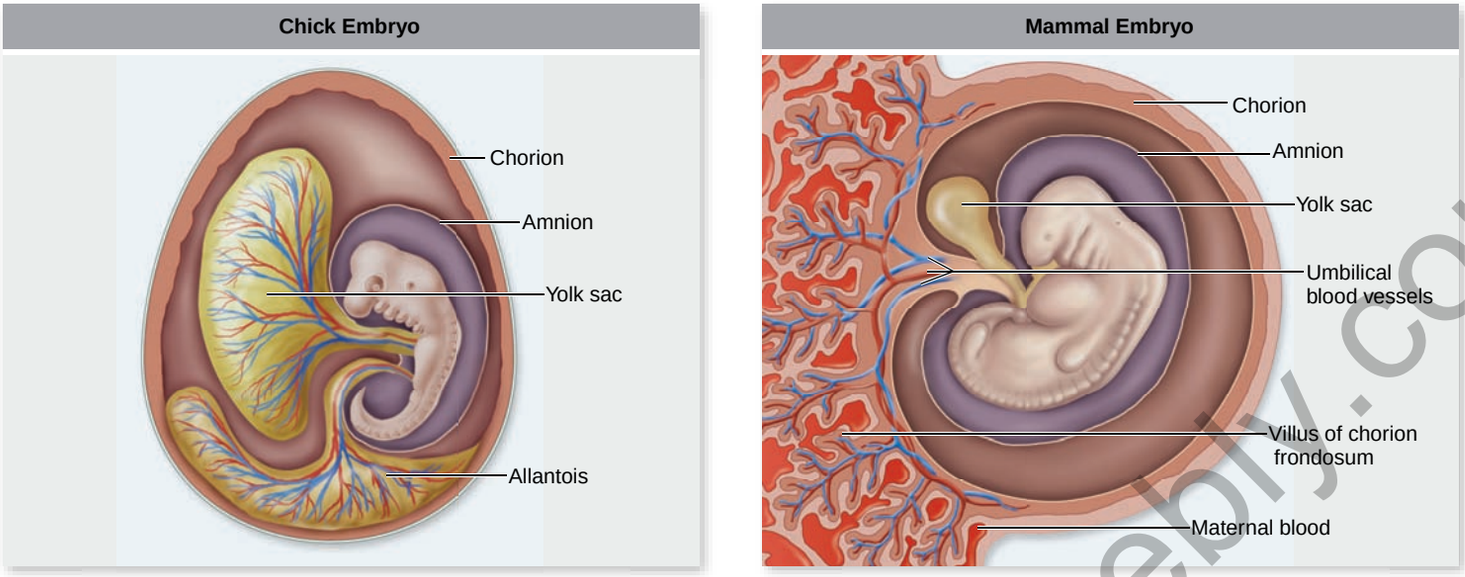


Figure 54.14 Mammalian gastrulation. ***a.*** Cross section of the mammalian blastocyst at the end of cleavage. ***b.*** The amniotic cavity forms between the inner cell mass (ICM) and the pole of the embryo. Meanwhile, the ICM flattens and delaminates into two layers that will become ectoderm and endoderm. ***b.*** and ***c.*** Cells of the lower layer migrate out to line the blastocoel cavity to form the yolk sac. ***d.*** A primitive streak forms the ectoderm layer, and cells destined to become mesoderm migrate into the interior, similar to gastrulation in birds.



a. *b.*

Figure 54.15 The extraembryonic membranes. The extraembryonic membranes in *(a)* a chick embryo and *(b)* a mammalian embryo share some of the same characteristics. However, in the chick, the allantois continues to grow until it eventually unites with the chorion just under the eggshell, where it is involved in gas exchange. In the mammalian embryo, the allantois contributes blood vessels to the developing umbilical cord.

Extraembryonic membranes are an adaptation to life on dry land

As an adaptation to terrestrial life, the embryos of reptiles, birds, and mammals develop within a fluid-filled *amniotic membrane*, or *amnion* (chapter 35). The amniotic membrane and several other membranes form from embryonic cells, but they are located outside of the body of the embryo. For this reason, they are known as **extraembryonic membranes.** The extraembryonic membranes include the amnion, chorion, yolk sac, and allantois.

In birds, the amnion and chorion arise from two folds that grow to completely surround the embryo (figure 54.15*a*). The amnion is the inner membrane that surrounds the embryo and suspends it in *amniotic fluid*, thereby mimicking the aquatic environments of fish and amphibian embryos. The chorion is located next to the eggshell and is separated from the other membranes by a cavity—the *extraembryonic coelom*.

The *yolk sac* plays a critical role in the nutrition of bird and reptile embryos; it is also present in mammals, although it does not nourish the embryo. The *allantois* is derived as an outpouching of the gut and serves to store the uric acid excreted in the urine of birds. During development, the allantois of a bird embryo expands to form a sac that eventually fuses with the overlying chorion, just under the eggshell. The fusion of the allantois and chorion form a functioning unit, the chorioallantoic membrane, in which embryonic blood vessels, carried in the allantois, are brought close to the porous eggshell for gas exchange. The chorioallantoic membrane is thus the respiratory membrane of a bird embryo.

In mammals, the trophoblast cells of the blastocyst implant into the endometrial lining of the mother's uterus and become the chorionic membrane (figure 54.15*b*). The part of the chorion in contact with endometrial tissue contributes to the placenta. The other part of the placenta is composed of modified endometrial tissue of the mother's uterus, as is described in more detail in a later section. The allantois in mammals contributes blood vessels to the structure that will become the umbilical cord, so that fetal blood can be delivered to the placenta for gas exchange.

Learning Outcomes Review 54.3

Gastrulation involves cell rearrangement and migration to produce ectoderm, mesoderm, and endoderm. In sea urchins, endoderm forms by invagination of the blastula; mesodermal cells form from other surface cells. In vertebrates with moderate to extensive amounts of yolk, surface cells move through a blastopore or a primitive streak, respectively. Mammalian gastrulation is similar to gastrulation in birds. Extraembryonic membranes of amniote species form from embryonic cells outside the embryo's body and include the yolk sac, amnion, chorion, and allantois.

- ***What kind of cellular behaviors are necessary for gastrulation?***

54.4 Organogenesis

Learning Outcomes

1. ***Describe examples of organogenesis.***
2. ***Describe neurulation and somitogenesis.***
3. ***Explain the migration and role of neural crest cells.***

Gastrulation establishes the basic body plan and creates the three primary germ layers of animal embryos. The stage is now

set for *organogenesis*—the formation of the organs in their proper locations—which occurs by interactions of cells within and between the three germ layers. Thus, organogenesis follows rapidly on the heels of gastrulation, and in many animals begins before gastrulation is complete. Over the course of subsequent development, tissues develop into organs and animal embryos assume their unique body form (see table 54.1).

Changes in gene expression lead to cell determination

All of the cells in an animal's body, with the exception of a few specialized ones that have lost their nuclei, have the same complement of genetic information. Despite the fact that all of its cells are genetically identical, an adult animal contains dozens to hundreds of cell types, each expressing some unique aspect of the total genetic information for that individual. The information for other cell types is not lost, but most cells within a developing organism progressively lose the capacity to express ever-larger portions of their genomes. What factors determine which genes are to be expressed in a particular cell?

To a large degree, a cell's location in the developing embryo determines its fate. By changing a cell's location, an experimenter can often alter its developmental destiny, as mentioned in chapter 19. But this is only true up to a certain point in the cell's development. At some stage, every cell's ultimate fate becomes fixed, a process referred to as *cell determination*.

A cell's fate can be established by inheritance of cytoplasmic determinants or by interactions with neighboring cells. The process by which a cell or group of cells instructs neighboring cells to adopt a particular fate is called *induction*. If a nonporous barrier, such as a layer of cellophane, is imposed between the inducer and the target tissue, no induction takes place. In contrast, a porous filter, through which proteins can pass, does permit induction to occur.

In these experiments, researchers concluded that the inducing cells secrete a paracrine signal molecule that binds to the cells of the target tissue. Such signal molecules are capable of producing changes in the patterns of gene transcription in the target cells. You will learn more about the origin of embryonic induction a little later in this chapter.

Development of selected systems in *Drosophila* illustrates organogenesis

In chapter 19, you saw how the creation of morphogen gradients in a fruit fly embryo leads to hierarchies of gene expression that direct cell fate decisions along both the anterior–posterior and dorsal–ventral axes. These two axes form a coordinate system to specify the position of tissues and organs within the *Drosophila* embryo. In this section we look at development of three different organs: salivary glands, the heart, and the tracheae of the respiratory system.

Salivary gland development

The fruit fly larva is a mobile eating machine, and thus it has very active salivary glands. The primordia of the salivary glands develop as simple tubular invaginations of ectodermal cells on the ventral surface of the third head segment.

Salivary glands develop only from an anterior strip of cells that express the *sex combs reduced (scr)* gene. No salivary glands form in *scr*-deficient embryos, whereas experimental expansion of *scr* expression along the anterior–posterior axis results in the formation of additional salivary gland primordia along the length of the embryo.

The *scr* gene is one of the homeotic genes in the Antennapedia complex, which encode transcription factors that bind to DNA via their homeodomains to regulate gene expression (see chapter 19). One downstream target of the *scr* gene is the *fork head (fkh)* gene, which has Scr-binding sites in its enhancer. The *fkh* gene is required for secretory cell development in salivary gland rudiments, and it encodes a transcription factor that directly activates expression of salivary gland-specific genes. Thus, action of the *scr* gene activates *fkh* expression at the proper anterior location for salivary gland formation.

The inhibitory action of a dorsally expressed protein, Decapentaplegic (Dpp), determines the ventral position of the salivary glands. Activation of the Dpp-signaling pathway represses salivary gland specification in neighboring cells. This restricts development of salivary gland rudiments to their specific ventral patch of ectoderm cells (figure 54.16). In mutant embryos deficient for Dpp or any of the downstream Dpp-signaling proteins,

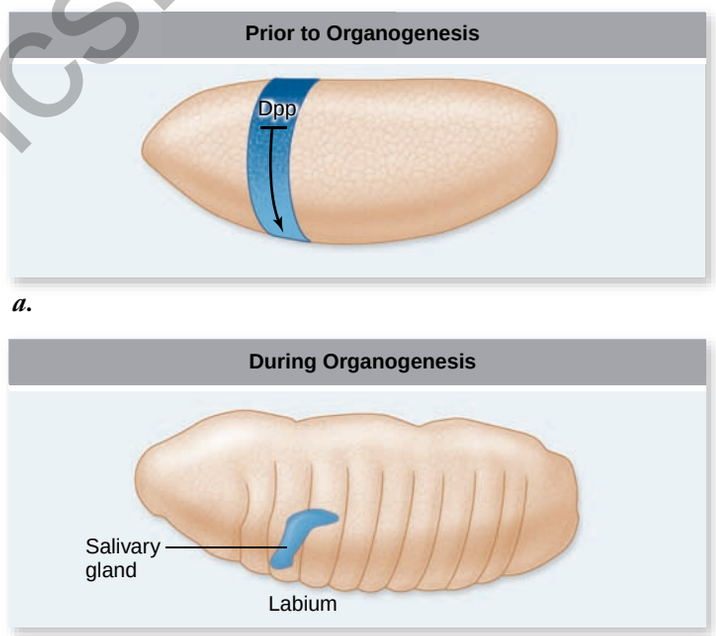


Figure 54.16 Salivary gland formation in *Drosophila*. Prospective salivary gland cells are determined by the intersection of the anterior–posterior and dorsal–ventral axes. ***a.*** Prior to organogenesis, the sex combs reduced *(scr)* gene is expressed in an anterior band of cells (shaded blue). At the same time, Decapentaplegic protein (Dpp) is released by cells on the dorsal side of the embryo, forming a gradient in the dorsal–ventral direction. Dpp specifies dorsal cell fates and inhibits formation of salivary gland rudiments. ***b.*** During organogenesis, the salivary glands develop in areas where Scr is expressed but Dpp is absent. Each salivary gland rudiment forms as a ventral invagination of the surface ectoderm on either side of the third head segment (the labium).

salivary gland rudiments are not restricted to this ventral patch, and they form from the entire ectoderm of the third segment.

Heart development

The heart is a mesoderm-derived structure in all animals, and it is the first organ to become functional during embryonic development. The dorsal vessel is the heart-equivalent structure in *Drosophila melanogaster*. The homeobox-containing gene *tinman* is expressed in the prospective heart mesoderm and in the developing dorsal vessel, and its activity is required for dorsal vessel development in *Drosophila* (figure 54.17).

Dorsal vessel development in *Drosophila* is also dependent on two other types of transcription factors (known as GATA and T-box factors). In an illuminating case of evolutionary conservation, scientists have discovered gene families similar to each of these three *Drosophila* genes in vertebrates. Moreover, members of these gene families play important roles in vertebrate heart specification.

This evolutionary conservation includes not just the structure of these genes, but their function as well. Researchers have discovered that specification of cardiac mesoderm is subject to inductive signals from adjoining germ layers in both *Drosophila* and vertebrates. In vertebrates, the heart develops in an internal location, and the inductive signals come from the underlying anterior endoderm. In *Drosophila*, the dorsal vessel forms in a more superficial location, and the signals come from the overlying ectoderm.

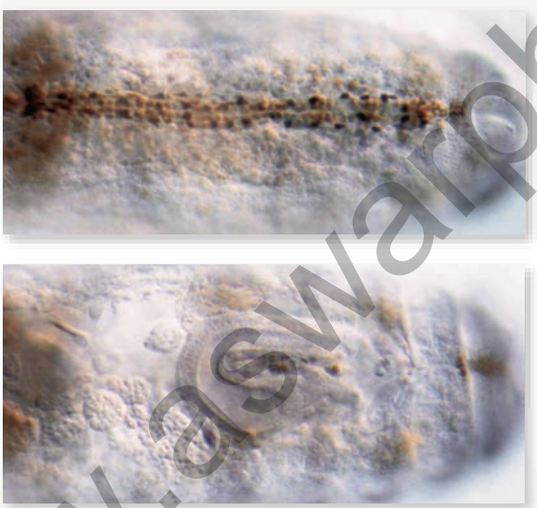
Despite the different sources, the signals that regulate the expression of these three key types of transcription factors are themselves conserved between *Drosophila* and vertebrates. Given the critical and conserved circulatory function of the heart, it is perhaps not surprising that similar gene families mediate the specification of heart mesoderm in both *Drosophila* and vertebrates.

SCIENTIFIC THINKING

Hypothesis: *The* tinman *gene is required for proper development of the dorsal vessel in Drosophila.*

Prediction: *The* tinman *gene must be expressed in precursor cells for the dorsal vessel. Loss of* tinman *function should result in loss of dorsal vessel.*

Test: *Analyze expression of* tinman *in whole mount embryos in wild type (top) and mutant (bottom) embryos.*



Result: *In the wild type embryo,* tinman *is expressed in a line of cells where the dorsal vessel forms. In mutant embryos with no expression, no dorsal vessel forms.*

Conclusion: *The function of* tinman *is necessary for dorsal vessel formation.*

Further Experiments: Tinman *is a homeobox containing gene. What does this suggest about its function? How could you follow up on this?*

Figure 54.17 A gene necessary for heart formation in *Drosophila*.

Tracheae: Branching morphogenesis

As you learned in chapters 34 and 49, insects exchange gases via a branching system of finer and finer tubes called *tracheae*. The repeated branching of simple epithelial tubes that leads to formation of the tracheal system is an example of **branching morphogenesis.**

Mutations in the *branchless* gene in *Drosophila* result in embryos with greatly reduced tracheal systems. The *branchless* gene encodes a member of the large family of **fibroblast growth factors (FGF),** which bind to receptor tyrosine kinase proteins (see chapter 9) to stimulate proliferation of target cells. In another interesting case of evolutionary conservation, the mammalian FGF homologue of the *branchless* gene is required for branching morphogenesis that creates the alveolar passageways in the mammalian lung.

In both animals, loose clusters of mesenchymal cells adjacent to distal regions of the epithelial tube secrete FGF. The FGF binds to a specific FGF receptor in the membrane of the epithelial cells, stimulating them to proliferate and to grow out into a new tube bud.

In vertebrates, organogenesis begins with neurulation and somitogenesis

The process of organogenesis in vertebrates begins with the formation of two morphological features found only in chordates: the *notochord* and the hollow **dorsal nerve cord** (see chapter 35). The development of the dorsal nerve cord is called *neurulation.*

Development of the neural tube

The notochord forms from mesoderm and is first visible soon after gastrulation is complete. It is a flexible rod located along the dorsal midline in the embryos of all chordates, although its function as a supporting structure is supplanted by the subsequent development of the vertebral column in the vertebrates. After the notochord has been laid down, the region of dorsal ectodermal cells situated above the notochord begins to thicken to form the *neural plate*.

The thickening is produced by the elongation of the dorsal ectoderm cells. Those cells then assume a wedge shape because of contracting bundles of actin filaments at their apical end. This change in shape causes the neural tissue to roll up into a **neural groove** running down the long axis of the embryo. The edges of the neural groove then move toward each

other and fuse, creating a long hollow cylinder, the **neural tube** (figure 54.18). The neural tube eventually pinches off from the surface ectoderm to end up beneath the surface of the embryo's back. Regional changes, which are under control of the *Hox* gene complexes (see chapter 19), then occur in the neural tube as it differentiates into the spinal cord and brain.

