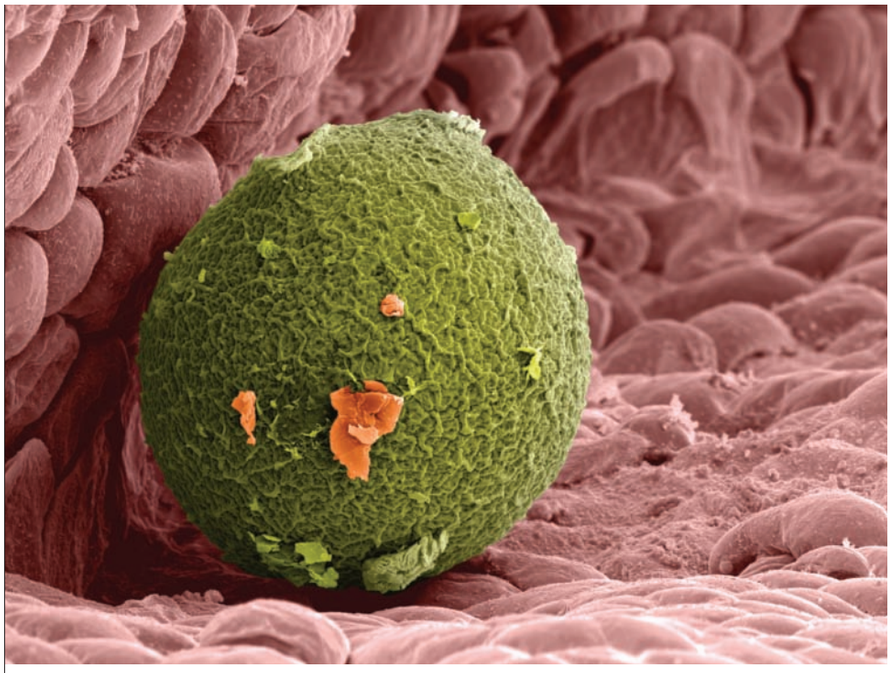
A newly fertilized human egg passing down the oviduct on its way to implantation in the wall of the uterus (colorized SEM).



Study Plan

47 Animal Reproduction

Why It Matters

It is 7 days after the October full moon and night is falling. All the inhabitants of the Samoan island of Tutuila who have access to a boat are gathered on the island's large lagoon. Some hold lanterns and look into the water; others have nets at the ready. They are awaiting the palolo worm *(Eunice viridis)*, which has appeared in the water as the moon rises on this same night of the lunar year for as long as the islanders can remember.

The moon peeks over the horizon and the excitement of the crowd rises. Then, there they are, untold thousands of blue and green worms, squirming in the water like animated spaghetti. The boaters scoop up the worms by the netfull and dump them into buckets. When the buckets are full, the islanders glide toward the shore where steaming pots are waiting, for palolo worms are a delicacy that the islanders savor only once a year. For the islanders, a night of feasting, singing, and dancing will follow as they cook and eat the worms. Their flavor has been described by some as similar to that of caviar; by others like, well, palolo worms.

The worms that squirm to the surface to delight the islanders are actually not complete individuals. They are tail sections about 10 to

Seapics

Figure 47.1
The palolo worm. Gametes are packed into segments of the tail section (in blue).

20 cm long that break from adults after they become filled with eggs or sperm. The adults are polychaete annelids that live in burrows in coral reefs of the Samoan and Fiji islands **(Figure 47.1).** These annelids develop tail segments once a year, just after the October full moon. On the seventh night following the full moon, the tails break off and swim to the surface, where—if Samoan gourmets do not net them first—they disintegrate and release eggs and sperm by the millions, turning the water of the lagoon milky. The anterior ends of the worms, safe in their burrows, will survive to produce tails for next year's mating frenzy. A biological clock in the worms, timed by periods of moonlight, precisely sets both the appearance of the mating swarm and indirectly, the appearance of the islanders with their boats.

The swarm of the palolo worms is only one of many adaptations that accomplish mating in animals. For animals that reproduce by eggs and sperm, the adaptations are as diverse as the number of species on Earth. This diversity allows individuals of the same species to find each other and unite eggs and sperm. Within the diversity, however, are underlying patterns that are shared by all animals.

Both the underlying patterns and the diversity of animal reproduction are the subjects of this chapter. We also discuss the development of eggs and sperm, and the union of egg and sperm that begins the development of a new individual. The next chapter continues with the events of development after eggs and sperm have united.

47.1 Animal Reproductive Modes: Asexual and Sexual Reproduction

Reproduction is part of a life cycle in which individuals grow, develop, and reproduce according to instructions encoded in DNA. Rather than survival of the individual, reproduction is the means of passing on the individual's genes to new generations of the species. As such, it is among the most vital functions of living organisms.

Two basic modes of reproduction operate in the animal kingdom. In **asexual reproduction,** a single individual gives rise to offspring without fusion of **gametes** (egg and sperm); that is, there is no genetic input from another individual. In **sexual reproduction,** male and female parents produce offspring through the union of egg and sperm generated by meiosis (meiosis is discussed in Chapter 11).

Asexual Reproduction Produces Offspring with Genes from Only One Individual

Many aquatic invertebrates and some terrestrial annelids and insects reproduce asexually. Asexual reproduction is rare among vertebrates. In asexual reproduction, one to many cells of a parent's body develop directly into a new individual. In a few animals that undergo asexual reproduction, the cells taking part are genetically varied products of meiosis, but in most they are products of mitosis. The offspring therefore are genetically identical to one another and to the parent: in other words, they are genetic clones of the parent. For this reason, asexual reproduction of this kind is also called *clonal reproduction*.

Genetic uniformity of offspring can be advantageous in environments that remain stable and uniform. Asexual reproduction tends to preserve gene combinations producing individuals that are successful in such environments. Further, individuals do not have to expend energy to produce gametes or find a mate. Asexual reproduction can also bring reproductive advantages to individuals living in sparsely settled populations, or to sessile animals, which cannot move from place to place.

Asexual reproduction involving mitosis occurs in animals by three basic mechanisms: *fission, budding,* and *fragmentation*. In **fission,** the parent separates into two or more offspring of approximately equal size. Planarians (flatworms), for instance, reproduce asexually by fission; depending on the species, they may divide by transverse or longitudinal fission. In **budding,** a new individual grows and develops while attached to the parent. Sponges, tunicates, and some cnidarians reproduce asexually by this mechanism. The offspring may break free from the parent, or remain attached to form a *colony*. In the cnidarian *Hydra,* for example, an offspring buds and grows from one side of the parent's body and then detaches to become a separate individual **(Figure 47.2).** Among many corals, the buds remain attached when their growth is complete, forming colonies of thousands of interconnected individuals. In **fragmentation,** pieces separate from a parent's body and develop *(regenerate)* into new individuals. Many species of cnidarians, flatworms, annelids, and some echinoderms can reproduce by fragmentation.