Generation of somites

While the neural tube is forming from dorsal ectoderm, the rest of the basic architecture of the body is being rapidly established by changes in the mesoderm. The sheets of mesoderm on either side of the developing notochord separate into a series of rounded regions called **somitomeres.** The somitomeres then separate into segmented blocks called **somites** (see figure 54.18). The mesoderm in the head region does not separate into discrete somites but remains connected as somitomeres, which form the skeletal muscles of the face, jaws, and throat.

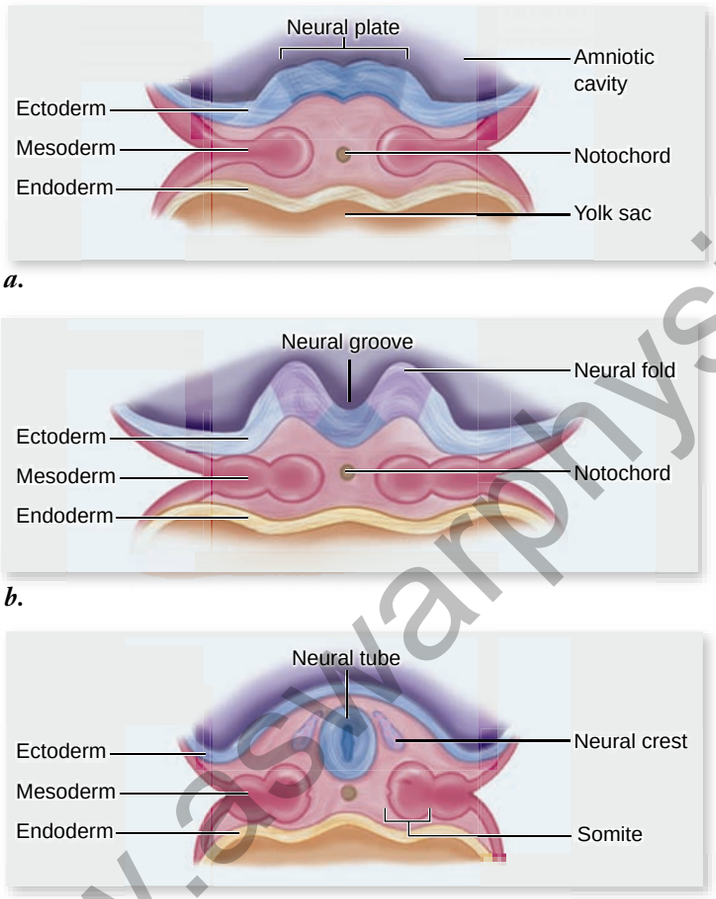


Figure 54.18 Mammalian neural tube formation.
a. The neural plate forms from ectoderm above the notochord. ***b.*** The cells of the neural plate fold together to form the neural groove. ***c.*** The neural groove eventually closes to form a hollow tube called the neural tube, which will become the brain and spinal cord. As the tube closes, some of the cells from the dorsal margin of the neural tube differentiate into the neural crest, migratory cells that form a variety of structures and are characteristic of vertebrates.

Somites form in an anterior–posterior wave with a regular periodicity that can be easily timed—for example, by using a vital dye, which marks cells without killing them, to mark each somite as it forms in a chick embryo. Cells at the presumptive boundary regions in the presomitic mesoderm instruct cells anterior to them to condense and separate into somites at specific times (for example, every 90 min in a chick embryo). This "clock" appears to be regulated by contact-mediated cell signaling between neighboring cells.

Somites themselves are transient embryonic structures, and soon after their formation, cells disperse and start differentiating along different pathways to ultimately form the skeleton, skeletal musculature, and associated connective tissues. The total number of somites formed is species-specific; for example, chickens form 50 somites, whereas some species of snakes form as many as 400 somites.

Some body organs, including the kidneys, adrenal glands, and gonads, develop within a strip of mesoderm that runs lateral to each row of somites. The remainder of the mesoderm, which is most ventrally located, moves out and around the endoderm and eventually surrounds it completely. As a result of this movement, the mesoderm becomes separated into two layers. The outer layer is associated with the inner body wall, and the inner layer is associated with the outer lining of the gut tube. Between these two layers of mesoderm is the *coelom* (see chapter 32), which becomes the body cavity of the adult. Figure 54.19 shows the major mesoderm lineages of amniote embryos.

Migratory neural crest cells differentiate into many cell types

Neurulation occurs in all chordates, and the process in the simple lancelet, a nonvertebrate chordate, is much the same as it is in a human. However, neurulation is accompanied by an additional step in vertebrates. Just before the neural groove closes

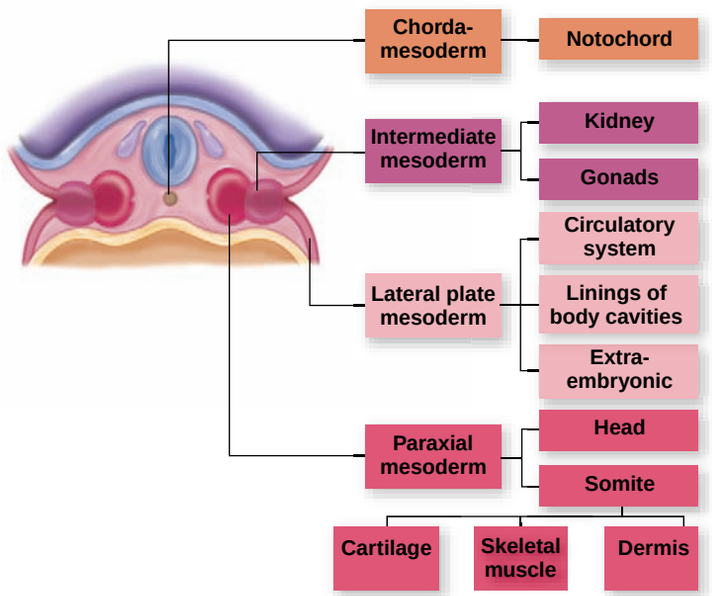


Figure 54.19 Mesoderm-derived structures of birds and mammals.

to form the neural tube, its edges pinch off, forming a small cluster of cells—the *neural crest*—between the roof of the neural tube and the surface ectoderm (figure 54.18*c*).

In another example of extensive cell movements during animal development, the neural crest cells then migrate away from the neural tube to colonize many different regions of the developing embryo. The appearance of the neural crest was a key event in the evolution of the vertebrates because neural crest cells, after reaching their final destinations, ultimately develop into many structures characteristic of the vertebrate body.

The differentiation of neural crest cells depends on their migration pathway and final location. Neural crest cells migrate along one of three pathways in the embryo. Cranial neural crest cells are anterior cells that migrate into the head and neck; trunk neural crest cells migrate along one of two different pathways (to be described shortly). Each population of neural crest cells develops into a variety of cell types.

Cranial neural crest cells' migration

Cranial neural crest cells contribute significantly to development of the skeletal and connective tissues of the face and skull, as well as differentiating into nerve and glial cells of the nervous system, and melanocyte pigment cells. Changes in the placement of cranial neural crest cells during development have led to the evolution of the great complexity and variety of vertebrate heads.

There are two waves of cranial neural crest cell migration. The first produces both dorsal and ventral structures, and the second produces only dorsal structures and makes much less cartilage and bone. Transplantation experiments indicate that the developmental potential of the cells in these two waves is identical. The differences in cell fate are due to the environment the migrating cells encounter and not due to prior determination of cell fate.

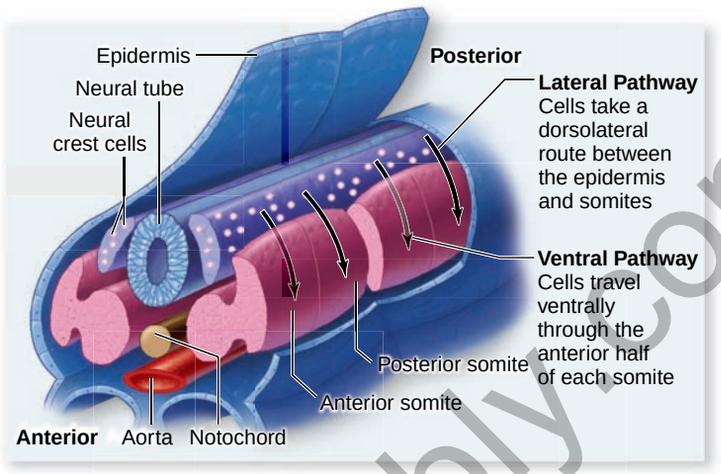
Trunk neural crest cells: Ventral pathway

Neural crest cells located in more posterior positions have very different developmental fates depending on their migration pathway. The first trunk neural crest cells that migrate away from the neural tube pass through the anterior half of each adjoining somite to ventral locations (figure 54.20*a*).

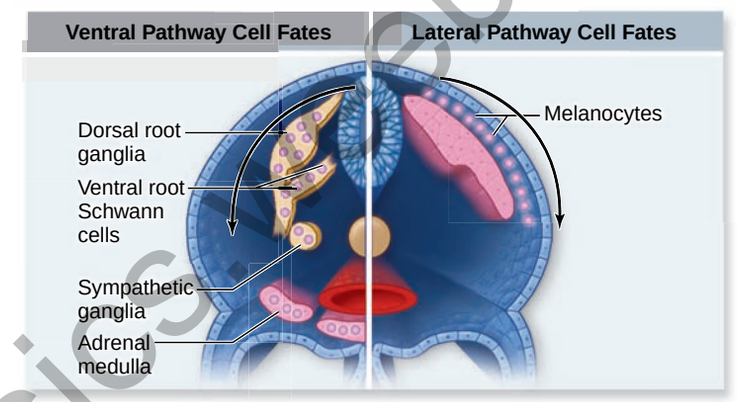
Some of these cells form the sensory neurons of the dorsal root ganglia, which send out projections to connect the periphery of the animal with the spinal cord (see chapter 44). Others become specialized as Schwann cells, which insulate nerve fibers to facilitate the rapid conduction of impulses along peripheral nerves. Still others form nerves of the autonomic ganglia, which regulate the activity of internal organs, and endocrine cells of the adrenal medulla (figure 54.20*b*). The chemical similarity of the hormone epinephrine and the neurotransmitter norepinephrine, which are released by sympathetic neurons of the autonomic nervous systems, may result because both adrenal medullary cells and sympathetic neurons derive from the neural crest.

Trunk neural crest cells: Lateral pathway

The second group of trunk neural crest cells migrate away from the neural tube in the space just under the surface ectoderm, to occupy this space around the entire body of the embryo. There, they will differentiate into the pigment cells of the skin



a.



b.

c.

Figure 54.20 Migration pathways and cell fates of trunk neural crest cells. ***a.*** The first wave of trunk neural crest cells migrates ventrally through the anterior half of each somite, whereas the second wave of cells leaves dorsally and migrates through the space between the epidermis and the somites. ***b.*** Ventral pathway neural crest cells differentiate into a variety of specialized cell types, but lateral pathway cells develop into the melanocytes (pigment cells) of the skin. ***c.*** A mutation in a gene that promotes survival of neural crest cells in all mammals leads to white spotting on the bellies and foreheads of both human babies and mice! Each individual is heterozygous for this mutation and thus has only half as much of the survival factor as unaffected individuals.

(figure 54.20*a*, *b*). Mutations in genes that affect the survival and migration of neural crest cells lead to white spotting in the skin on ventral surfaces, as well as internal problems in other neural crest-derived tissues (figure 54.20*c*).

Because the fate of a neural crest cell is dictated by its migration pathway, many studies have been done to identify the molecules that control the migration pathways of neural crest cells. Cell adhesion molecules on cell surfaces and in the extracellular matrix are expected to play prominent roles. For example, prospective neural crest cells down-regulate the expression of *N*-cadherin on their surfaces, which enables them to break away from the neural tube. Then, soon after leaving the neural tube, integrin receptors appear on the surfaces of neural crest cells, allowing them to interact with proteins in the extracellular matrix pathways along which they will migrate.

Neural crest derivatives are important in vertebrate evolution

Primitive chordates such as lancelets are filter feeders, using the rapid beating of cilia to draw water into their mouths, which then exits through slits in their pharynx. These pharyngeal slits evolved into the vertebrate gill chamber, a structure that provides a greatly improved means of gas exchange. Thus, evolution of the gill chamber was certainly a key event in the transition from filter feeding to active predation, which requires a much higher metabolic rate.

In the development of the gill chamber, some of the cranial neural crest cells form cartilaginous bars between the embryonic pharyngeal slits. Other cranial neural crest cells induce portions of the mesoderm to form muscles along the cartilage, and still others to form neurons that carry impulses between the central nervous system and these muscles.

Many of the unique vertebrate adaptations that contribute to their varied ecological roles involve structures that arise from neural crest cells. The vertebrates became fast-swimming predators with much higher metabolic rates. This accelerated metabolism permitted a greater level of activity than was possible among the more primitive chordates. Other evolutionary changes associated with the derivatives of the neural crest provided better detection of prey, a greatly improved ability to orient spatially during prey capture, and the means to respond quickly to sensory information. The evolution of the neural crest and of the structures derived from it were thus crucial steps in the evolution of the vertebrates (figure 54.21).

Learning Outcomes Review 54.4

Genetic control of organogenesis relies on conserved families of cell-signaling molecules and transcription factors. The control of heart development in *Drosophila* and mammals uses some of the same proteins. The process of neurulation forms the basic nervous system in vertebrates. Somitogenesis is the division of mesoderm into somites. Neural crest cells arise from the neural tube and migrate to many sites to form a variety of cell types. The evolution of the neural crest led to the appearance of many vertebrate-specific adaptations.

- ***Are neural crest cells determined prior to migration?***

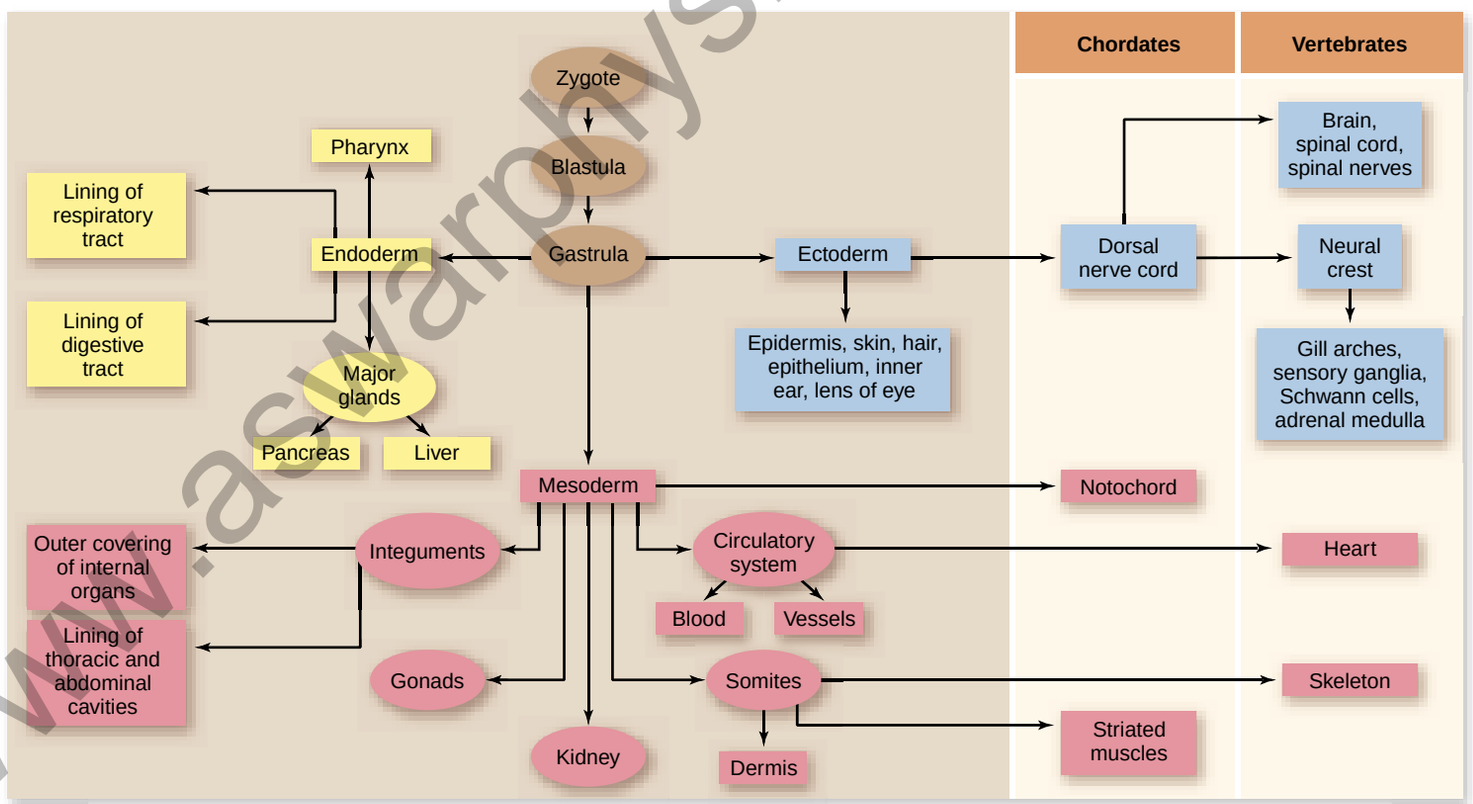


Figure 54.21 Germ-layer derivation of the major tissue types in animals. The three germ layers that form during gastrulation give rise to all the organs and tissues in the body, but the neural crest cells that form from ectodermal tissue give rise to structures that are prevalent in vertebrates, such as gill arches and bones of the face and skull.