Some animals produce offspring by the growth and development of an egg without fertilization. The offspring may be haploid or diploid depending on the

species. This form of asexual reproduction is called **parthenogenesis** (*parthenos* = virgin; *genesis* = birth). Because the egg from which a parthenogenetic offspring is produced derives from meiosis in the female parent, the offspring are not genetically identical to the parent or to each other. (How chromosome segregation and genetic recombination during meiosis produces gametes with gene combinations different from the parent is described shortly.)

Parthenogenesis occurs in some invertebrates, including certain aphids, water fleas, bees, and crustaceans. In bees, for instance, haploid male drones are produced parthenogenetically from unfertilized eggs produced by reproductive females (queens) while new queens and sterile workers develop from fertilized eggs. Parthenogenesis also occurs in some vertebrates, for example, in certain fish, salamanders, amphibians, lizards, and turkeys. In these animals, an egg, produced by meiosis, typically doubles its chromosomes to produce a diploid cell that begins development. In single-sex species where females have two identical sex chromosomes, the offspring are female, whereas in single-sex species where males have two identical sex chromosomes, the offspring are male. For instance, all whiptail lizards *(Cnemidophorus)* are females, produced solely by parthenogenesis. Interestingly, these females go through the motions of mating and copulation with each other.

Sexual Reproduction Generates Diversity among Offspring

Animals reproduce sexually by the union of sperm and eggs produced by meiosis. The overriding advantage of sexual reproduction is the generation of genetic diversity among offspring. This diversity increases the chance that, in a changing environment, at least some offspring will grow and reproduce successfully. Diversity also increases the chance that offspring may be able to live and reproduce in environments previously unoccupied by the species.

Two mechanisms that are part of meiosis give rise to the genetic diversity in eggs and sperm: *genetic recombination* (see Section 11.2) and the *independent assortment* of chromosomes of maternal and paternal origin (see Section 12.1). Genetic recombination mixes the alleles of parents into new combinations within chromosomes; independent assortment selects random combinations of maternal and paternal chromosomes to be placed in gamete nuclei. Additional variability is generated at fertilization when eggs and sperm from genetically different individuals fuse together at random to initiate the development of new individuals. To these sources of variability are added random DNA mutations, which are the ultimate source of variability for both sexual and asexual reproduction.

The disadvantages of sexual reproduction include the expenditure of energy and raw materials in producing gametes and finding mates. The need to find mates can also expose animals to predation and takes time from finding food and shelter and caring for existing offspring.

Dr. Stanley Flegler/Visuals Unlimited

Figure 47.2
Asexual reproduction by budding in *Hydra* (colorized SEM).

With these advantages and disadvantages in mind, we now turn to the mechanisms of sexual reproduction, which include both cellular and whole-organism activities. We begin with the cellular mechanisms in the next section.

Study Break

What are the advantages and disadvantages of asexual reproduction? Of sexual reproduction?

47.2 Cellular Mechanisms of Sexual Reproduction

The cellular mechanisms of sexual reproduction are **gametogenesis**, the formation of male and female gametes, and **fertilization**, the union of gametes that initiates development of a new individual. The pairing of a male and a female for the purpose of sexual reproduction is **mating.**

Gametogenesis Involves the Coordinated Events of Meiosis and Sperm and Egg Development

Gametes in most animals form from **germ cells,** a cell line that is set aside early in embryonic development and remains distinct from the other, **somatic cells** of the body. During development, the germ cells collect in specialized gamete-producing organs, the **gonads**—the

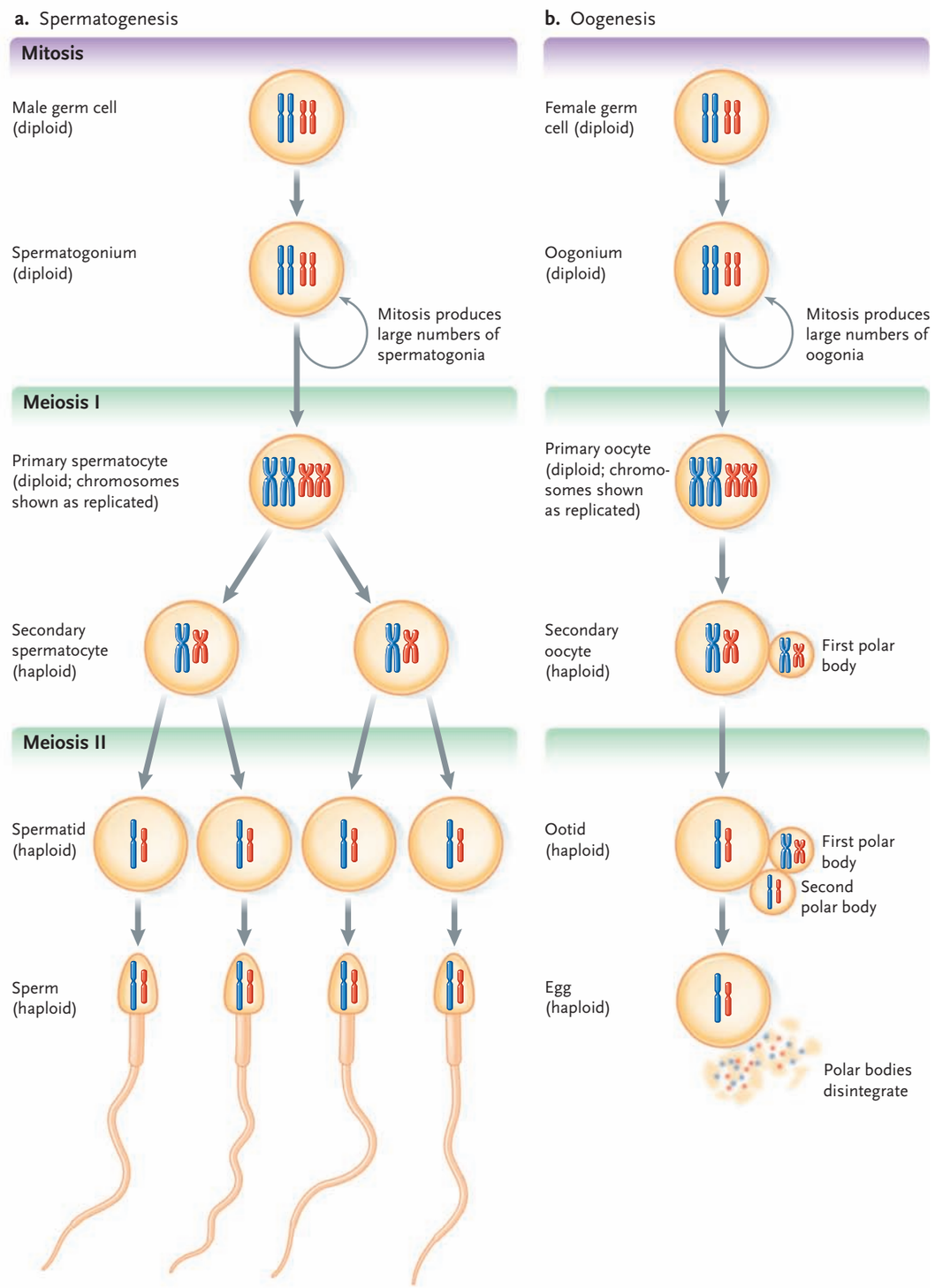


Figure 47.3
The mitotic and meiotic divisions producing eggs and sperm from germ cells. **(a)** Spermatogenesis. **(b)** Oogenesis. The first polar body may or may not divide, depending on the species, so that either two or three polar bodies may be present at the end of meiosis. Two are shown in this diagram.

testes (singular, *testis*) in males and **ovaries** in females. Mitotic divisions of the germ cells produce **spermatogonia** in males and **oogonia** in females; these are the cells that enter meiosis to give rise to gametes **(Figure 47.3).** In some animals, the germ cells also give rise to families of cells that assist gamete development.