54.5 Vertebrate Axis Formation

Learning Outcomes

1. *Describe the Spemann-Mangold experiment.*
2. *Explain the function of the organizer.*
3. *Distinguish between primary and secondary inductive events.*

In animal development, the relative position of cells in particular germ layers determines, to a large extent, the organs that develop from them. In *Drosophila*, you have seen that formation of morphogen gradients in the syncytial blastoderm establishes the anterior–posterior and dorsal–ventral axes of the embryo. The *Hox* gene complexes in vertebrates function similarly to the homeotic genes of *Drosophila* to specify the position of organs along the anterior–posterior axis. But how is cell fate selection along the dorsal–ventral axis accomplished in vertebrate embryos? Put another way, how do cells of the dorsal ectoderm "know" they are above the mesoderm-derived notochord, and thus fated to develop into the neural tube? The solution to this puzzle is one of the outstanding accomplishments of experimental embryology.

The Spemann organizer determines dorsal–ventral axis

The renowned German biologist Hans Spemann and his student Hilde Mangold solved this puzzle early in the 20th century. Normally, cells derived from the dorsal lip of the blastopore of a gastrulating amphibian embryo give rise to the notochord. Spemann and Mangold removed cells of the dorsal lip from one embryo and transplanted them to a different location on another embryo (figure 54.22). The new location corresponded to that of the animal's future belly. They found that some of the embryos developed two notochords: a normal dorsal one, and a second one along the belly. Moreover, a complete set of dorsal axial structures (e.g., notochord, neural tube, and somites) formed at the ventral transplantation site in most of these embryos.

By using genetically different donor and host blastulas, Spemann and Mangold were able to show that the second notochord produced by transplanting dorsal lip cells contained host cells as well as transplanted ones. The transplanted dorsal lip cells had thus acted as *organizers*, stimulating cells that would normally form skin and belly structures to develop into dorsal axial structures. The belly cells must clearly contain the genetic information for dorsal axial developmental program, but they do not express it in the normal course of their development. Signals from the transplanted dorsal lip cells, however, must have caused them to do so.

How the organizer works

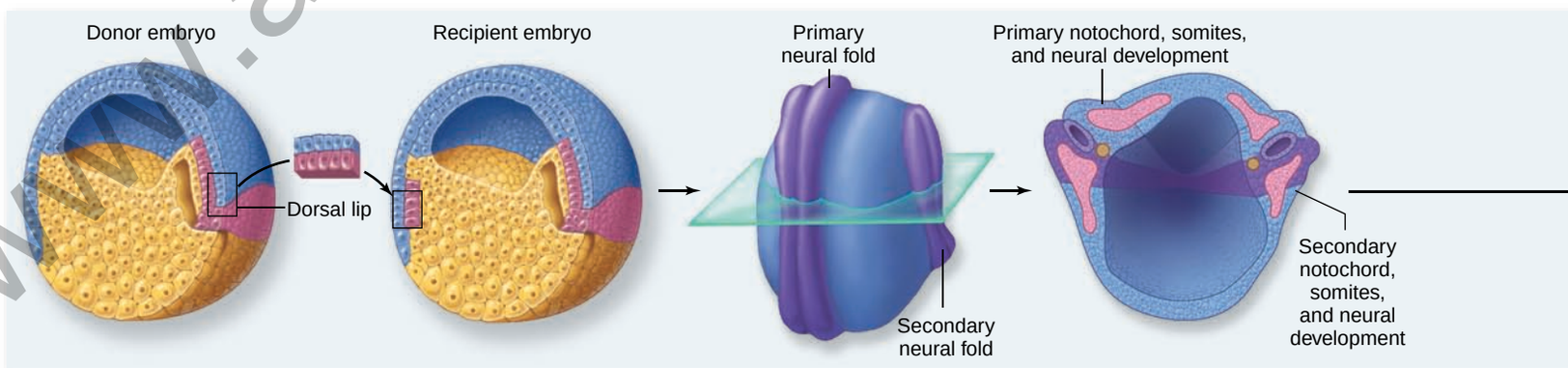
An organizer is a cluster of cells that release diffusible signal molecules, which then convey positional information to other cells. As seen earlier, organizers can have a profound influence on the development of surrounding tissues. Working as signal beacons, they inform surrounding cells of their distance from the organizer. The closer a particular cell is to an organizer, the higher the concentration of the signal molecule *(morphogen)* it experiences. Organizers and the diffusible morphogens that they release are thought to be part of a widespread mechanism for determining relative position and cell fates during vertebrate development.

The action of morphogens

The action of morphogens can be studied by using isolated portions of the blastula. The blastula can be bisected into an animal half (the animal cap) and vegetal half (the vegetal cap). If animal caps are removed from a frog blastula and cultured alone, they will form only ectoderm-derived epidermal cells. Similarly, cultured vegetal caps will form only endodermal cells. However, if animal caps are cultured combined with vegetal caps, the animal caps will form mesodermal structures.

The molecules involved in this induction have not been unambiguously identified. Members of the transforming growth factor beta (TGF-β) family have been implicated. These include activin, and *Xenopus* nodal-related proteins (Xnrs). Evidence for the inducing action of these molecules ranges from indirect: the

Figure 54.22 Spemann and Mangold's dorsal lip transplant experiment. Tissue from the dorsal lip of a donor embryo induced the formation of a second axis in the future belly region of a second, recipient embryo.



timing and pattern of expression correlates with inducing tissue, to depleting developing embryos of these proteins with specific reagents that block gene expression.

The origin of the organizer

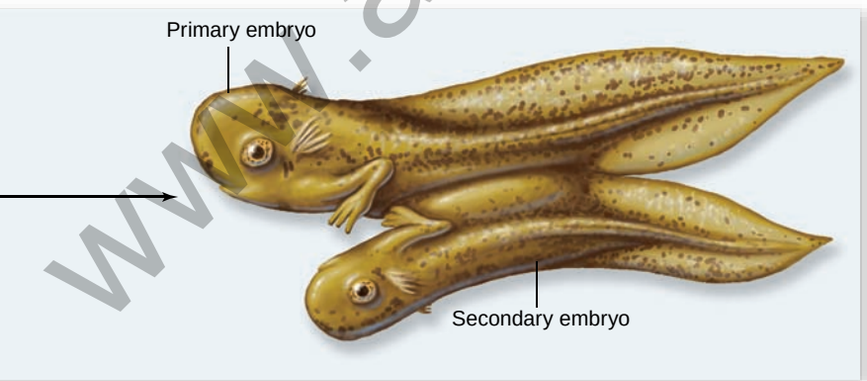
How do cells of the frog blastopore's dorsal lip become the Spemann organizer and how do they acquire their ability to specify cell fate along the dorsal–ventral axis? In frogs, as in fruit flies, this process starts during oogenesis in the mother. At that time, maternally encoded dorsal determinants are put into the developing oocyte, one of which accumulates at the vegetal pole of the unfertilized egg. At fertilization, cytoplasmic rearrangements cause this determinant to shift to the future dorsal side of the egg.

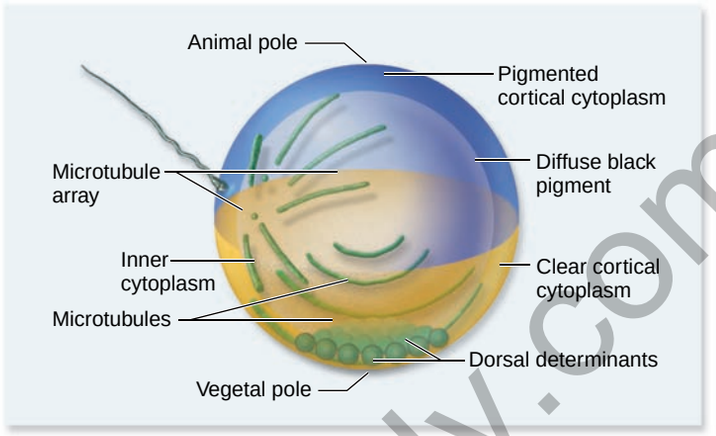
First, a signal from the point of sperm entry initiates the assembly of a microtubule array, which enables the egg's plasma membrane and the underlying cortical cytoplasm to rotate over the surface of the deeper cytoplasm. This physical rotation shifts this maternally encoded dorsal determinant to the opposite side of the egg from the point of sperm entry (figure 54.23*a*, *b*). In some frogs, a gray crescent forms opposite the sperm entry point, as mentioned earlier, and this crescent marks the future site of the dorsal lip.

Cells that form in this area during cleavage (called the Nieuwkoop center for the scientist who did the previously mentioned animal cap studies) receive the dorsal determinants that moved during cortical rotation. The dorsal determinants cause a change in gene expression in these cells, producing a signaling molecule that induces the cells above them to develop into the dorsal lip of the blastopore (figure 54.23*c*).

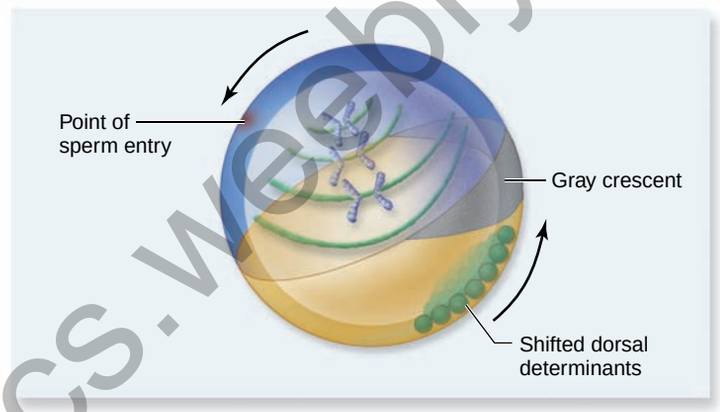
Maternally encoded dorsal determinants activate Wnt signaling

Experiments carried out over the last 15 years suggest that the maternally encoded dorsal determinants in *Xenopus* are mRNAs for proteins that function in the intracellular **Wnt** signaling pathway. *Wnt* genes encode a large family of cell-signaling proteins that affect the development of a number of structures in both vertebrates and invertebrates. Turning on the Wnt pathway in the dorsal vegetal cells of the Nieuwkoop center leads ultimately to activation of a transcription factor, which moves into the nucleus to activate the expression of genes necessary for organizer specification.

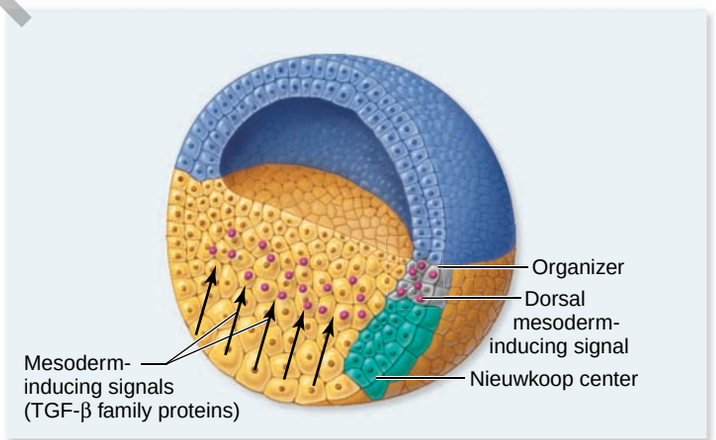




a.



b.



c.

Figure 54.23 Creation of the Spemann organizer.
a. Dorsal determinants are localized at the vegetal pole of the unfertilized frog egg. At fertilization, a microtubule array forms at the site of sperm entry. These microtubules organize parallel microtubules to line the vegetal half of the egg between the cortex and cytoplasm. ***b.*** The cortical cytoplasm and dorsal determinants ride on this parallel array of microtubules, shifting to a site opposite sperm entry. ***c.*** Cells that inherit these shifted dorsal determinants form the Nieuwkoop center, which releases diffusible signaling molecules that specify the cells in the overlying dorsal marginal zone to become the organizer. The organizer forms at the area of the gray crescent, visible following the cytoplasmic rearrangements at fertilization.

Signaling molecules from the Spemann organizer inhibit ventral development

It has taken decades to establish the identity and function of the molecules that are synthesized by cells of the Spemann organizer to subsequently specify dorsal mesoderm cell fates in frogs. A surprising finding of recent experiments indicates that dorsal lip cells do not directly *activate* dorsal development. Instead, dorsal mesoderm development is a result of the *inhibition* of ventral development.

A protein called **bone morphogenetic protein 4 (BMP4)** is expressed in all marginal zone cells (the prospective mesoderm) of a frog embryo. Cells with receptors for BMP4 have the potential to develop into mesodermal derivatives. The specific mesodermal fate depends on how many receptors bind BMP4: More BMP4 binding induces a more ventral mesodermal fate.

The organizer functions by secreting a host of *inhibitory* molecules that can bind to BMP4 and prevent its binding to receptor. Such molecules are referred to as BMP4 antagonists. Up to 13 different proteins have been identified in the Spemann organizer, most of which appear to function as BMP4 antagonists. These include the proteins Noggin, Chordin, Dickkopf, and Cerebrus. Noggin and BMP4 are also involved in toe and finger joint formation, so humans homozygous for a *Noggin* mutation have fused joints.

Thus, the gradient of *inhibitory* molecules that emanates from the Spemann organizer leads to a declining level of BMP4 *function* in the ventral-to-dorsal direction. Cells farthest from the organizer bind the highest levels of BMP4 and differentiate into ventral mesoderm structures such as blood and connective tissues. Cells that are midway from the organizer bind intermediate amounts of BMP4, differentiate into intermediate mesoderm, and form organs such as the kidneys and gonads. BMP4 binding is completely inhibited by the high levels of antagonists in the organizer itself. Thus, these cells adopt the most dorsal of mesoderm fates and develop into somites. The influence of the organizer also extends to ectoderm as inhibition of BMP4 in ectoderm leads to formation of neural tissue instead of epidermis (figure 54.24).

Evidence indicates that organizers are present in all vertebrates

In chicks, a group of cells at the anterior limit of the primitive streak called *Hensen's node* functions similarly to the dorsal lip of the blastopore: Hensen's node induces a second axis when transplanted to another area of a chick embryo. Recent studies have shown that cells of Hensen's node act like the Spemann organizer, secreting molecules that inhibit ventral development. These molecules are the same as those found in frog embryos. Therefore, these experiments once again illustrate the evolutionary conservation of particular genes in animal development.

In addition, notochord signaling acts to pattern the neural tube. The notochord produces the signaling molecule sonic hedgehog (Shh), which is related to a signaling molecule in

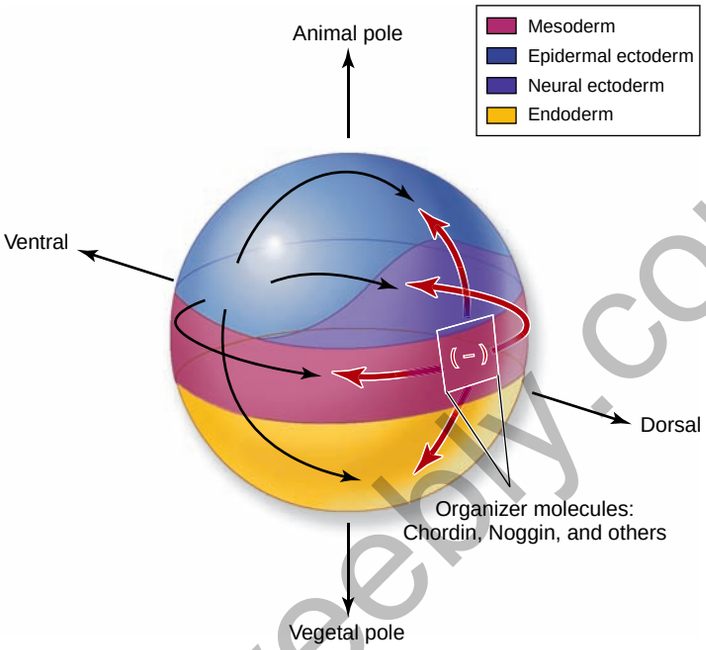


Figure 54.24 Function of the Spemann organizer.
The organizer is a hotbed of secreted molecules that bind to and antagonize the action of BMP4, a morphogen that at high levels specifies ventral mesoderm cell fates.

Drosophila called hedgehog. Signaling by Shh specifies ventral cell fate with dose-related effects similar to those described for the TGF-β family proteins discussed earlier. In this way, induction by the notochord causes somites to form vertebrae, ribs, muscle, and skin, depending on the levels of Shh cells are exposed to.

Induction can be primary or secondary

The process of induction that Spemann initially discovered appears to be a fundamental mode of development in vertebrates. Inductions between the three primary germ layers—ectoderm, mesoderm, and endoderm—are referred to as **primary inductions.** The differentiation of the central nervous system during neurulation by the interaction of dorsal ectoderm and dorsal mesoderm to form the neural tube is an example of primary induction.