Meiosis reduces the number of chromosomes from the diploid level characteristic of somatic cells of the species, in which there are two copies of each chromosome, to the haploid level of gametes, in which there is one copy of each chromosome. The fusion of a haploid sperm and egg during fertilization restores the diploid number of chromosomes and produces a **zygote**, the first cell of a new individual.

During the meiotic divisions, the developing gametes are known as **spermatocytes** or **oocytes;** at the end of meiosis they become *spermatids* or *ootids*. When meiosis is complete, the haploid cells develop into mature sperm cells, also called **spermatozoa** (singular, *spermatozoon*) or simply *sperm;* and egg cells, also called **ova** (singular, *ovum*) or simply *eggs*. The process of producing sperm is called **spermatogenesis** and the process of producing eggs is called **oogenesis.** The sperm of most animal species are motile cells, driven through a watery medium by the whiplike beating of a flagellum that extends from the posterior end of the cell. The eggs of all animals are nonmotile cells, typically much larger than sperm of the same species.

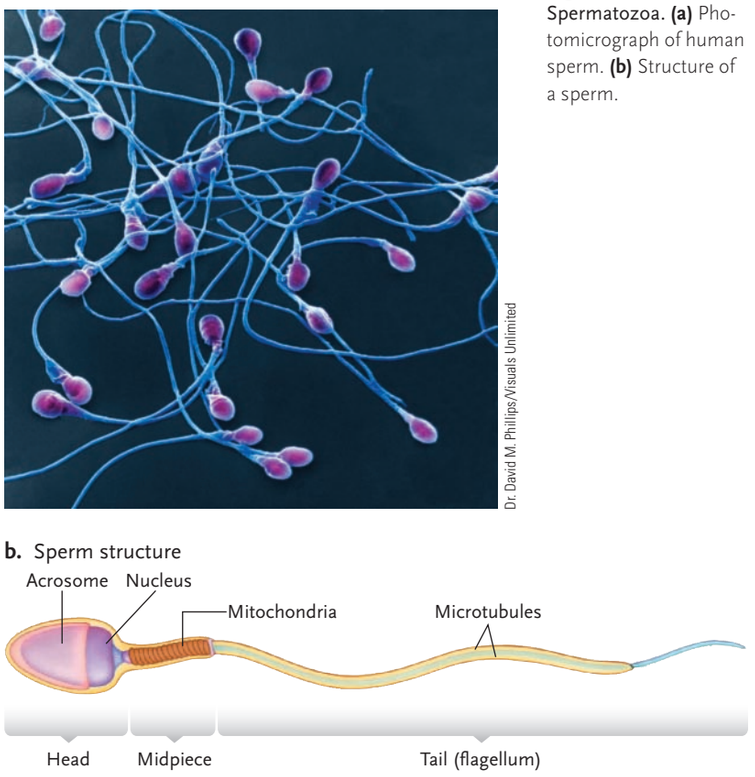


Figure 47.4
Spermatozoa. **(a)** Photomicrograph of human sperm. **(b)** Structure of a sperm.

Spermatogenesis. The events of spermatogenesis produce haploid cells, specialized to deliver their nuclei to eggs of the same species. Two meiotic divisions produce four haploid spermatids (see Figure 47.3a), which develop into mature sperm **(Figure 47.4).** During maturation, most of the cytoplasm is lost, except for mitochondria, which surround the base of a flagellum. These mitochondria produce the ATP used as the energy source for flagellar beating. At the head of the sperm, a specialized secretory vesicle, the **acrosome,** forms a cap over the nucleus. The acrosome contains enzymes and other proteins that help the sperm attach to and penetrate the surface coatings of an egg of the same species.

Oogenesis. In oogenesis, only one of the cell products of meiosis develops into a functional egg, which retains almost all of the parent cell's cytoplasm. The other products form nonfunctional cells called **polar bodies** (see Figure 47.3b). The unequal cytoplasmic divisions concentrate nutrients and other molecules required for development in the egg. In most species, the polar bodies eventually disintegrate and do not contribute to fertilization or embryonic development.

The oocytes of most animals do not actually complete meiosis until fertilization. For example, mammals follow a complex pattern in which oocytes stop developing at the end of the first meiotic prophase, within a few weeks after a female is born. The oocytes remain in the ovary at this stage until the female is sexually mature. In humans, some oocytes may remain in prophase of the first meiotic division for perhaps 50 years.Then, one to several oocytes advance to the metaphase of the second meiotic division and are released from the ovary at intervals ranging from days to months, or at certain seasons, depending on the species. As in other animals, meiosis is completed at fertilization to produce the fully mature egg **(Figure 47.5).** Mature eggs are the largest cell type of an animal species.

An egg typically has specialized features, which include stored nutrients required for at least the early stages of embryonic development; egg coats of one or more kinds, which protect the egg from mechanical injury and infection and, in some species, protect the embryo after fertilization; and mechanisms that prevent the egg from being fertilized by more than one sperm cell (discussed shortly).

Egg coats are surface layers added during oocyte development or fertilization in many species. The **vitelline coat,** called the **zona pellucida** in mammals (see Figure 47.5) is a gel-like matrix of proteins, glycoproteins, or polysaccharides immediately outside of the plasma membrane of the egg cell. Insect eggs have additional outer protein coats that form a hard, water-

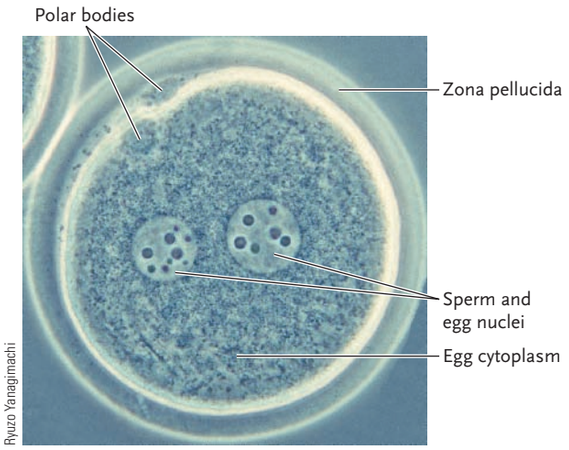


Figure 47.5
A mature hamster egg that has been fertilized.

impermeable layer for preventing desiccation. Amphibians and some echinoderms instead have an additional outer egg jelly layer (see Figure 47.8) that protects the egg from drying.

In birds, reptiles, and one group of egg-laying mammals, the **monotremes**, the egg white, a thick solution of proteins, surrounds the vitelline coat. Outside the white is the *shell* of the egg, flexible and leathery in reptiles and mineralized and brittle in birds. Both the egg white and the shell are added while the egg—fertilized or not—is in transit through the **oviduct**, the tube through which the egg moves from the ovary to the outside of the body. In mammals, the egg is surrounded by **follicle cells** during its development. These cells, which grow from ovarian tissue, nourish the developing egg. They also make up part of the zona pellucida while the egg is in the ovary, and remain as a protective layer after it is released.

The amount of stored nutrients in an egg varies with the animal. Mammalian eggs are microscopic, containing few stored nutrients. In mammals, the embryo develops inside the mother and is supplied with nutrients by the mother's body. In contrast, the relatively huge eggs of birds and reptiles contain all the nutrients required for complete embryonic development: the "yolk" contains the egg cell, and the "white" contains the nutrients. No matter what the size of an animal egg, however, most of the volume is cytoplasm, and the egg nucleus is microscopic or nearly so in all species.

Fertilization Requires an Internal or External Aquatic Medium

Eggs and sperm are delivered from the ovaries and testes to the site of fertilization by oviducts in females and by sperm ducts in males; in many species, external accessory sex organs participate in the delivery. **Figure 47.6** shows examples of invertebrate and vertebrate reproductive systems. The nonmotile eggs move through the oviducts on currents generated by the beating of cilia lining the oviducts, or by contractions of the oviducts or the body wall.

Depending on the species, fertilization may take place externally, in a watery medium outside the body of both parents, or internally, in a watery fluid inside the body of the female. In **external fertilization**, which occurs in most aquatic invertebrates, bony fishes, and amphibians, sperm and eggs are shed into the surrounding water. The sperm swim until they collide with an egg of the same species. The process is helped by synchronization of female and male gamete release, and by the enormous quantities of gametes released. In some animals, such as sea urchins and amphibians, the sperm are attracted to the egg by diffusible attractant molecules released by the egg.

Most amphibians, even terrestrial species such as toads, mate in an aquatic environment. Frogs typically mate by a reflex response called *amplexus*, in which the male clasps the female tightly around the body with his forelimbs **(Figure 47.7).** The embrace stimulates the female to shed a mass of eggs into the water through the *cloaca*—the cavity in reptiles, birds, amphibians, and many fishes into which both the intestinal and genital tracts empty. As the eggs are released, they are fertilized by sperm released by the male.

Internal fertilization takes place in invertebrates such as annelids, some arthropods, and some mollusks, and in vertebrates such as reptiles, birds, mammals, some fishes, and some salamanders. In these animals, the sperm are released by the male close to or inside the entrance of the reproductive tract of the female. The sperm swim through fluids in the reproductive tract until they reach and fertilize each egg. In some species, molecules released by the egg attract the sperm to its outer coats. The physical act involving the introduction of the male's accessory sex organ (for example, penis) into a female's accessory sex organ (for example, vagina) to accomplish internal fertilization is known as **copulation**. Internal fertilization makes terrestrial life possible by providing the aquatic medium required for fertilization inside the female's body without the danger of gametes drying by exposure to the air.

Sharks and rays have evolved a form of internal fertilization in which the male uses a pair of modified pelvic fins as accessory sex organs to channel sperm directly inside the female's cloaca. Male reptiles, birds, and mammals also have accessory sex organs that place sperm directly inside the reproductive tract of females, where fertilization takes place. In reptiles and birds, sperm fertilize eggs as they are released from the ovary and travel through the oviducts, before the shell is added. In mammals, the male's penis delivers sperm into the female's vagina. Unlike the cloaca, which has both sexual and excretory functions, the vagina is specialized for reproduction. Fertilization takes place when sperm swim into the tubular oviducts containing the eggs.

Fertilization Involves Fusion of a Sperm and an Egg, Which Activates the Egg for Development

Once a sperm touches the outer surface of an egg of the same species **(Figure 47.8a),** receptor proteins in the sperm plasma membrane bind the sperm to the vitelline coat or zona pellucida. In most animals, only a sperm from the same species as the egg can recognize and bind to the egg surface.

Species recognition is highly important in animals that carry out external fertilization, because the water surrounding the egg may contain sperm of many different species. It is less important in internal fertilization, because structural adaptations and behavioral patterns of mating usually limit sperm transfer from males to females of the same species.

Fertilization. After the initial attachment of sperm to egg, the events of fertilization proceed in rapid succession **(Figure 47.8b).** The actual attachment event triggers the **acrosome reaction**, in which enzymes contained in the acrosome are released from the sperm and digest a path through the egg coats. The sperm, with its tail still beating, follows the path until its plasma membrane touches and fuses with the plasma membrane of the egg. Fusion introduces the sperm nucleus into the egg cytoplasm and activates the egg to complete meiosis and begin development.

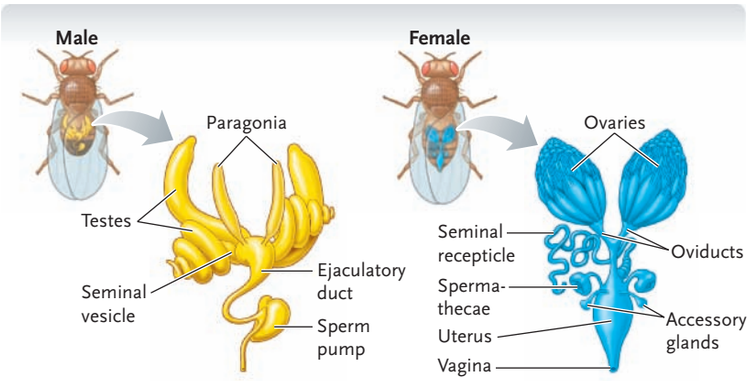
Egg Activation and Blocks to Polyspermy. Two mechanisms can prevent more than one sperm from fertilizing the egg: a *fast block* within seconds of fertilization, and a *slow block* within minutes.