Inductions between tissues that have already been specified to develop along a particular developmental pathway are called **secondary inductions.** An example of secondary induction is the development of the lens of the vertebrate eye. The eye develops as an extension of the forebrain, a stalk that grows outward until it comes into contact with the surface ectoderm (figure 54.25). At a point directly above the growing stalk, a layer of the surface ectoderm pinches off, forming a transparent lens. The formation of lens from the surface ectoderm requires induction by the underlying neural ectoderm.

This was shown by transplantation experiments performed by Spemann. When the optic stalks of the two eyes have just started to project from the brain prior to lens

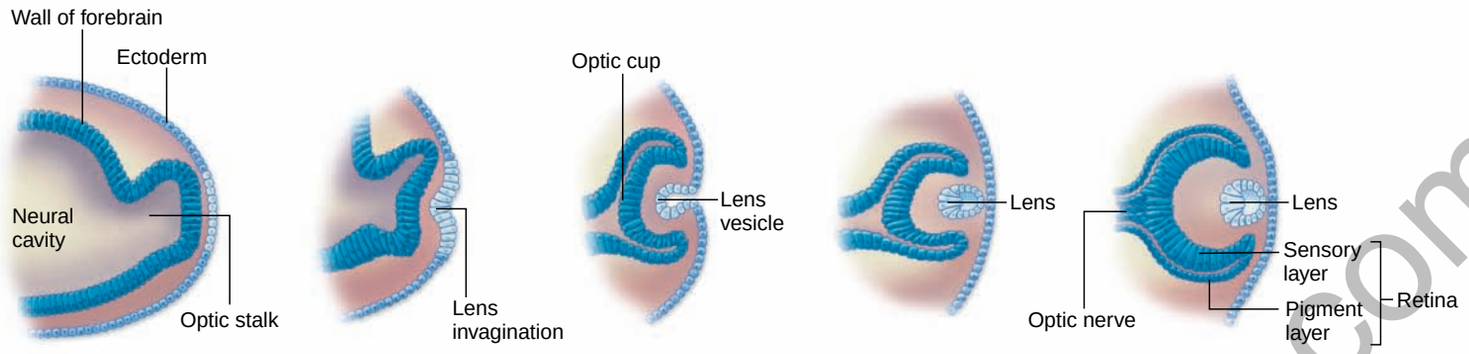


Figure 54.25 Development of the vertebrate eye by induction. An extension of the optic stalk grows until it contacts the surface ectoderm, where it induces a section of the ectoderm to pinch off and form the lens. Other structures of the eye develop from the optic stalk, with lens cells reciprocally inducing the formation of photoreceptors in the optic cup.

formation, one of the budding stalks can be removed and transplanted underneath surface ectoderm in a region that would normally develop into the epidermis of the skin (such as that of the belly). When this is done, a lens forms from belly ectoderm cells in the region above where the budding stalk was transplanted. This lens forms due to inductive signals from the underlying optic stalk.

Learning Outcomes Review 54.5

The Spemann-Mangold experiment showed that transplanted cells of the dorsal lip of the blastopore act as organizers stimulating development of a notochord. Hensen's node plays an equivalent role in vertebrates. By inhibiting BMP4, the organizer induces ectoderm to form neural tissue and mesoderm to form dorsal mesoderm. Primary inductions between germ layers lead to development of the vertebrate nervous system, whereas secondary inductions result in formation of structures such as the lens of the eye.

- ***How can the organizer function by inhibiting the action of other molecules?***

54.6 Human Development

Learning Outcomes

1. ***Describe the major developmental events in first trimester.***
2. ***Explain the role of the placenta.***
3. ***Describe the hormonal control of the birth process.***

Human development from fertilization to birth takes an average of 266 days, or about 9 months. This time is commonly divided into three periods called *trimesters*. We describe here the development of the embryo as it takes place during these trimesters. Later, we summarize the process of birth, nursing of the infant, and postnatal development.

During the first trimester, the zygote undergoes rapid development and differentiation

About 30 hr after fertilization, the zygote undergoes its first cleavage; the second cleavage occurs about 30 hr after that. By the time the embryo reaches the uterus, 6 to 7 days after fertilization, it has differentiated into a blastocyst. As mentioned earlier, the blastocyst consists of an inner cell mass, which will become the body of the embryo, and a surrounding layer of trophoblast cells (see figure 54.10).

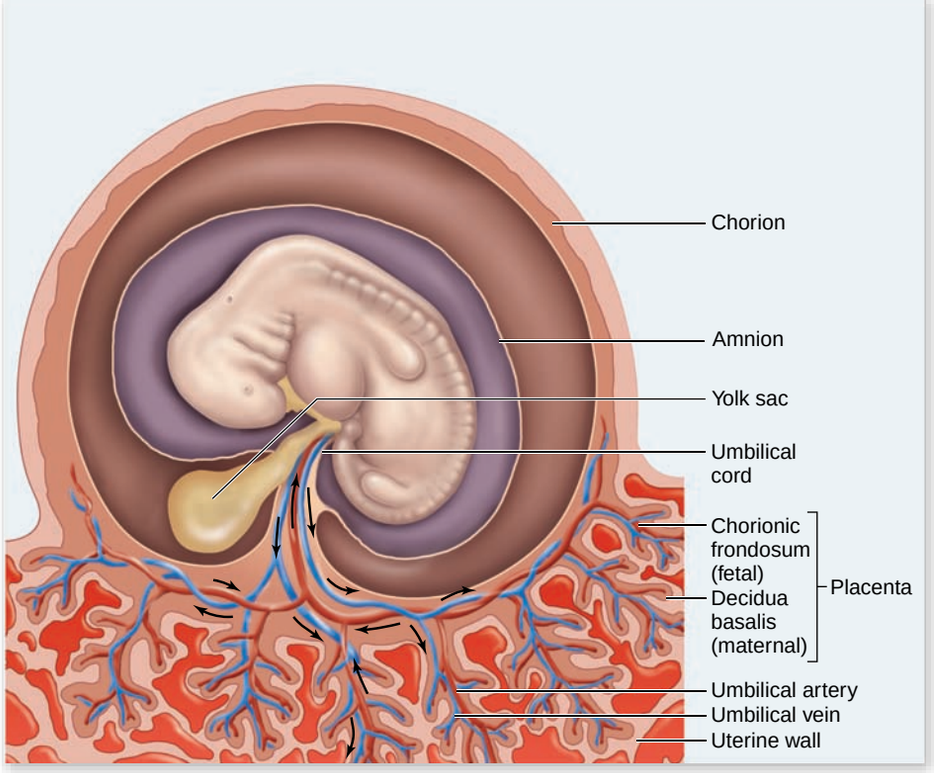
The trophoblast cells of the blastocyst digest their way into the endometrial lining of the uterus in the process known as **implantation.** The blastocyst begins to grow rapidly and initiates the formation of the amnion and the chorion.

Development in the first month

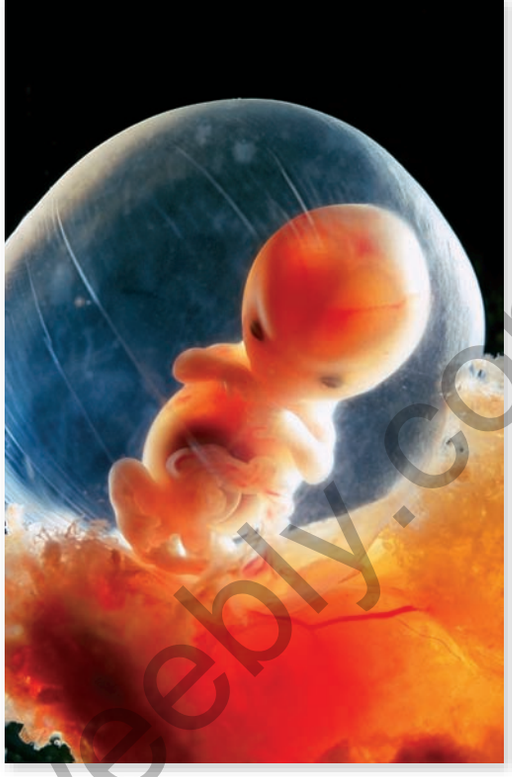
During the second week after fertilization, the developing chorion and the endometrial tissues of the mother engage to form the placenta (figure 54.26). Within the placenta, the mother's blood and the blood of the embryo come into close proximity but do not mix. Gases are exchanged, however, and the placenta provides nourishment for the embryo, detoxifies certain molecules that may pass into the embryonic circulation, and secretes hormones. Certain substances, such as alcohol, drugs, and antibiotics, are not stopped by the placenta and pass from the mother's bloodstream into the embryo.

One of the hormones released by the placenta is human chorionic gonadotropin (hCG), which was discussed in chapter 53. This hormone is secreted by the trophoblast cells even before they become the chorion, and it is the hormone assayed in pregnancy tests. Human chorionic gonadotropin maintains the mother's corpus luteum. The corpus luteum, in turn, continues to secrete estradiol and progesterone, thereby preventing menstruation and further ovulations.

Gastrulation also takes place in the second week after fertilization, and the three germ layers are formed. Neurulation occurs in the third week. The first somites appear, which give rise to the muscles, vertebrae, and connective tissues. By the end of the third week, over a dozen somites are evident, and the blood vessels and gut have begun to develop. At this point, the embryo is about 2 mm long.



a.



b.

Figure 54.26 Structure of the placenta. ***a.*** The placenta contains a fetal component, the chorionic frondosum, and a maternal component, the decidua basalis. Deoxygenated fetal blood from the umbilical arteries (shown in blue) enters the placenta, where it picks up oxygen and nutrients from the mother's blood. Oxygenated fetal blood returns in the umbilical vein (shown in red) to the fetus. ***b.*** Note that the 7-week embryo is surrounded by a fluid-filled amniotic sac.

Organogenesis begins during the fourth week (figure 54.27*a*). The eyes form. The tubular heart develops its four chambers and starts to pulsate rhythmically, as it will for the rest of the individual's life. At 70 beats per minute, the heart is destined to beat more than 2.5 billion times during a lifetime of 70 years. Over 30 pairs of somites are visible by the end of the fourth week, and the arm and leg buds have begun to form. The embryo has increased in length to about 5 mm. Although the developmental scenario is now far advanced, many women are still unaware they are pregnant at this stage. Most spontaneous abortions (miscarriages), which frequently occur in the case of a defective embryo, occur during this period.

The second month

Organogenesis continues during the second month (figure 54.27*b*). The miniature limbs of the embryo assume their adult shapes. The arms, legs, knees, elbows, fingers, and toes can all be seen—as well as a short bony tail. The bones of the embryonic tail, an evolutionary reminder of our past, later fuse to form the coccyx.

Within the abdominal cavity, the major organs, including the liver, pancreas, and gallbladder, become evident. By the end of the second month, the embryo has grown to about 25 mm in length, weighs about 1 g, and begins to look distinctly human. The ninth week marks the transition from embryo to fetus. At this time, all of the major organs of the body have been established in their proper locations.

The third month

The nervous system develops during the third month, and the arms and legs start to move (figure 54.27*c*). The embryo begins to show facial expressions and carries out primitive reflexes such as the startle reflex and sucking.

At around 10 weeks, the secretion of hCG by the placenta declines, and the corpus luteum regresses as a result. However, menstruation does not occur because the placenta itself secretes estradiol and progesterone (figure 54.28).

The high levels of estradiol and progesterone in the blood during pregnancy continue to inhibit the release of FSH and LH, thereby preventing ovulation. They also help maintain the uterus and eventually prepare it for labor and delivery, and they stimulate the development of the mammary glands in preparation for lactation after delivery.

During the second trimester, the basic body plan develops further

Bones actively enlarge during the fourth month (figure 54.27*d*), and by the end of the month, the mother can feel the baby kicking. By the end of the fifth month, the rapid heartbeat of the fetus can be heard with a stethoscope, although it can also be detected as early as 10 weeks with a fetal monitor.

Growth begins in earnest in the sixth month; by the end of that month, the fetus weighs 600 g (1.3 lb) and is over 300 mm (1 ft) long. Most of its prebirth growth is still to come, however. The fetus cannot yet survive outside the uterus without special medical intervention.

During the third trimester, organs mature to the point at which the baby can survive outside the womb

The third trimester is predominantly a period of growth and maturation of organs. The weight of the fetus doubles several

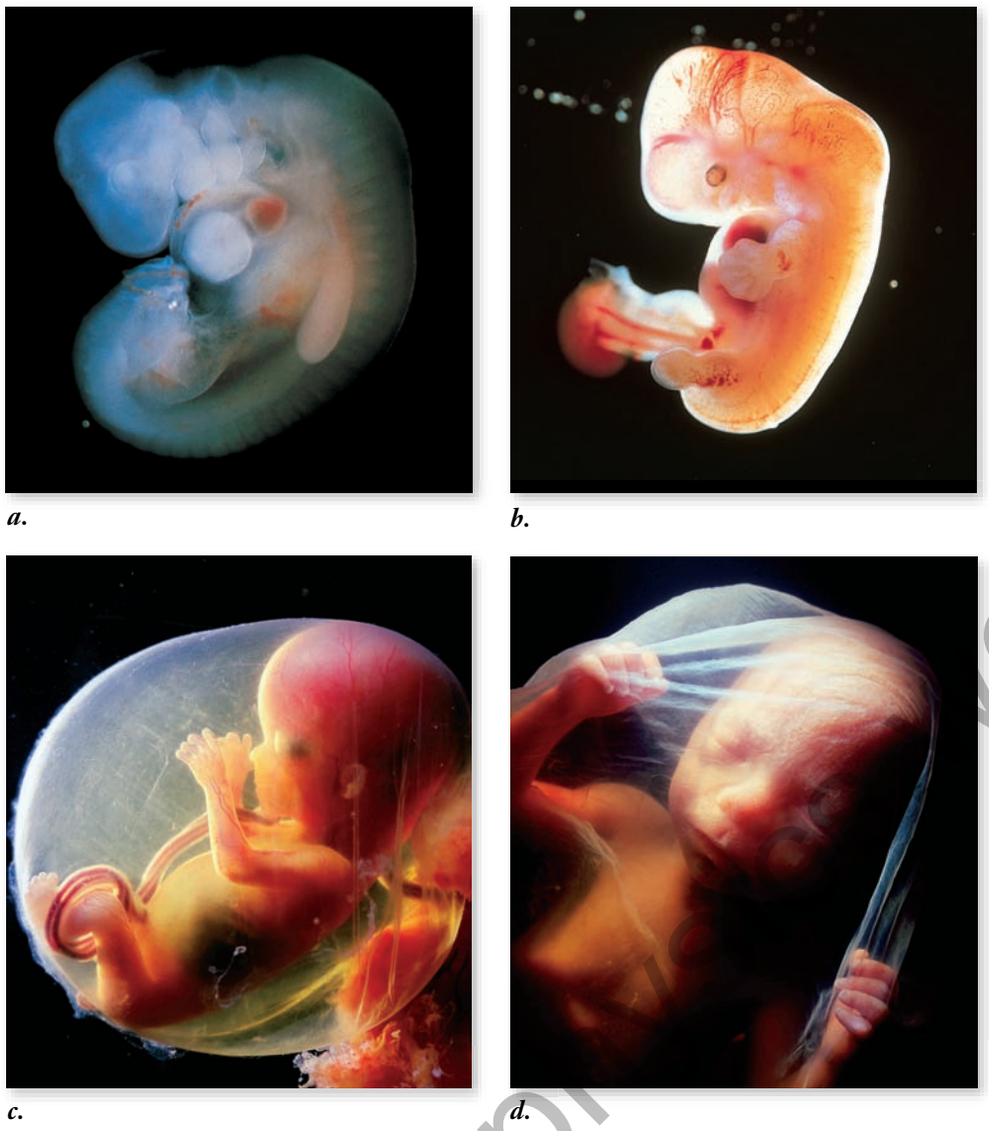
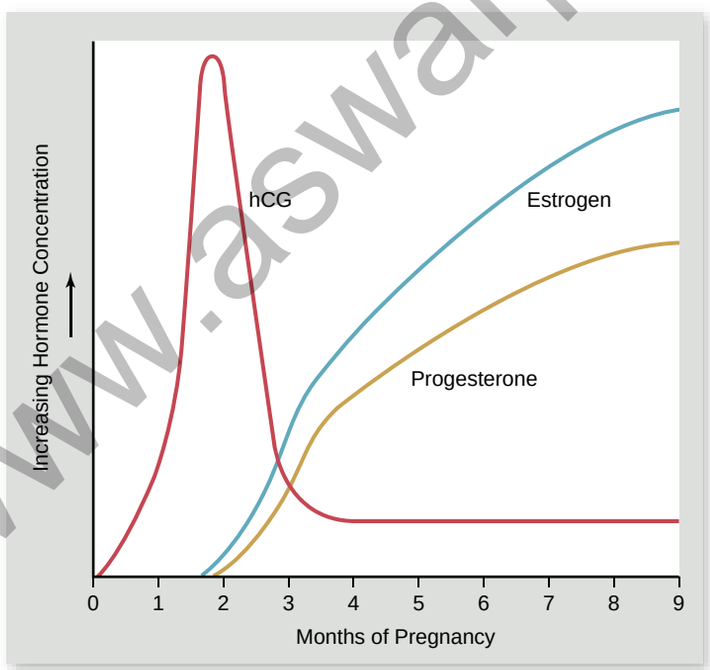


Figure 54.27 The developing human. *(a)* 4 weeks, *(b)* end of 5th week, *(c)* 3 months, and *(d)* 4 months.



times, but this increase in bulk is not the only kind of growth that occurs. Most of the major nerve tracts in the brain, as well as many new neurons (nerve cells), are formed during this period. Neurological growth is far from complete when birth takes place, however. If the fetus remained in the uterus until its neurological development was complete, it would grow too large for safe delivery through the pelvis. Instead, the infant

Figure 54.28 Hormonal secretion by the placenta. The placenta secretes human chorionic gonadotropin (hCG), which peaks in the second month and then declines. After 5 weeks, it secretes increasing amounts of estrogen and progesterone.