In many invertebrate species, such as the sea urchin, the fusion of egg and sperm opens ion channels in the egg's plasma membrane, spreading a wave of electrical depolarization over the egg surface, much like the nerve impulse traveling along a neuron. The depolarization alters the egg plasma membrane so that it cannot fuse with any additional sperm, thereby eliminating the possibility that more than one set of paternal chromosomes enters the egg. Because it occurs within a few seconds after fertilization, the barrier set up by the wave of depolarization is called the **fast block to polyspermy.**

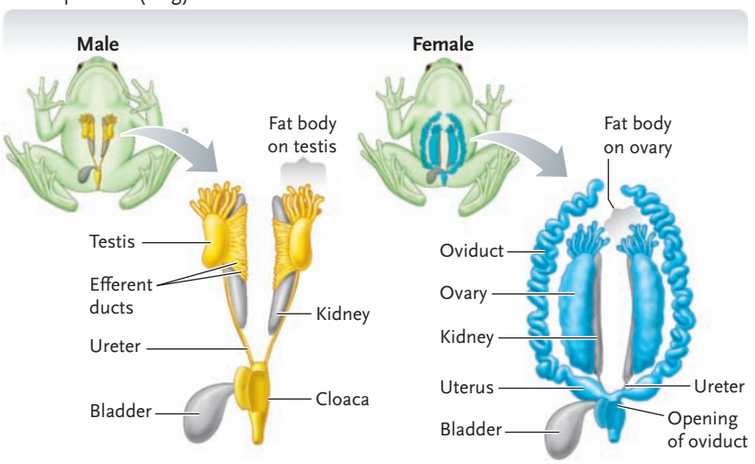
The fast block depends on a change in the egg's membrane potential from negative to positive. For example, Laurinda Jaffe, of the University of Connecticut Health Center, found that if the membrane potential of a sea urchin egg was artificially kept at a negative value, no fast block was set up, and additional sperm could fuse with the plasma membrane. If the membrane was instead kept positive before sperm contact, fertilization was entirely blocked.

In vertebrates, the wave of membrane depolarization following sperm–egg fusion is not as pronounced, and does not prevent additional sperm from fusing

a. *Drosophila* (fruit fly)



b. Amphibian (frog)



c. Mammal (cat)

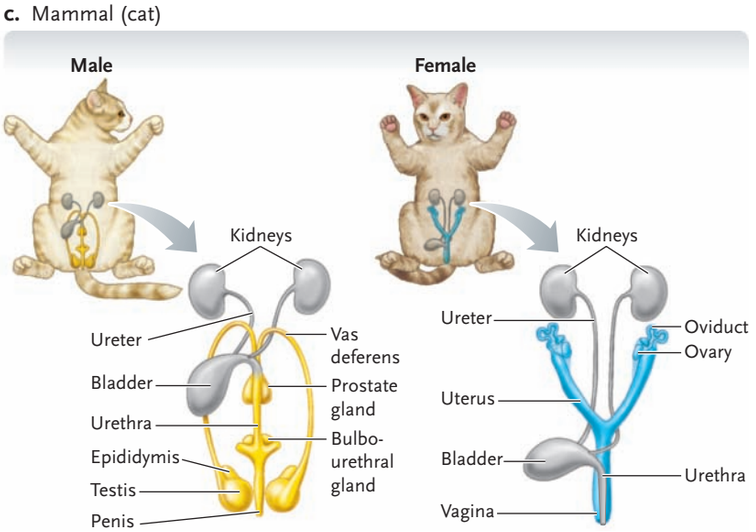


Figure 47.6
Some reproductive systems. **(a)** An insect, *Drosophila* (fruit fly). **(b)** An amphibian, a frog. **(c)** A mammal, a cat. Female systems are shown in blue, and male systems in yellow.

Hans Pfletschinger

Figure 47.7
A male leopard frog *(Rana pipiens)* clasping a female in a mating embrace known as amplexus. The tight squeeze by the male frog stimulates the female to release her eggs, which can be seen streaming from her body, embedded in a mass of egg jelly. Sperm released by the male fertilize the eggs as they pass from the female.

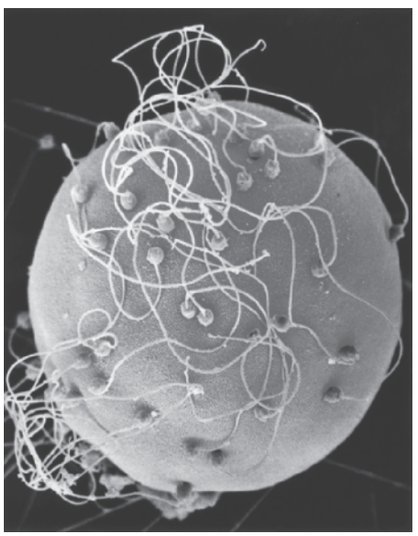
with the egg. However, any additional sperm nuclei entering the egg cytoplasm usually break down and disappear, so that only the first sperm nucleus to enter fuses with the egg nucleus.

In both invertebrates and vertebrates, fusion of egg and sperm triggers the release of stored calcium (Ca^{2+}) ions from the endoplasmic reticulum into the cytosol. The Ca^{2+} ions activate control proteins and enzymes that initiate intense metabolic activity in the fertilized egg, including a rapid increase in cellular oxidations and synthesis of proteins and other molecules.

The Ca^{2+} ions also trigger the **cortical reaction**, in which **cortical granules**, secretory vesicles just under the plasma membrane, fuse with the egg's plasma membrane and release their contents to the outside (see Figure 47.8b). Enzymes released from the cortical granules alter the egg coats within minutes after fertilization, so that no further sperm can attach and penetrate to the egg. Once this barrier, termed the **slow block to polyspermy**, is set up, no further sperm can reach the egg plasma membrane in any animal species.

The importance of Ca^{2+} to cortical granule release has been demonstrated experimentally: if Ca^{2+} is added to the cytoplasm, the granules are released in