Inquiry question

The high levels of estradiol and progesterone secreted by the placenta prevent ovulation and thus formation of any additional embryos during pregnancy. What would be the expected effect of these high hormone levels in the absence of pregnancy?

is born as soon as the probability of its survival is high, and its brain continues to develop and produce new neurons for months after birth.

Critical changes in hormones bring on birth

In some mammals, changing hormone levels in the developing fetus initiate the process of birth. The fetuses of these mammals have an extra layer of cells in their adrenal cortex, which secrete corticosteroids that induce the uterus of the mother to manufacture prostaglandins. Prostaglandins trigger powerful contractions of the uterine smooth muscles.

In humans, fetal secretion of cortisol increases during late pregnancy, which appears to stimulate estradiol secretion by the placenta. The mother's uterus releases prostaglandins, possibly as a result of the high levels of estradiol secreted by the placenta. Estradiol also stimulates the uterus to produce more oxytocin receptors, and as a result, the uterus becomes increasingly sensitive to oxytocin.

Prostaglandins begin the uterine contractions, but then sensory feedback from the uterus stimulates the release of oxytocin from the mother's posterior-pituitary gland. Working together, oxytocin and prostaglandins further stimulate uterine contractions, forcing the fetus downward (figure 54.29). This positive feedback mechanism accelerates during labor. Initially, only a few contractions occur each hour, but the rate eventually increases to one contraction every 2 to 3 min. Finally, strong contractions, aided by the mother's voluntary pushing, expel the fetus, which is now a newborn baby, or *neonate*.

After birth, continuing uterine contractions expel the placenta and associated membranes, collectively called the *afterbirth*. The umbilical cord is still attached to the baby, and to free the newborn, a doctor or midwife clamps and cuts the cord. Blood clotting and contraction of muscles in the cord prevent excessive bleeding.

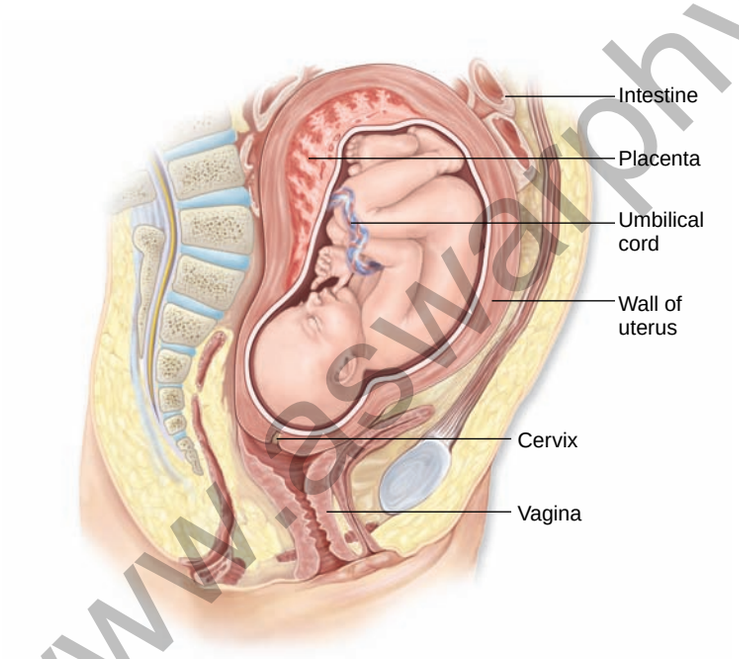


Figure 54.29 Position of the fetus just before birth.
A developing fetus causes major changes in a woman's anatomy. The stomach and intestines are pushed far up, and considerable discomfort often results from pressure on the lower back. In a normal vaginal delivery, the fetus exits through the cervix, which must dilate (expand) considerably to permit passage.

Nursing of young is a distinguishing feature of mammals

Milk production, or *lactation*, occurs in the alveoli of mammary glands when they are stimulated by the anterior-pituitary hormone prolactin. Milk from the alveoli is secreted into a series of alveolar ducts, which are surrounded by smooth muscle and lead to the nipple.

During pregnancy, high levels of progesterone stimulate the development of the mammary alveoli, and high levels of estradiol stimulate the development of the alveolar ducts. However, estradiol blocks the actions of prolactin on the mammary glands, and it inhibits prolactin secretion by promoting the release of prolactin-inhibiting hormone from the hypothalamus. During pregnancy, therefore, the mammary glands are prepared for, but prevented from, lactating. The growth of mammary glands is also stimulated by the placental hormones human chorionic somatomammotropin, a prolactin-like hormone, and human somatotropin, a growth hormone-like hormone.

When the placenta is discharged after birth, the concentrations of estradiol and progesterone in the mother's blood decline rapidly. This decline allows the anterior-pituitary gland to secrete prolactin, which stimulates the mammary alveoli to produce milk. Sensory impulses associated with the baby's suckling trigger the posterior-pituitary gland to release oxytocin. Oxytocin stimulates contraction of the smooth muscle surrounding the alveolar ducts, thus causing milk to be ejected by the breast. This pathway is known as the *milk let-down reflex*, and it is found in other mammals as well. The secretion of oxytocin during lactation also causes some uterine contractions, as it did during labor. These contractions help restore the tone of uterine muscles in mothers who are breast-feeding.

The first milk produced after birth is a yellowish fluid called colostrum, which is both nutritious and rich in maternal antibodies. Milk synthesis begins about 3 days following the birth and is referred to as the milk "coming in." Many mothers nurse for a year or longer. When nursing stops, the accumulation of milk in the breasts signals the brain to stop secreting prolactin, and milk production ceases.

Postnatal development in humans continues for years

Growth of the infant continues rapidly after birth. Babies typically double their birth weight within 2 months. Because different organs grow at different rates and cease growing at different times, the body proportions of infants are different from those of adults. The head, for example, is disproportionately large in newborns, but after birth it grows more slowly than the rest of the body. Such a pattern of growth, in which different components grow at different rates, is referred to as **allometric growth.**

In most mammals, brain growth is mainly a fetal phenomenon. In chimpanzees, for instance, the brain and the cerebral

portion of the skull grow very little after birth, whereas the bones of the jaw continue to grow. As a result, the head of an adult chimpanzee looks very different from that of a fetal or infant chimpanzee. In human infants, by contrast, the brain and cerebral skull grow at the same rate as the jaw. Therefore, the jaw–skull proportions do not change after birth, and the head of a human adult looks very similar to that of a human fetus or infant.

The fact that the human brain continues to grow significantly for the first few years of postnatal life means that adequate nutrition and a safe environment are particularly crucial during this period for the full development of a person's intellectual potential.

Learning Outcomes Review 54.6

The critical stages of human development occur in the first trimester of gestation; the subsequent 6 months involve growth and maturation. Growth of the brain is not complete at birth and must be completed postnatally. Hormones in the mother's blood maintain the nutritive uterine environment for the developing fetus; changes in hormone secretion and levels stimulate birth (prostaglandins and oxytocin) and lactation (oxytocin and prolactin).

- ***Why are teratogens (agents that cause birth defects) most potent in the first trimester?***

Chapter Review

54.1 Fertilization

A sperm must penetrate to the plasma membrane of the egg for membrane fusion to occur.

The sperm's acrosome releases digestive enzymes to penetrate the egg's external layers (see figure 54.1). Fusion with the egg's membrane allows the sperm nucleus to pass into the egg's cytoplasm.

Membrane fusion activates the egg.

Fusion of membranes triggers egg activation by the release of calcium (see figure 54.2). Blocks to polyspermy include changes in membrane potential and alterations to the external coat of the egg. Upon egg activation, meiosis is completed (see figures 54.4 and 54.5).

The fusion of nuclei restores the diploid state.

Fertilization is complete when the haploid sperm nucleus fuses with the haploid egg nucleus.

54.2 Cleavage and the Blastula Stage

The blastula is a hollow mass of cells.

Cleavage is a rapid series of cell divisions that produces blastomeres, which form a hollow ball of cells called a blastula.

Cleavage patterns are highly diverse and distinctive.

Cleavage patterns are primarily influenced by the amount of yolk (see table 54.2). With little or no yolk, cleavage is holoblastic (involving the whole egg); where more yolk is present, cleavage is meroblastic (involving the blastodisc only). Cleavage in mammals is holoblastic.

Blastomeres may or may not be committed to developmental paths.

In many animals, unequal segregation of cytoplasmic determinants commits each blastomere to a different path. Mammals exhibit regulative development in which the fate of early blastomeres is not predetermined.

54.3 Gastrulation

Gastrulation produces the three germ layers.

During gastrulation the three germ layers differentiate: endoderm, ectoderm, and mesoderm (see table 54.3). Cells move during gastrulation using a variety of cell shape changes.

Gastrulation patterns also vary according to the amount of yolk.

The amount of yolk also influences cell movement. In frogs, a layer of cells involutes through the dorsal lip of the blastopore. In birds, surface cells migrate through the primitive streak. Mammalian gastrulation is similar to that of birds.

Extraembryonic membranes are an adaptation to life on dry land.

The yolk sac, amnion, chorion, and allantois prevent dessication and nourish and protect the developing embryo (see figure 54.15).

54.4 Organogenesis

Changes in gene expression lead to cell determination.

A cell's location in the developing embryo often determines its fate. Differentiation can be established by inheritance of cytoplasmic determinants and by interactions with other cells (induction).

Development of selected systems in* Drosophila *illustrates organogenesis.

The development of salivary glands, the dorsal vessel, and tracheae all demonstrate the action of gene expression on development.

In vertebrates, organogenesis begins with neurulation and somitogenesis (see figures 55.18–55.20).

Neurulation is the formation of the neural tube from ectoderm near the notochord; somitogenesis is the establishment of mesoderm into units called somites.

Migratory neural crest cells differentiate into many cell types.

Neural crest cells migrate widely to become connective tissue, nerve and glial cells, melanocytes, sensory neurons, and other cells.

Neural crest derivatives are important in vertebrate evolution.

Many of the unique adaptations of vertebrates have arisen from neural crest cells (see figure 54.21).

54.5 Vertebrate Axis Formation

The Spemann organizer determines dorsal–ventral axis.

Organizers are a cluster of cells that produce gradients of diffusible signal molecules, conveying positional information to other cells.

Maternally encoded dorsal determinants activate Wnt signaling.
Turning on the Wnt pathway activates organizer specification.

Signaling molecules from the Spemann organizer inhibit ventral development.
Morphogens can either activate or inhibit development along a certain path. The Spemann organizer induces formation of the dorsum by inhibiting ventral development (see figure 54.24).

Evidence indicates that organizers are present in all vertebrates.
Cells at the anterior edge of the primitive streak, termed Hensen's node, function similarly to the Spemann organizer.

Induction can be primary or secondary.
Primary induction occurs between the three germ layers; secondary induction occurs between already determined tissues.

54.6 Human Development

During the first trimester, the zygote undergoes rapid development and differentiation.
Implantation of the blastocyst occurs at the end of the first week of pregnancy. During the second week, the embryonic chorion and the mother's endometrial tissues form the placenta, and gastrulation occurs. Organogenesis begins during the fourth week. The eighth week marks the transition from embryo to fetus.

During the second trimester, the basic body plan develops further.

During the third trimester, organs mature to the point at which the baby can survive outside the womb.

Critical changes in hormones bring on birth.
Birth is initiated by secretions of steroids from the fetal adrenal cortex that induce prostaglandins, which cause contractions.

Nursing of young is a distinguishing feature of mammals.
Nursing involves a neuroendocrine reflex, causing the release of oxytocin and the milk let-down response.

Postnatal development in humans continues for years.
Postnatal development continues with different organs growing at different rates—called allometric growth.

Review Questions

UNDERSTAND

1. Which of the following events occur immediately after fertilization?
   a. Egg activation
   b. Polyspermy defense
   c. Cytoplasm changes
   d. All of these occur after fertilization
2. Which of the following plays the greatest role in determining how cytoplasmic division occurs during cleavage?
   a. Number of chromosomes
   b. Amount of yolk
   c. Orientation of the vegetal pole
   d. Sex of the zygote
3. Gastrulation is a critical event during development. Why?
   a. Gastrulation converts a hollow ball of cells into a bilaterally symmetrical structure.
   b. Gastrulation causes the formation of a primitive digestive tract.
   c. Gastrulation causes the blastula to develop a dorsal–ventral axis.
   d. All of these are significant events that occur during gastrulation.
4. Gastrulation in a mammal would be most similar to gastrulation in
   a. a gecko.
   b. a tuna.
   c. an eagle.
   d. no other species; mammalian gastrulation is unique.
5. Somites
   a. begin forming at the tail end of the embryo and then move forward in a wavelike fashion.
   b. are derived from endoderm.
   c. develop into only one type of tissue per somite.
   d. may vary in number from one species to the next.
6. Of the following processes, which occurs last?
   a. Cleavage
   b. Neurulation
   c. Gastrulation
   d. Fertilization

APPLY

1. Your cousin just had twins. She tells you that twinning occurs when two sperm fertilize the same egg. You reply that
   a. yes, she is right, that is the most common source of twinning.
   b. no, only one sperm survives passage through the uterine cervix, so two sperm are never present at fertilization.
   c. no, cortical granules are used to prevent additional sperm penetration.
   d. no, twinning occurs when unfertilized eggs divide spontaneously and thus is parthenogenic in nature.
2. In the Spemann experiment, when the dorsal lip is transplanted, the recipient embryo then has a second source of molecules that
   a. specifies ventral fate.
   b. inhibits the molecules that specify ventral fate.
   c. specifies dorsal fate.
   d. inhibits the molecules that specify dorsal fate.

3. Suppose that a burst of electromagnetic radiation were to strike the blastomeres of only the animal pole of a frog embryo. Which of the following would be most likely to occur?
   a. A change or mutation relevant to the epidermis or skin
   b. A switching of the internal organs so that reverse orientation (left/right) occurs along the midline of the body
   c. The migration of the nervous system to form outside of the body
   d. Failure of the reproductive system to develop
4. Which of the following would qualify as a secondary induction?
   a. The formation of the lens of the eye due to induction by the neural ectoderm
   b. Differentiation during neurulation by the dorsal ectoderm and mesoderm
   c. Both of these
   d. Neither of these
5. Your Aunt Ida thinks that babies can stimulate the onset of their own labor. You tell her that
   a. among mammals the onset of labor has been most closely linked to a change in the phases of the Moon.
   b. it is the mother's circadian clock that determines the onset of labor.
   c. body weight determines the onset of labor.
   d. changes in fetal hormone levels can affect the onset of labor.
6. Drug or alcohol exposure during which of the following stages is most likely to have a profound effect on the neural development of the fetus?
   a. Preimplantation
   b. First trimester
   c. Second trimester
   d. Third trimester
7. Axis formation in amniotic embryos could be affected by
   a. mutations in cells in the dorsal lip of the blastopore.
   b. mutations in cells in the primitive streak.
   c. both of these.
   d. neither of these.

SYNTHESIZE

1. Suppose you discover a new species whose development mechanisms have not been documented before. How could you determine at what stage the cell fate is determined?
2. You look up from your studying to see your dog, Fifi, acting silly again. Using this as a teachable moment, compare and contrast the homeoboxes in your dog and the fruit fly she just ate.
3. Why doesn't a woman menstruate while she is pregnant?
4. Spemann and Mangold were able to demonstrate that some cells act as "organizers" during development. What types of cells did they use? How did they determine that these cells were organizers?

ONLINE RESOURCE

www.ravenbiology.com

Understand, Apply, and Synthesize—enhance your study with animations that bring concepts to life and practice tests to assess your understanding. Your instructor may also recommend the interactive eBook, individualized learning tools, and more.

Chapter 55

Behavioral Biology

Chapter Outline

Introduction

The study of behavior is at the center of many disciplines of biology. Observing behavior provides important insights into the workings of the brain and nervous system, the influences of genes and the environment, when and how animals reproduce, and how they adapt to their environment. Behavior is shaped by natural selection and is controlled by internal mechanisms involving genes, hormones, neurotransmitters, and neural circuits. In this chapter, we explore how behavioral biology integrates approaches from several branches of biological science to provide a detailed understanding of the mechanisms that underscore behavior and its evolution.

55.1 The Natural History of Behavior

Learning Outcomes

1. *Contrast the proximate and ultimate causation of behavior.*
2. *Explain instinct theory.*
3. *Describe the physiological factors that might be the basis for innate behaviors.*

Observing animal behavior and making inferences about what one sees is at once simple and profound. Behavior is what an animal does. It is the most immediate way an animal responds adaptively to its environment by tracking environmental cues and signals such as odors, sounds, or visual signals associated with food, predators, or mates. Behavior also concerns thinking and cognition, monitoring one's social environment, and making decisions as to whether or not to cooperate or act altruistically. Behavior allows animals to survive and reproduce and is thus critical to the evolutionary process. The work of behavioral biologists has provided important insights into animal behavior, including the very meaning of human behavior.

Behavior can be analyzed in terms of mechanisms (cause) and evolutionary origin (adaptive nature)

Why does an animal behave in a particular way? Consider hearing a bird sing. We could ask how it vocalizes or determine the time of the year it sings most frequently. We could also ask about the function of the song, that is, ask why it sings. Answers to questions about how birds sing consider the role of internal factors such as hormones and nerve cells and other physiological processes. Such questions concern proximate causation: the mechanisms that are the reason for behavior. To analyze the proximate cause of bird song, we could measure hormone levels or study the development of brain regions and neural circuits associated with singing. For example, a male songbird may sing during the breeding season because of an increased level of the steroid sex hormone testosterone, which binds to receptors in the brain and triggers the production of song. Additionally, neural connections between the brain and the syrinx (the bird's vocal organ) must develop to allow songs to be produced. These explanations describe the proximate cause of bird song.

Asking about the function of a behavior (once again, bird song) is to ask why it evolved. To answer this question, we would determine how it influenced survival or reproductive success. A male bird sings to defend a territory from other males and to attract a female with which to reproduce. This is the ultimate, or evolutionary, explanation for the male's vocalization. Now we can understand its ultimate causation, or adaptive value. Researchers often study behavior from both perspectives to fully appreciate its mechanisms and ecological function, and thus its role in evolution. Behavior can be analyzed at four levels: (1) physiology (how it is influenced by hormones, nerve cells, and other internal factors); (2) ontogeny (how it develops in an individual), (3) phylogeny (its origin in groups of related species), and (4) adaptive significance (its role in survival and fitness). We'll begin by tracing the history of the study of mechanisms of behavior by focusing on the work of ethologists—biologists who first began to study behavior at the turn of the 20th century.

Ethology emphasizes the study of instinct and its origins

Ethology is the study of the natural history of behavior, with an emphasis on behaviors that form an animal's instincts, or programmed behaviors. Ethologists observed that individuals of a given species behaved in stereotyped ways, showing the same pattern of behavior in response to a particular stimulus. Because their behavior seemed reflexive, they considered it to be instinctive, or *innate*. Behaviors were thought to be programmed by the nervous system, which in turn was designed by genes, and responses would occur without experience. Ethologists based their instinct model on observations and experiments of simple behaviors such as egg retrieval by geese. Geese incubate their eggs in a nest. If an egg falls out of the nest, the goose will roll the egg back into the nest with a side-to-side motion of its neck while the egg is tucked beneath its bill (figure 55.1). Even if the egg is removed during retrieval, the goose will still complete the egg-retrieval sequence, as if driven by a program activated by the initial sight of the egg outside the nest.

This example is one paradigm of instinct theory and illustrates the way ethologists conceptualized the mechanisms of behavior. Egg retrieval behavior is triggered by a *key stimulus* (sometimes called a *sign stimulus*); this is the egg out of the nest. Early ethologists thought the nervous system regulated behavior via the *innate releasing mechanism*, a neural circuit involved

Figure 55.1 Innate egg-rolling response in geese. The series of movements used by a goose to retrieve an egg is a fixed action pattern. Once it detects the sign stimulus (in this case, an egg outside the nest), the goose goes through the entire set of movements: It will extend its neck toward the egg, get up, and roll the egg back into the nest with a side-to-side motion of its neck while the egg is tucked beneath its bill.

in the perception of the key stimulus and the triggering of a motor program, the *fixed action pattern*, in this case the act of guiding the egg back to the nest. Ethologists generalized that the key stimulus is a cue or signal in the environment that initiates neural events that cause behavior. The innate releasing mechanism involves the sensory apparatus that detects the signal and the neural circuit controlling muscles to generate the fixed action pattern.

Learning Outcomes Review 55.1

Proximate causation of behavior involves the immediate mechanisms that bring about an action; ultimate causation refers to the adaptive value of a behavior. Ethology is the study of the nature of behavior, emphasizing instinct and the regulation of behavior by internal factors such as genes, nerve cells, and hormones. Ethologists are also interested in the origins of behavior.

- ***Why is it important to understand the phylogeny (evolutionary origins) of behavior?***

55.2 Nerve Cells, Neurotransmitters, Hormones, and Behavior

Learning Outcomes

1. ***Relate the structure of neural circuits to their function.***
2. ***Describe the role of hormones and neurotransmitters in behavior.***

Although early ethologists had little understanding of neurobiology, they hypothesized elements of the nervous system (the innate releasing mechanism) controlled behavior. Today, neuroethologists—researchers who examine the neurobiology of behavior—can describe in detail how information in the environment is processed by sensory cells and how nerve impulses are transmitted to other neurons and muscles to form neural circuits that regulate behaviors important to survival. Behavior reflects the organization of the peripheral and central nervous system, and studying behavior can help us understand how neurons function individually and in combination with other neurons in circuits (see chapters 44 and 45).

Behaviors that must occur rapidly, like those used to capture prey or flee predators, involve neural mechanisms that enable such functions. Some moths have an earlike sensory organ equipped with sensory neurons designed to detect the ultrasonic cries of bats, the first step in evading predation. Specialized cells in the frog's retina detect moving objects like insects and release the tongue in fractions of a second once suitable prey is sighted. Likewise, the jaws of a predatory ant snap shut when prey trigger sensory hairs between the mandibles. Rapid responses to predators or prey often involve large nerve cell axons that can quickly transmit impulses to muscles. In the example of "trap jaw" ants, large axons of the mandibular motor neuron—the fastest neuron yet identified—fire nerve impulses that close the jaws in only 33 msec. Neural circuits that enable quick responses often are made up of few sensory and motor neurons, and their connecting nerve cells.

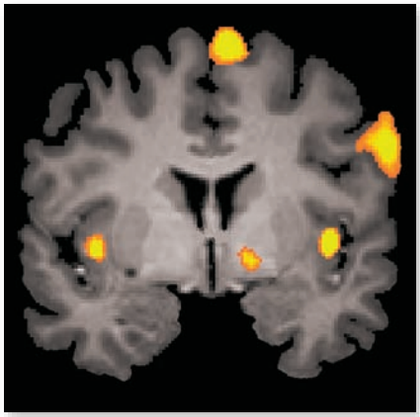


Figure 55.2
Functional Magnetic Resonance Imaging (fMRI). MRIs reveal neural activity in specific regions of the brain. In this case, activity in part of the brain called the nucleus accumbens is associated with viewing images of food.

Behavioral biologists examine the relationship of hormones to behavior to understand the endocrine mechanisms that are the foundation of reproduction, parental care, aggression, and stress (see chapter 46). In this way, the effects of the steroid sex hormones estrogen and testosterone on behavior have been determined. Testosterone in the male, for example, regulates territorial behavior and courtship, whereas estrogen in the female controls her mating behavior. Glucocorticoid hormones are involved in stress.

Neuroscientists may measure levels of neurotransmitters such as serotonin and dopamine in the nervous system or blood and associate these chemicals with behavior (see chapter 44). These chemicals are released by nerve cells and can affect activity in different brain regions. Serotonin has been shown to influence aggression in an incredibly wide range of animals including lobsters, mice, and humans. Researchers may inject a neurotransmitter or pharmacologically change its level in the brain to examine how it affects behavior.

The techniques of neuroethology include identifying and mapping individual neurons, their dendrites and connections to other neurons, and how their impulses and neurochemicals regulate behavior. Today, techniques such as functional magnetic resonance imaging (fMRI) are generating exciting data on the specialized functions of different regions of the human brain. One striking example concerns how the brain responds to images of food (figure 55.2). In contrast to expectation, the brain's response does not occur in the visual cortex, the region associated with object recognition, but in a circuit in the nucleus accumbens in the forebrain, normally involved in reward and pleasure.

Learning Outcomes Review 55.2

Instinctive behaviors appear to involve programmed circuits in the nervous system that are likely to be genetically controlled. Research in neuroethology supports the instinct concept of behavior by describing the organization of neural circuits governing behavior. Chemical signals provided by hormones and by neurotransmitters such as serotonin and dopamine cause behaviors to occur.

- ***If a male songbird is injected with testosterone two weeks earlier than when these birds normally start to sing in the spring, what would you expect to happen?***

55.3 Behavioral Genetics

Learning Outcomes

1. *Discuss the types of studies that have provided evidence to link genes and behavior.*
2. *Explain how single genes can influence behavior.*
3. *Describe the role of genes in complex behaviors such as aggression, parental care, and pair bonding.*

Instinct theory assumed that genes play a role in behavior, but ethologists did not conclusively demonstrate the role genes can play. The study of genes and behavior has often been highly controversial, as ethologists and social scientists engaged in a seemingly endless debate over whether behavior is determined more by an individual's genes (nature) or by its learning and experience (nurture). One problem with this nature/nurture controversy is that the question is framed as an "either/or" proposition, which fails to consider that both instinct and experience can have significant roles, often interacting in complex ways to shape behavior.

Behavioral genetics deals with the contribution that heredity makes to behavior. It is obvious that genes, the units of heredity, are passed from one generation to the next and guide the development of the nervous system and potentially the behavioral responses it regulates. But animals may also develop in a rich social environment and have experiences that guide behavior. The importance of "nature" and "nurture" to behavior can be seen by first reviewing the history of studies in behavioral genetics and next examining the importance of experience and development. We'll then consider their interaction.

Artificial selection and hybrid studies link genes and behavior

Pioneering research indicated that behavioral differences among individuals result from genetic differences. Research on a variety of animals demonstrated that hybrids showed behaviors involved in nest building and courtship that were intermediate between those of parents. These early efforts to define the role of genes in behavior demonstrated that behavior can have a heritable component, but fell short of identifying the genes involved. With the development of molecular biology, far greater precision was added to the analysis of the genetics of behavior.

Learning itself can be influenced by genes. In one classic study, rats had to find their way through a maze of blind alleys and only one exit, where a reward of food awaited them. Some rats quickly learned to zip through the maze to the food, making few mistakes, but other rats made more errors in learning the correct path. Researchers bred rats that made few errors with one another to establish a "maze-bright" group, and error-prone rats were interbred, forming a "maze-dull" group. Offspring in each group were then tested for their maze-learning ability. The offspring of maze-bright rats learned to negotiate the maze with fewer errors than their parents, while the offspring of maze-dull parents performed more poorly. Repeating this artificial selection method for several generations led to two behaviorally distinct types of rat with very different maze-learning abilities (figure 55.3). This type of study suggests the ways in which natural selection could shape behavior over time, making genes for certain abilities more prevalent.

Inquiry question

What would happen if, after the seventh generation, rats were randomly assigned mates regardless of their ability to learn the maze?

Some behaviors appear to be controlled by a single gene

Artificial selection and hybrid studies only suggested a role for genes in behavior. Subsequent research took advantage of advances in molecular biology and identified the genes involved. Fruit flies, *Drosophila*, have traditionally provided a useful model system in which the effect of single genes have been identified.

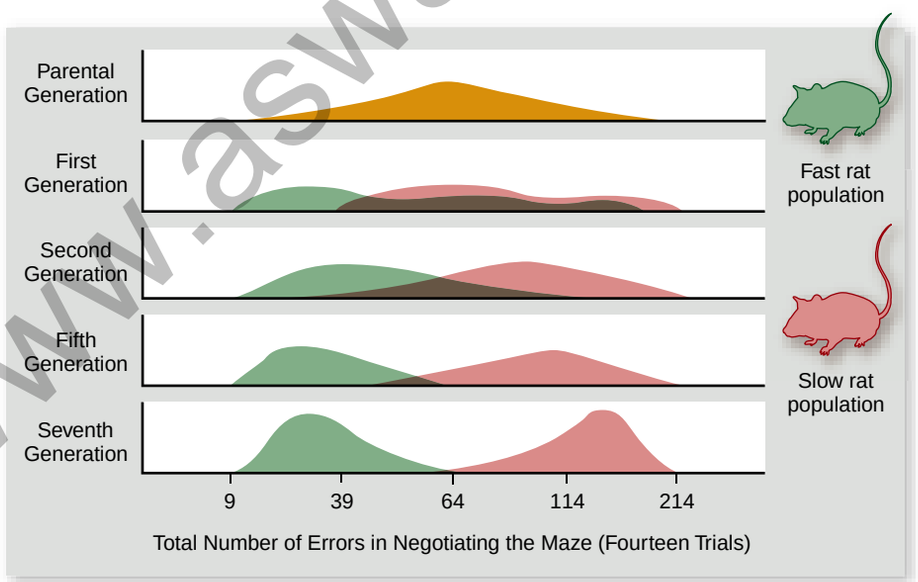


Figure 55.3 The genetics of learning. Rats that made the fewest errors in the parental population were interbred to select for rats that had improved maze-learning ability (green), and rats that made the most errors were interbred to select for rats that were error prone (red).

Inquiry question

What would happen if, after the seventh generation, rats were randomly assigned mates regardless of their ability to learn the maze?

Single genes have also been shown to influence behavior in animals ranging from mice to humans.

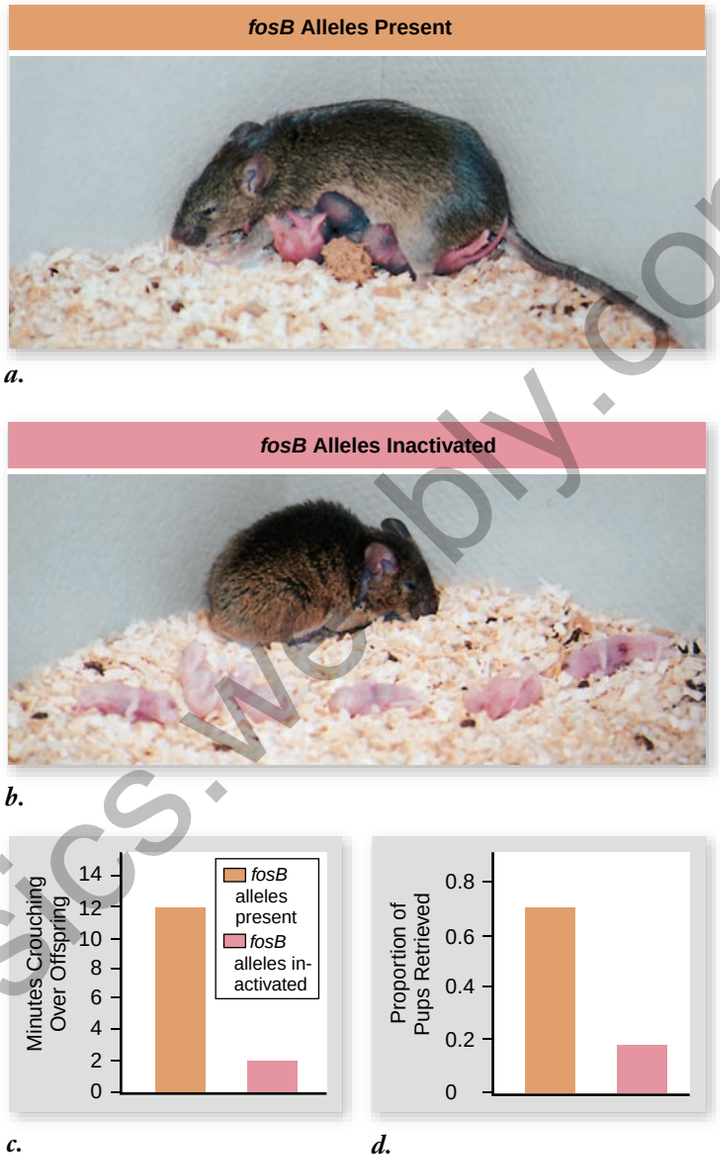
In fruit flies, individuals that possess alternative alleles for a particular gene differ greatly in their feeding behavior as larvae: Larvae with one allele move around a great deal as they eat, whereas individuals with the alternative allele move hardly at all. A wide variety of experimentally induced mutations at other genes affect courtship behavior in males and females. For example, *fru* is a regulatory gene whose transcription products govern the design of the courtship center of the fruit fly brain. This gene turns on other genes involved in the neural circuitry of courtship.

Single genes in mice are associated with spatial memory and parenting. For example, some mice with a particular mutation have trouble remembering recently learned information about where objects are located. This is apparently because they lack the ability to produce the enzyme α-calcium-calmodulin-dependent kinase II, which plays an important role in the functioning of the hippocampus, a part of the brain important for spatial learning.

It is particularly interesting that genes are involved in behavior as complex as maternal care: The presence or absence of *fosB* determines whether female mice nurture their young in particular ways. Females with both *fosB* alleles disabled initially investigate their newborn babies, but then ignore them, in stark contrast to the caring and protective maternal behavior displayed by normal females (figure 55.4). The cause of this inattentiveness appears to result from a chain reaction. When mothers of new babies initially inspect them, information from their auditory, olfactory, and tactile senses is transmitted to the hypothalamus, where *fosB* alleles are activated. The *fosB* alleles produce a protein, which in turn activates other enzymes and genes that affect the neural circuitry of the hypothalamus. These modifications in the brain cause the female to behave maternally. If mothers lack the *fosB* alleles, this process is stopped midway. No protein is activated, the brain's neural circuitry is not rewired, and maternal behavior does not result. The "maternal instincts" of mice can thus be defined genetically!