a. Sperm adhering to egg



David M. Phillips/Visuals Unlimited

b. Steps in fertilization

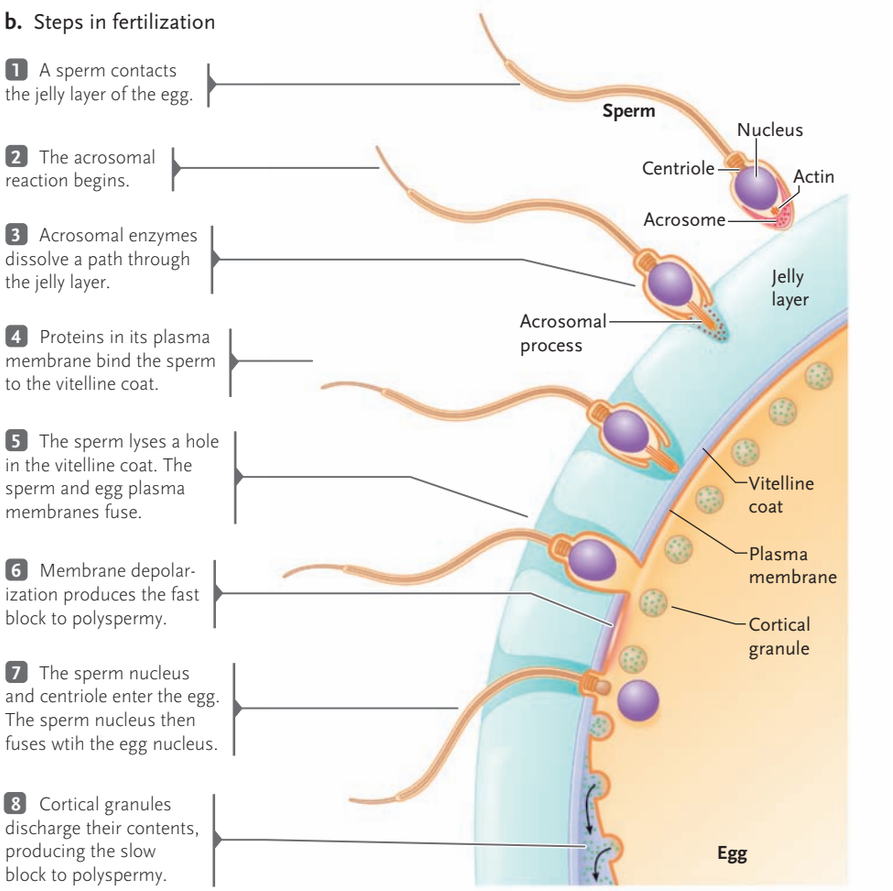


Figure 47.8
Fertilization. **(a)** Sperm adhering to the surface coat of a sea urchin egg. Of the many sperm that may initially adhere to the outer surface of an egg, usually only one accomplishes fertilization. **(b)** Steps of fertilization in a sea urchin.

unfertilized eggs; conversely, if Ca^{2+}-binding chemicals are added to the cytoplasm of unfertilized eggs, so that the Ca^{2+} concentration cannot rise, cortical granule release does not occur after fertilization.

After the sperm nucleus enters the egg cytoplasm, microtubules move the sperm and egg nuclei together in the egg cytoplasm and they fuse. The chromosomes of the egg and sperm nuclei then assemble together and enter mitosis. The subsequent, highly programmed events of embryonic development, which convert the fertilized egg into an individual capable of independent existence, are described in the next chapter.

Of the structures in a sperm cell, only the paternal chromosomes, the microtubule organizing center, and one or two centrioles (see Section 10.3 and Figure 10.11) survive in the egg. Therefore, with the exception of the microtubule organizing center and centrioles, all the cytoplasmic structures of the embryo, and of the new individual, are maternal in origin. The centrioles of the new individual are normally paternal in origin.

Reproductive Systems May Be Oviparous or Viviparous in Animals with Internal Fertilization

In animals with internal fertilization, three major types of support for embryonic development have evolved: *oviparity,* meaning egg laying; *viviparity,* meaning live bearing; and *ovoviparity,* meaning live bearing from eggs that hatch internally. **Oviparous** animals (*ovum* = egg; *parere* = to give birth to) lay eggs that contain the nutrients needed for development of the embryo outside the mother's body. Examples are insects, spiders, most reptiles, and birds. The only oviparous mammals are the *monotremes:* the echidnas and *Ornithorhynchus anatinus* (the duck-billed platypus), both of which inhabit Australia.

Viviparous animals (*vivus* = alive) retain the embryo within the mother's body and nourish it during at least early embryo development. All mammals except the monotremes are viviparous. Viviparity is seen also in all other vertebrate groups except for the crocodiles, turtles, and birds.

In viviparous animals, development of the embryo takes place in a specialized saclike organ, the **uterus** *(womb)*. Among mammals, one group, called the *placental mammals* or *eutherians,* has a specialized temporary structure, the **placenta**, that connects the embryo with the uterus. The placenta facilitates the transfer of nutrients from the mother's blood to the embryo and of wastes in the opposite direction. Humans are placental mammals. The other group of mammals, the *marsupials* or *metatherians,* originally were called nonplacental mammals because of a belief that they lacked a placenta. In fact, they do have a placenta, but it derives from a different tissue than that of eutherians and does not connect the embryo and the uterus. Instead it provides nutrients to the embryo from an attached membranous sac containing yolk for only the early stages of its development. In many metatherians, the embryo is then born and crawls over the mother's fur to reach the **marsupium,** an abdominal pouch in which it attaches to nipples and continue its development **(Figure 47.9).** Kangaroos, koalas, wombats, and opossums are marsupials.

John Cancalosi/Peter Arnold, Inc.

Figure 47.9
Developing offspring of a marsupial mammal, an opossum, attached to nipples in the marsupium (pouch) of the mother.

In some animals, such as some fishes, lizards, and amphibians, many snakes, and many invertebrates, fertilized eggs are retained within the body and the embryo develops using the nutrients provided by the egg. There is no uterus or placenta involved. When development is complete the eggs hatch inside the mother and the young are released to the exterior. Animals showing this form of reproduction are known as **ovoviviparous** animals.

Hermaphroditism Is a Variation on Sexual Reproduction

Some animals have evolved modified mechanisms that they use as their normal sexual reproduction process. One of these mechanisms is **hermaphroditism** (from *Hermes* + *Aphrodite,* a Greek god and goddess), in which both mature egg-producing and mature sperm-producing tissue is present in the same individual. That is, hermaphroditic individuals are able to produce both eggs and sperm. Most flatworms, earthworms, land snails, and numerous other invertebrates are hermaphroditic; in humans and other mammals, hermaphroditism is a rare, abnormal condition.

Most hermaphroditic animals do not fertilize themselves. In those animals, self-fertilization is prevented by anatomical barriers that prevent individuals from introducing sperm into their own body, or by mechanisms in which the egg and sperm mature at different times. The prevention of self-fertilization maintains the genetic variability of sexual reproduction.

Hermaphroditism takes two forms: **simultaneous hermaphroditism**, in which individuals develop functional ovaries and testes at the same time, and

a.

Robin Chittenden; Frank Lane Picture Agency/Corbis

b. Sex organs

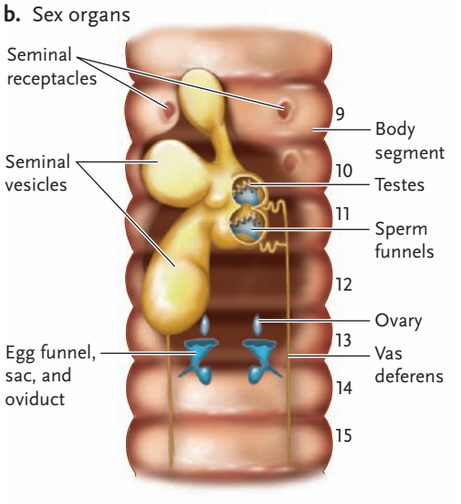


Figure 47.10
Simultaneous hermaphroditism in the earthworm. **(a)** Copulation by a mating pair of earthworms, in which each earthworm releases sperm that fertilizes eggs in its partner. **(b)** Sex organs in the earthworm.

sequential hermaphroditism, in which individuals change from one sex to the other. The two earthworms shown in **Figure 47.10** provide a common example of simultaneous hermaphroditism. The only known vertebrate simultaneous hermaphrodites are hamlets (genus *Hypoplectrus*), a group of predatory sea basses. Sequential hermaphroditism is seen among a number of invertebrates (for example, the gastropod, the slipper shell *Crepidula fornicata*) and some ectothermic vertebrates, notably fishes (for example, the clownfish, genus *Amphiprion*). In some species the initial sex is male (as with the slipper shell and the clownfish), and in others it is female.