Another fascinating example of the genetic basis of behavior concerns prairie and montane voles, two closely related species of North American rodents that differ profoundly in their social behavior. Male and female prairie voles form monogamous pair bonds and share parental care, whereas montane voles are promiscuous (meaning they mate with multiple partners and go their separate ways). The act of mating leads to the release of the neuropeptides vasopressin and oxytocin, and the response to these peptides differs dramatically in each species. Injection of either peptide into prairie voles leads to pair bonding even without mating. Conversely, injecting a chemical that blocks the action of these neuropeptides causes prairie voles not to form pair bonds after mating. By contrast, montane voles are unaffected by either of these manipulations.

These different responses have been traced to interspecific differences in brain structure (figure 55.5). The prairie vole has many receptors for these peptides in a particular part of the brain, the nucleus accumbens, which seems to be involved in the expression of pair-bonding behavior. By contrast, few such receptors occur in the same brain region in the montane vole. In laboratory experiments with prairie voles, blocking these receptors tends to prevent pair-bonding, whereas stimulating them



a.

b.

c.

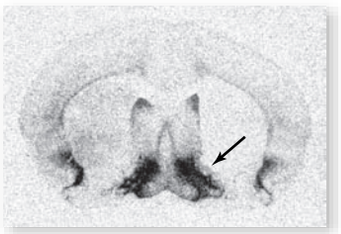
d.

Figure 55.4 Genetically caused defect in maternal care.
a. In mice, normal mothers take very good care of their offspring, retrieving them if they move away and crouching over them. ***b.*** Mothers with the mutant *fosB* allele perform neither of these behaviors, leaving their pups exposed. ***c.*** Amount of time female mice were observed crouching in a nursing posture over offspring. ***d.*** Proportion of pups retrieved when they were experimentally moved.

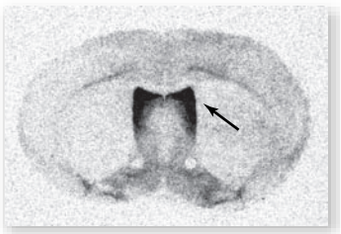
Inquiry question

Why does the lack of *fosB* alleles lead to maternal inattentiveness?

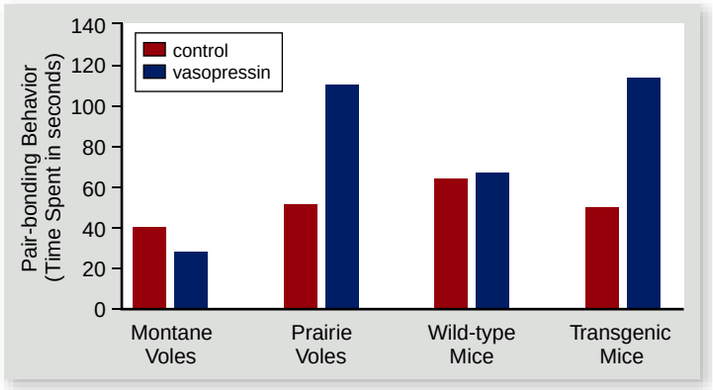
leads to pair-bonding behavior. The gene that codes for the peptide receptors has also been identified, and a difference in the DNA structure between the species has been discovered. To test the hypothesis that this genetic difference was responsible for the differences in behavior, scientists created transgenic mice with the prairie vole version of the gene, and sure enough, when injected with vasopressin, the transgenic mice exhibited pair-bonding behavior very similar to that of prairie voles, whereas normal mice showed no response (see figure 55.5). The



a. Prairie vole



b. Montane vole



c.

Figure 55.5 Genetic basis of differences in pair-bonding behavior in two rodent species. ***a.*** and ***b.*** The prairie *(Microtus ochrogaster)* and montane *(M. montanus)* voles differ in the distribution of one type of vasopressin receptor in the brain. ***c.*** Transgenic mice created with the prairie-vole version of the receptor genes respond to injections of vasopressin by exhibiting heightened levels of pair-bonding behavior in 5-min trials compared with their response to a control injection. By contrast, normal wild-type mice (control) show no increase in such behaviors.

vasopressin receptor gene varies in structure among primate species that vary in degree of pair bonding. In human males, the gene has recently been found to be associated with the strength of marital bonds and satisfaction in marriage.

The production of monoamine oxidases (MAOs), enzymes that degrade neurotransmitters such as serotonin and dopamine, are controlled by single genes. Transgenic mice that lack MAOA (monoamine oxidase-A) are highly aggressive. In humans, a single point mutation results in the lack of the ability to produce MAOA, resulting in antisocial behavior and violence. MAO abnormalities are also associated with mood disorders in humans.

Learning Outcomes Review 55.3

A relationship between genes and behavior has been demonstrated in many ways, including artificial selection experiments and studies on the effects of single genes. Genes can regulate behavior by producing molecular factors that influence the function of the nervous system; mutations altering these factors have been found to affect behavior.

- ***What would you infer about the role of genes in pair-bonding in prairie voles if you learned that males sometimes seek to copulate with females other than their own mate?***

55.4 Learning

Learning Outcomes

1. ***Describe the mechanisms of learning.***
2. ***Define learning preparedness.***
3. ***Explain how instinct influences learning preparedness.***

Instincts can guide an animal's actions, but behavior can also develop from previous experiences, a process termed learning. Traditionally, psychologists studied the mechanisms of learning using laboratory rodents, but today both proximate and ultimate causes of learning are understood by integrating learning into an ecological and evolutionary framework.

Learning mechanisms include habituation and association

Habituation is a simple form of learning defined as a decrease in response to a repeated stimulus that has no positive or negative consequences. Initially, the stimulus may evoke a strong response, but the response declines with repeated exposure. For example, young birds see many types of objects moving overhead. At first, they may respond by crouching and remaining still. But frequently seen objects, such as falling leaves or members of their own species flying overhead, have no positive or negative consequence to the nestlings. Over time, the young birds may habituate to such stimuli and stop responding. Thus, habituation can be thought of as learning not to respond to a stimulus.

One ecological context in which habituation has adaptive value is prey defense. Birds that feed on insects search for suitable prey in a visually complex environment. Insects that have camouflaged bodies appear to be twigs or leaves, which are commonly encountered as birds search for prey. Because birds see these objects very frequently, they habituate to their appearance. Insects that look like twigs or leaves are therefore protected because they do not trigger an attack, and they survive to reproduce.

More complex forms of learning concern changes in behavior through an association between two stimuli or between a stimulus and a response. In associative learning, for example, (figure 55.6) a behavior is modified, or conditioned, through the association. The two major types of associative learning—classical conditioning and operant conditioning—differ in the way the associations are established. In **classical conditioning,** the paired presentation of two different kinds of stimuli causes the animal to form an association between the stimuli. Classical conditioning is also called **Pavlovian conditioning,** after the Russian psychologist Ivan Pavlov, who first described it.

Pavlov presented meat powder, an unconditioned stimulus, to a dog and noted that the dog responded by salivating, an unconditioned response. If an unrelated stimulus, such as the ringing of a bell, was repeatedly presented at the same time as the meat powder, the dog would soon salivate in response to the sound of the bell alone. The dog had learned to associate the unrelated sound stimulus with the meat powder stimulus. Its

a. *b.* *c.*

Figure 55.6 Learning what is edible. Associative learning is involved in predator–prey interactions. ***a.*** A naive toad is offered a bumblebee as food. ***b.*** The toad is stung, and ***(c)*** subsequently avoids feeding on bumblebees or any other insects having black-and-yellow coloration. The toad has associated the appearance of the insect with pain and modifies its behavior.

response to the sound stimulus was, therefore, conditioned, and the sound of the bell is referred to as a conditioned stimulus.

In **operant conditioning,** an animal learns to associate its behavioral response with a reward or punishment. American psychologist B. F. Skinner studied operant conditioning in rats by placing them in an apparatus that came to be called a "Skinner box." As the rat explored the box, it would occasionally press a lever by accident, causing a pellet of food to appear. Soon it learned to associate pressing the lever (the behavioral response) with obtaining food (the reward). This sort of trial-and-error learning is of major importance to most vertebrates. Learning provides flexibility that allows behavior to be fine-tuned to an environment.

Instinct governs learning preparedness

Psychologists once believed that any two stimuli could be linked through learning and that animals could be conditioned to perform any learnable behavior. This view has changed. Today, researchers believe that instinct guides learning by determining what type of information can be learned. Animals may have innate predispositions toward forming certain associations. For example, if a rat is offered a food pellet at the same time it is exposed to X-rays (which later produce nausea), the rat remembers the taste of the food pellet but not its size, and in the future will avoid food with that taste, but will readily eat pellets of the same size if they have a different taste. Similarly, pigeons can learn to associate food with colors, but not with sounds. In contrast, they can associate danger with sounds, but not with colors.

These examples of learning preparedness demonstrate that what an animal can learn is biologically influenced—that is, learning is possible only within the boundaries set by evolution. Innate programs for learning have evolved because they lead to adaptive responses. In nature, food that is toxic to a rat is likely to have a particular taste; thus, it is adaptive to be able to associate a taste with a feeling of sickness that may develop hours later. The seed a pigeon eats may have a distinctive color that the pigeon can see, but it makes no sound the pigeon can hear.

An animal's ecology is key to understanding its learning capabilities. Some species of birds, such as Clark's nutcracker, feed on seeds. When seeds are abundant, these birds store them in buried caches so they will have food during the winter. Seed caches (up to 2000!) may be buried and then recovered as long as nine months later. One would expect these birds to have an extraordinary spatial memory, and this is indeed what has been found (figure 55.7). Clark's nutcracker, and other seed-hoarding birds, have an unusually large hippocampus, the center for memory storage in the brain. This illustrates how feeding ecology (caching seeds to survive the winter) affects the evolution of brain anatomy (an enlarged hippocampus).

Learning Outcomes Review 55.4

Habituation is a diminishing response to a repeated stimulus that is neither positive nor negative. Association may occur as either classical conditioning or operant conditioning. Animals can change their behavior through learning in a variety of ways. Although learning mechanisms may be similar across species, animals also differ in their learning abilities according to their ecology.

- ***In some rodents, males travel far while females remain close to the nest. Do males or females have greater spatial memory? What experiment could you conduct to test your hypothesis?***

Figure 55.7 The Clark's nutcracker has an extraordinary memory. A Clark's nutcracker (*Nucifraga columbiana)* can remember the locations of up to 2000 seed caches months after hiding them. After conducting experiments, scientists have concluded that the birds use features of the landscape and other surrounding objects as spatial references to memorize the locations of the caches.

55.5 The Development of Behavior

Learning Outcomes

1. *Discuss the role of the critical period in imprinting.*
2. *Explain how social contact can influence growth and development.*
3. *Explain how the study of song learning in white-crowned sparrows illustrates the interaction of instinct and learning.*

Behavioral biologists recognize that behavior has both genetic and learned components. Thus far in this chapter, we have discussed the influence of genes and learning separately. But as you will see, these factors interact during development to shape behavior.

Parent–offspring interactions influence how behavior develops

As an animal matures, it may form social attachments to other individuals or develop preferences that will influence behavior later in life. This process of behavioral development is called **imprinting.** The success of imprinting is highest during a critical period (roughly 13 to 16 hours after hatching in geese). During this time, information required for normal development must be acquired. In **filial imprinting,** social attachments form between parents and offspring. For example, young birds like ducks and geese begin to follow their mother within a few hours after hatching, and their following response results in a social bond between mother and young. The young birds' initial experience, through imprinting, can determine how social behavior develops later in life. The ethologist Konrad Lorenz showed that geese will follow the first object they see after hatching and direct their social behavior toward that object, even if it is not their mother! Lorenz raised geese from eggs, and when he offered himself as a model for imprinting, the goslings treated him as if he were their parent, following him dutifully (figure 55.8).

Interactions between parents and offspring are key to the normal development of social behavior. The psychologist Harry Harlow gave orphaned rhesus monkey infants the opportunity to form social attachments with two surrogate "mothers," one made of soft cloth covering a wire frame and the other made only of wire (figure 55.9). The infants chose to spend time with the cloth mother, even if only the wire mother provided food, indicating that texture and tactile contact, rather than provision of food, may be among the key qualities in a mother that promote infant social attachment. If infant monkeys are deprived of normal social contact, their development is abnormal. Greater degrees of deprivation lead to greater abnormalities in social behavior during childhood and adulthood. Studies of orphaned human infants similarly suggest that a constant "mother figure" is required for normal growth and psychological development.

Figure 55.8 An unlikely parent. The eager goslings follow Konrad Lorenz as if he were their mother. He is the first object they saw when they hatched, and they have used him as a model for imprinting. Lorenz won the 1973 Nobel Prize in medicine or physiology for this work.

Recent research has revealed a biological need for the stimulation that occurs during parent–offspring interactions early in life. Female rats lick their pups after birth, and this stimulation inhibits the release of a brain peptide that can block normal growth. Pups that receive normal tactile stimulation also have more brain receptors for glucocorticoid hormones, thus a greater tolerance for stress, and longer-lived brain cells. Premature human infants who are massaged gain weight rapidly. These studies indicate that the need for normal social interaction is based in the brain, and that touch and

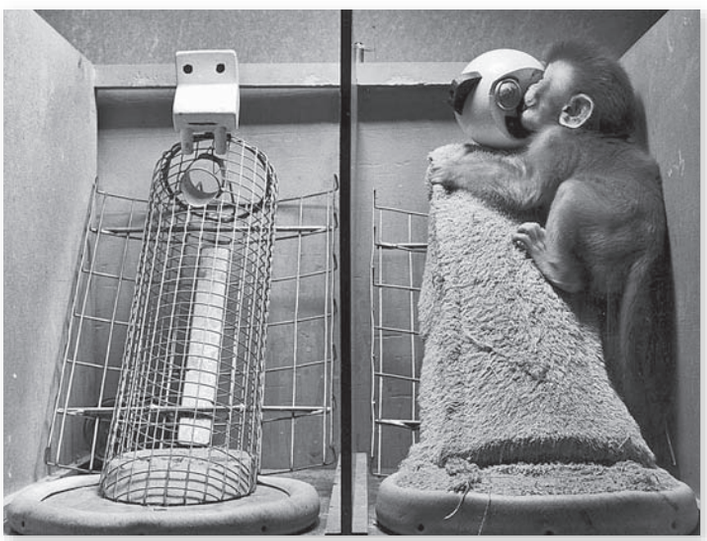


Figure 55.9 Choice trial on infant monkeys. Given a choice between a wire frame that provided food and a similar frame covered with cloth and given a monkey-like head, orphaned rhesus monkeys *(Macaca mulatta)* chose the monkeylike figure over the food.

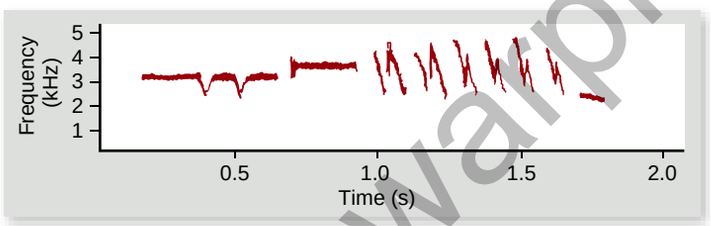
other aspects of contact between parents and offspring are important for physical as well as behavioral development.

Instinct and learning may interact as behavior develops

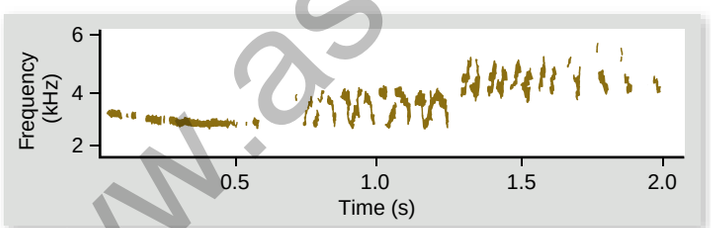
We began this chapter by considering the proximate and ultimate causation of bird song. Let's continue with the classic studies by Peter Marler on song learning in white-crowned sparrows to examine how innate programs and experience each contribute to the development of behavior.

Mature male white-crowned sparrows sing a species-specific courtship song during the mating season. Through a series of elegant experiments, Peter Marler asked if the song was the result of an instinctive program, learning, or both. Marler reared male birds in soundproof incubators equipped with speakers and microphones to control what a bird heard as it matured, and then recorded the song it produced as an adult. Males that heard no song at all during development sang a poorly developed song as adults (figure 55.10), indicating that instinct alone did not guide song production. In a second study, males were played only the song of a different species, the song sparrow. These males sang a poorly structured song as well. This experiment showed that males would not imitate any song they heard to learn to sing. But birds that heard the song of their own species, or that heard the songs of both the white-crowned sparrow and the song sparrow, sang a fully developed, white-crowned sparrow song as adults.

These results suggest males have a selective **genetic template,** or innate program, that guides them to learn the appropriate song. During a critical period in development, the template will accept the white-crowned sparrow song as a model. Thus, song acquisition depends on learning, but only the song of the correct species can be learned; the genetic template limits what can be learned.



a.



b.

Figure 55.10 Song development in birds. *a.* The sonograms of songs produced by male white-crowned sparrows (*Zonotrichia leucophrys*) that had been exposed to their own species' song during development are different from ***(b)*** those of male sparrows that heard no song during rearing. This difference indicates that the genetic program itself is insufficient to produce a normal song.