Study Break

1. What are egg coats, and what is their function? What egg coats do mammalian and bird eggs have?
2. How is the slow block to polyspermy brought about?

47.3 Sexual Reproduction in Humans

Except for structural details, human reproduction is typical of that of eutherian (placental) mammals. Internally, these mammals have a pair of gonads, either ovaries or testes. The gonads have a dual function in mammals, as they do in all vertebrates: they both produce gametes and secrete hormones responsible for sexual development and mating behavior (see Section 40.4). Males have ducts that carry sperm from the testes to the exterior. Females have an oviduct that leads from each ovary to the uterus, in which fertilized eggs implant and proceed through embryonic development. Nutrients from the mother and wastes from the embryo are exchanged through the placenta. After birth, the newborn offspring is nourished with milk secreted by the mother's mammary glands.

In this section we survey reproductive structures and functions in humans as representative of eutherian mammals. Our story of human development continues in the next chapter, which traces the process from fertilization to birth.

Human Female Sexual Organs Function in Oocyte Production, Fertilization, and Embryonic Development

Human females have a pair of ovaries suspended in the abdominal cavity **(Figure 47.11).** An oviduct leads from each ovary to the uterus, which is a hollow, saclike organ with walls containing smooth muscle. The uterus is lined by the endometrium, formed by layers of connective tissue with embedded glands and richly supplied with blood vessels. If an egg is fertilized and begins development, it must implant in the endometrium to continue developing. The lower end of the uterus, the **cervix**, opens into a muscular canal, the **vagina**, which leads to the exterior. Sperm enter the female reproductive tract via the vagina and, at birth, the baby passes from the uterus to the outside through the vagina.

At the birth of a female, each ovary contains about 1 million oocytes, arrested at the end of the first meiotic prophase. Of these oocytes, about 200,000 to 400,000 survive until a female becomes sexually mature; about 400 are **ovulated**—released into the oviducts as immature eggs—during a woman's lifetime. The egg is released into the abdominal cavity and pulled into the nearby oviduct by the current produced by the beating of the cilia lining the oviduct. The cilia also propel the egg through the oviduct and into the uterus. Fertilization of the egg occurs in the oviduct.

The external female sex organs, collectively called the **vulva**, surround the opening of the vagina. Two folds of tissue, the **labia minora**, run from front to rear on either side of the opening to the vagina. These folds are partially covered by a pair of fleshy, fat-padded

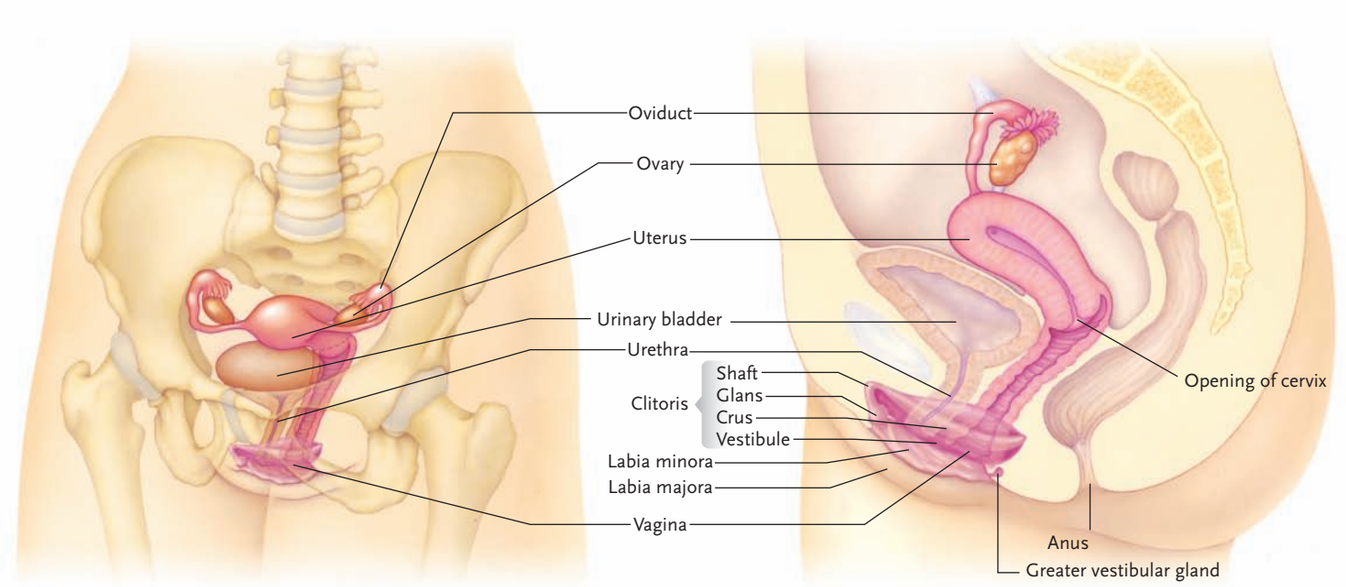


Figure 47.11
The reproductive organs of a human female.

folds, the **labia majora**, which also run from front to rear on either side of the vagina. At the anterior end of the vulva, the labia minora join to partly cover the head of the **clitoris.** The rest of the clitoris is within the body. The clitoris contains erectile tissue and has the same embryonic origins as the penis. A pair of **greater vestibular glands**, with openings near the entrance to the vagina, secretes a mucus-rich fluid that lubricates the vulva. The opening of the urethra, which conducts urine from the bladder, is located between the clitoris and the vaginal opening. Most nerve endings associated with erotic sensations are concentrated in the clitoris, in the labia minora, and around the opening of the vagina. When a human female is born, a thin flap of tissue, the **hymen**, partially covers the opening of the vagina. This membrane, if it has not already been ruptured by physical exercise or other disturbances, is broken by the first sexual intercourse.

Ovulation in Human Females Occurs in a Monthly Cycle

Reproduction in human females is under neuroendocrine control, involving complex interactions between the hypothalamus, pituitary, ovaries, and uterus. Under this control, approximately every 28 days from puberty to menopause, a female releases an egg from one of her ovaries. The cyclic events in the ovary leading to ovulation are known as the **ovarian cycle.** This cycle is coordinated with the **uterine cycle**, or **menstrual cycle** (*menstruus* = monthly), events in the uterus that prepare it to receive the egg if fertilization occurs.

The Ovarian Cycle. The ovarian cycle produces a mature egg **(Figure 47.12).** The starting point for the cycle is a primary oocyte in prophase of meiosis division I. The beginning of the cycle is triggered by an increase in the release of **gonadotropin-releasing hormone (GnRH)** by the hypothalamus. This hormone stimulates the pituitary to release **follicle-stimulating hormone (FSH)** and **luteinizing hormone (LH)** into the bloodstream **(Figure 47.13a).** FSH stimulates 6 to 20 primary oocytes in the ovaries to be released from prophase of meiosis I and continue through the meiotic divisions. As the primary oocytes develop into secondary oocytes—which arrest in metaphase of meiosis II—they become surrounded by cells that form a **follicle** (day 2 of the cycle; **Figure 47.13b**). During this follicular phase, the follicle grows and develops and, at its largest size, becomes filled with fluid and may reach 12 to 15 mm in diameter. Usually only one follicle develops to maturity with release of the egg (secondary oocyte) by ovulation. If two or more follicles develop and their eggs are ovulated, multiple births can result.