Figure 55.11 Brood parasite. Cuckoos lay their eggs in the nests of other species of birds. Because the young cuckoos (large bird to the right) are raised by a different species (such as this meadow pipit, smaller bird to the left), they have no opportunity to learn the cuckoo song; the cuckoo song they later sing is innate.

But learning plays a prominent role as well. If a young male becomes deaf after it hears its species' song during the critical period, it will sing a poorly developed song as an adult. Therefore, the bird must hear the correct song at the right time, and then "practice" listening to himself sing, matching what he hears to the model his genetic template has accepted.

Although this explanation of song development stood unchallenged for many years, white-crowned sparrow males can learn another species' song under certain conditions. If a live male strawberry finch is placed in a cage next to a young male sparrow, the young sparrow will learn to sing the strawberry finch's song. This finding indicates that social stimuli—in this case, being able to see, hear, and interact with another bird—is more effective than a tape-recorded song in altering the innate template that guides song development.

The males of some bird species may have no opportunity to hear the song of their own species. In such cases, it appears that the males instinctively "know" their own species' song. For example, cuckoos are **brood parasites;** females lay their eggs in the nest of another species of bird, and the young that hatch are reared by the foster parents (figure 55.11). When the cuckoos become adults, they sing the song of their own species rather than that of their foster parents. Because male brood parasites would most likely hear the song of their host species during development, it is adaptive for them to ignore such "incorrect" stimuli. They hear no adult males of their own species singing, so no correct song models are available. In these species, natural selection has produced a completely genetically guided song. Other birds can also sing a correct species-typical song, even if reared in isolation.

Inquiry question

Imagine there is only one bird species on an island. Do you think instinct, learning, or both will guide song development?

Studies on twins reveal a role for both genes and environment in human behavior

The interaction of genes and the environment can be seen in humans by comparing the behavior of identical twins (which are genetically the same), raised in the same environment or separated at birth and raised apart in different environments. Data on human twins raised together or raised apart allows researchers to determine whether similarities in behavior result from their genetic similarity or from shared environmental experiences. Twins studies indicate many similarities in a wide range of personality traits even though twins were raised in very different environments. Other studies show that antisocial behavior in humans, for which genetic factors such as MAOA deficiencies are known in individuals in the study sample, results from a combination of genes and experience during childhood. These similarities indicate that genetics plays a role in behavior even in humans, although the relative importance of genetics versus environment is still debated.

Learning Outcomes Review 55.5

During the critical period, offspring must engage in certain social interactions for normal behavioral development. Parent–offspring contact stimulates the release of physiological factors, such as hormones and brain receptors, crucial to growth and brain development. In white-crowned sparrows, young males must hear their species' song to sing it correctly, indicating that both instinct and learning affect song development.

- ***Some researchers have tried to link IQ and genes in humans. Why would this research be seen as controversial?***

55.6 *Animal Cognition*

Learning Outcome

1. ***Explain why behavioral biologists today are more open to considering that animals can think.***

For many decades, students of animal behavior flatly rejected the notion that nonhuman animals can think. Now serious attention is given to animal awareness. The central question of whether animals show **cognitive behavior**—that is, they process information and respond in a manner that suggests thinking—is widely supported (figure 55.12).

In a series of classic experiments conducted in the 1920s, a chimpanzee was left in a room with bananas hanging from the ceiling out of reach. Also in the room were several boxes lying on the floor. After some unsuccessful attempts to jump up and grab the bananas, the chimp stacked the boxes beneath the suspended bananas, and climbed up to claim its prize (figure 55.13). Field researchers have observed that Japanese macaques learned

a. ***b.***

Figure 55.12 Animal thinking? ***a.*** This chimpanzee is stripping the leaves from a twig, which it will then use to probe a termite nest. This behavior strongly suggests that the chimpanzee is consciously planning ahead, with full knowledge of what it intends to do. ***b.*** This sea otter is using a rock as an "anvil," against which it bashes a clam to break it open. A sea otter will often keep a favorite rock for a long time, as though it has a clear idea of its future use of the rock. Behaviors such as these suggest that animals have cognitive abilities.

to wash sand off potatoes and to float grain to separate it from sand. Chimpanzees pull leaves off a tree branch and then stick the branch into the entrance of a termite nest to "fish" for food. Chimps also crack open nuts using pieces of wood in a "hammer and anvil" technique. Even more remarkable is that parents appear to teach nut cracking to their offspring!

Recent studies have found that chimpanzees and other primates show amazing behaviors that provide strong evidence of cognition. Chimpanzees will eat the leaves of medicinal plants when infected with certain parasites. Chimps also cooperate with other chimps in ways that suggest an understanding of past success. Cognitive ability is not limited to primates: Ravens and other corvid birds also show extraordinary insight and problem-solving ability (figure 55.14).

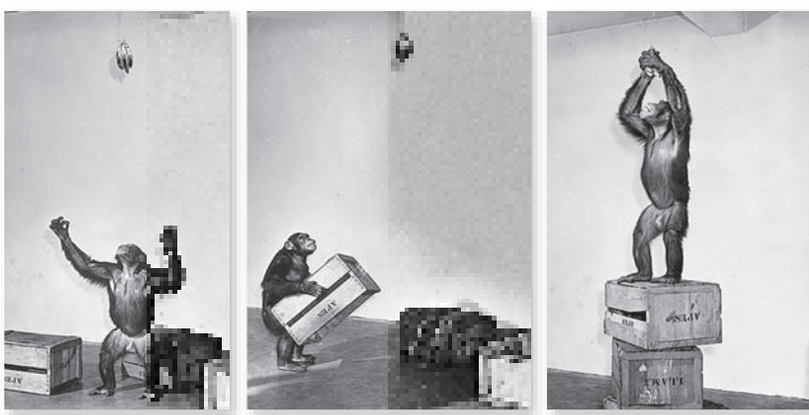


Figure 55.13 Problem solving by a chimpanzee. Unable to get the bananas by jumping, the chimpanzee devises a solution.

Figure 55.14 Problem solving by a raven. Confronted with a problem it has never previously faced, the raven figures out how to get the meat at the end of the string by repeatedly pulling up a bit of string and stepping on it.

Learning Outcome Review 55.6

Research has provided compelling evidence that some nonhuman animals are able solve problems and use reasoning, cognitive abilities once thought uniquely human.

- ***How could you determine whether a chimpanzee had the ability to count objects?***

55.7 *Orientation and Migratory Behavior*

Learning Outcomes

1. ***Define migration.***
2. ***Distinguish between orientation and navigation.***
3. ***Describe different systems for navigation.***

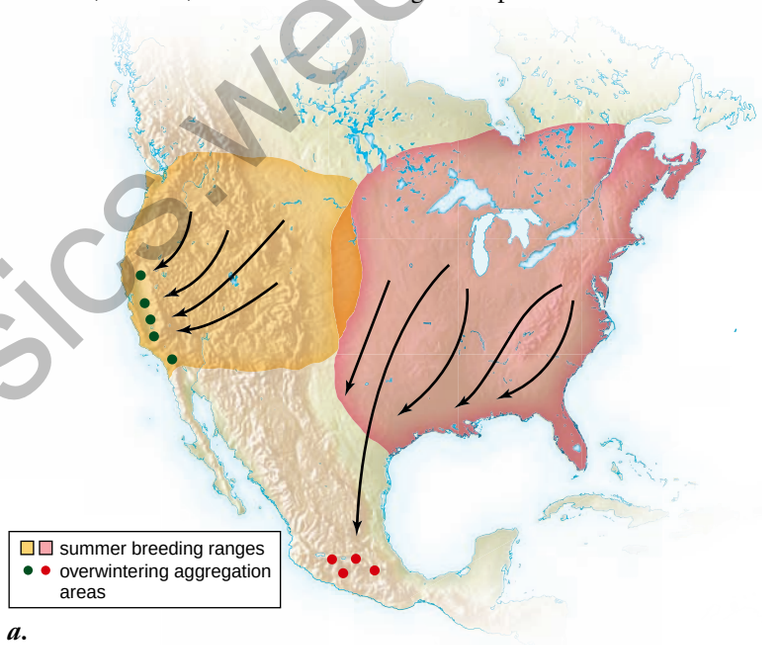
Monarch butterflies and many birds travel thousands of miles over continents to overwintering sites in the tropics. Many animals travel away from a nest and then return. To do so, they track cues in the environment, often showing exceptional skill at orientation. Animals with a homing instinct, such as pigeons, recognize complex features of the environment to return to their home. Despite decades of study, our understanding of animal orientation is far from complete.

Migration often involves populations moving large distances

Long-range, two-way movements are known as migrations. Each fall, ducks, geese, and many other birds migrate south along flyways from Canada across the United States, heading as far as South America, and then returning each spring.

Monarch butterflies also migrate each fall from central and eastern North America to their overwintering sites in several small, geographically isolated areas of coniferous forest in the mountains of central Mexico (figure 55.15). Each August, the butterflies begin a flight southward and at the end of winter, the monarchs begin the return flight to their summer breeding ranges. Two to five generations may be produced as the butterflies fly north: butterflies that migrate in the autumn to the precise locations in Mexico have never been there before!

Recent geographic range expansions by some migrating birds have revealed how migratory patterns change. When colonies of bobolinks became established in the western United States, far from their normal range in the Midwest and East, they did not migrate directly to their winter range in South America. Instead, they migrated east to their ancestral range, and then south along the original flyway (figure 55.16). Rather than changing the original migration pattern, they simply added a new segment. Scientists continue to study the western bobolinks to learn whether, in time, a more efficient migration path will evolve or



a.

b.

c.

Figure 55.15 Migration of monarch butterflies *(Danaus plexippus).* ***a.*** Monarchs from western North America overwinter in areas of mild climate along the Pacific coast. Those from eastern North America migrate over 3000 kilometers to Mexico. ***b.*** Monarch butterflies arrive at the remote forests of the overwintering grounds in Mexico, where they ***(c)*** form aggregations on the tree trunks.

whether the birds will always follow their ancestral course. The behavior of butterflies and birds accentuate the mysteries of the mechanism employed during migration.

Migrating animals must be capable of orientation and navigation

To get from one place to another, animals must have a "map" (that is, know where to go) and a "compass" (use environmental cues to guide their journey). Orientation requires following a bearing such as a source of light, but navigation is the ability to set or adjust a bearing, and then follow it. The former is analogous to using a compass, while the latter is like using a compass in conjunction with a map. The nature of the "map" animals use is unclear.

Birds and other animals navigate by looking at the sun during the day and the stars at night. The indigo bunting is a short-distance nocturnal migrant bird. It flies during the day using the Sun as a guide, and compensates for the movement of the Sun in the sky as the day progresses. These birds use the positions of constellations around the North Star in the night sky as a compass.

Many migrating birds also have the ability to detect Earth's magnetic field and to orient themselves with respect to it when cues from the Sun or stars are not available. In an indoor cage, they will attempt to move in the correct geographic direction, even though there are no visible external cues. However, the placement of a magnet near the cage can alter the direction in which the birds attempt to move. Researchers have found magnetite, a magnetized iron ore, in the eyes and upper beaks of some birds, but how these sensory organs function is not known.

The first migration of a bird appears to be innately guided by both celestial cues (the birds fly mainly at night) and Earth's magnetic field. When the two cues are experimentally manipulated to give conflicting directions, the information provided by the stars seems to override the magnetic information. Recent studies, however, indicate that celestial cues indicate the general direction for migration, whereas magnetic cues indicate the specific migratory path (perhaps a turn the bird must make midroute). Experiments on starlings indicate that inexperienced birds migrate by orientation, but older birds that have migrated previously use true navigation (figure 55.17).

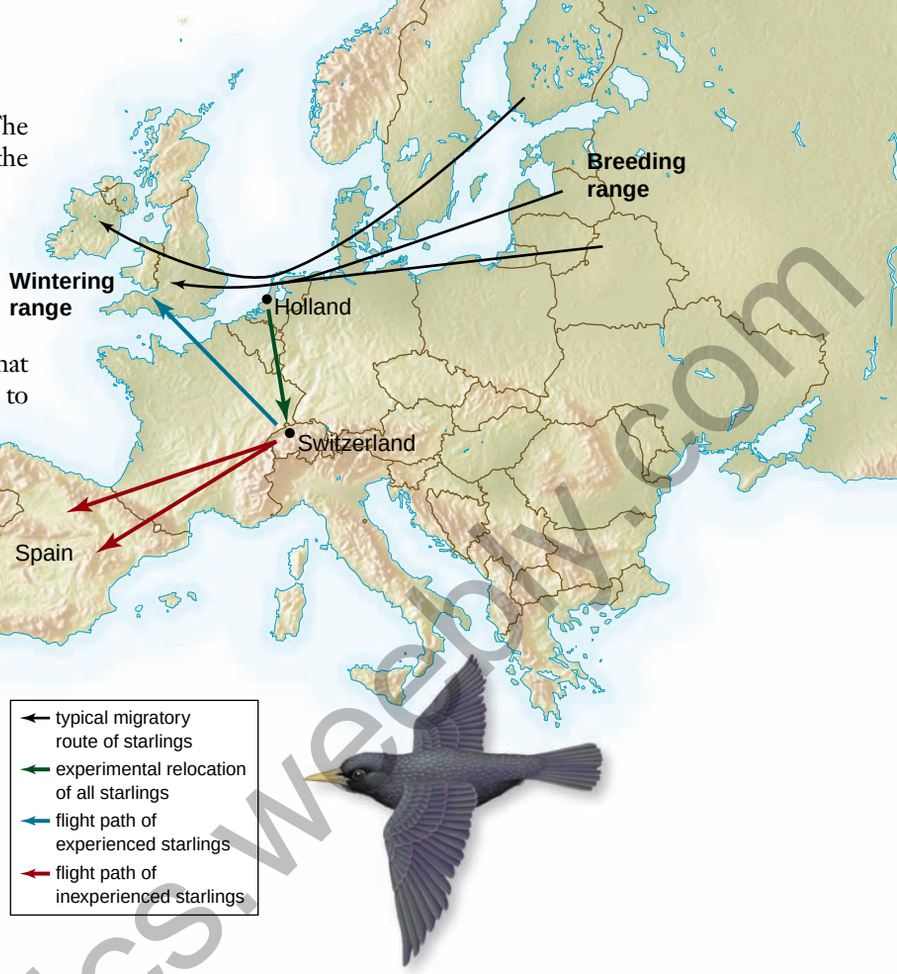


Figure 55.17 Migratory behavior of starlings *(Sturnus vulgaris).* The navigational abilities of inexperienced birds differ from those of adults that have made the migratory journey before. Starlings were captured in Holland, halfway along their full migratory route from Baltic breeding grounds to wintering grounds in the British Isles; these birds were transported to Switzerland and released. Experienced older birds compensated for the displacement and flew toward the normal wintering grounds (blue arrow). Inexperienced young birds kept flying in the same direction, on a course that took them toward Spain (red arrows). These observations imply that inexperienced birds fly by orientation, but experienced birds learn true navigation.

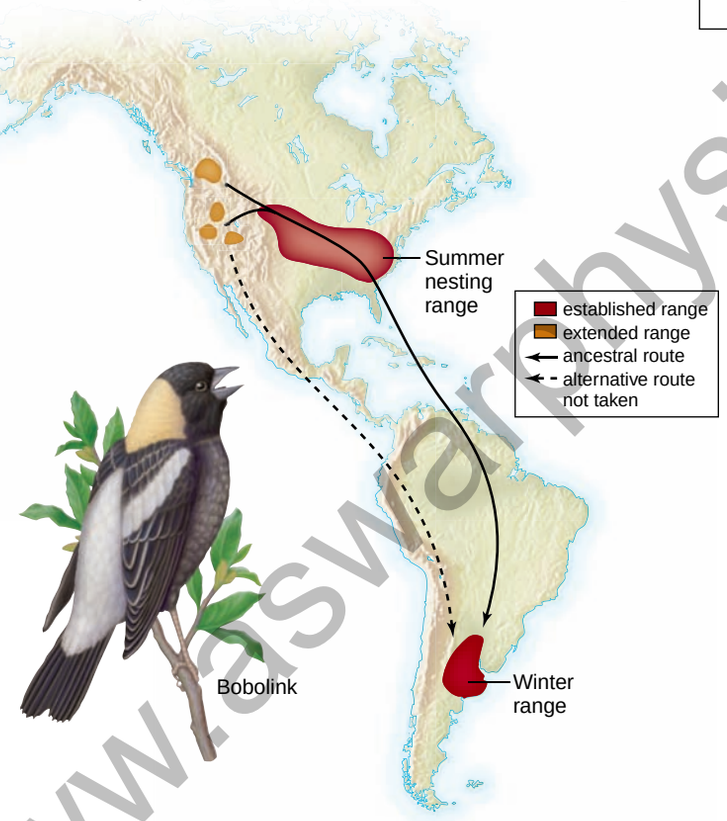


Figure 55.16 Birds on the move. The summer range of bobolinks *(Dolichonyx oryzivorus)* recently extended to the far western United States from their established range in the Midwest. When birds in these newly established populations migrate to South America in the winter, they do not fly directly to the winter range; instead, they first fly to the Midwest and then use the ancestral flyway, going much farther than if they flew directly to their winter range.