As the follicle enlarges, FSH and LH interact to stimulate the follicular cells to secrete **estrogens** (female sex hormones), primarily **estradiol** (see Section 40.4) **(Figure 47.13c).** Initially, the estrogens are secreted in low amounts; at this level, the estrogens have a negative feedback effect on the pituitary, inhibiting its secretion of FSH. As a result, FSH secretion declines briefly. However, estrogen secretion increases steadily, and its level peaks at about 12 days after follicle development begins (day 14 of cycle). The high estrogen level now has a positive feedback effect on the hypothalamus and pituitary, increasing the release of GnRH and stimulating the pituitary to release a burst of FSH and LH. The increased estrogen levels also convert the mucus secreted by the uterus to a thin and watery consistency, making it easier for sperm to swim through the uterus.

The burst in LH secretion stimulates the follicle cells to release enzymes that digest away the wall of the

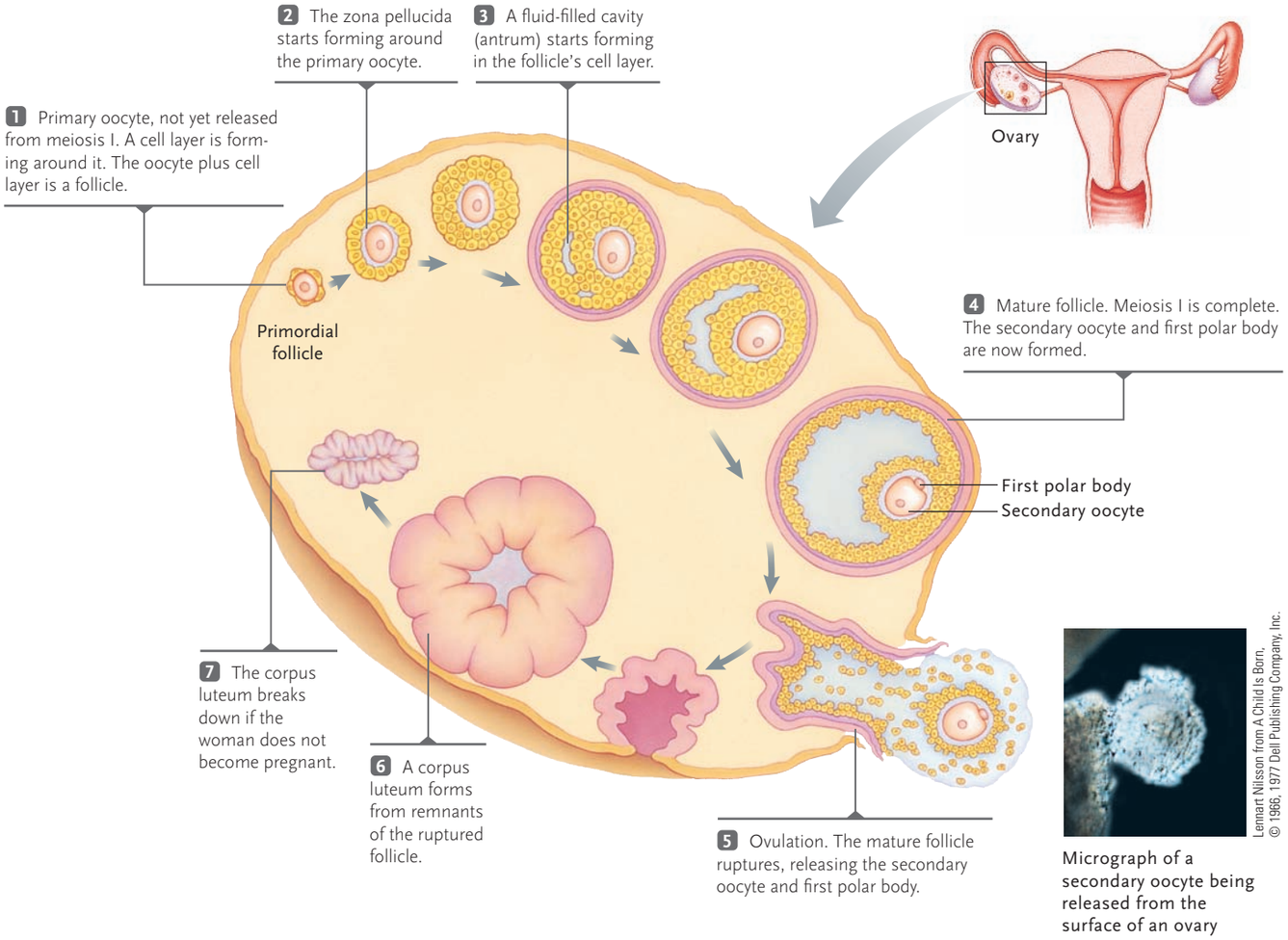


Figure 47.12
The growth of a follicle, ovulation, and formation of the corpus luteum in a human ovary.

follicle, causing it to burst and release the egg (see Figure 47.12); this is ovulation. LH also initiates the last phase of the menstrual cycle, the *luteal phase*. That is, LH causes the follicle cells remaining at the surface of the ovary to grow into an enlarged, yellowish structure, the **corpus luteum** (*corpus* = body; *luteum* = yellow; see Figure 47.12). Acting as an endocrine gland, the corpus luteum secretes several hormones: estrogens, large quantities of **progesterone**, and **inhibin**. Progesterone, a female sex hormone, stimulates growth of the uterine lining and inhibits contractions of the uterus. Both progesterone and inhibin have a negative feedback effect on the hypothalamus and pituitary. Progesterone inhibits the secretion of GnRH. Without GnRH, the pituitary does not release FSH and LH. FSH secretion from the pituitary is also inhibited directly by inhibin. The fall in FSH and LH levels diminishes the signal for follicular growth, and no new follicles begin to grow in the ovary.

If fertilization does not occur, the corpus luteum gradually degenerates as cells are phagocytized and blood supply is cut off. By about 10 days after ovulation, little tissue remains, meaning that estrogen, progesterone, and inhibin are no longer secreted. In the absence of progesterone, *menstruation* begins (described in the next section). As progesterone and inhibin levels decrease, FSH and LH secretion is no longer inhibited, and a new monthly cycle begins.

The Uterine (Menstrual) Cycle. The hormones that control the ovarian cycle also control the uterine (menstrual) cycle **(Figure 47.13d),** keeping the processes connected physiologically. Day 0 of the monthly cycle in the figure is the beginning of follicular development in the ovary (see Figure 47.13b); in the uterus, this correlates with the time at which menstrual flow begins.

Menstrual flow results from the breakdown of the endometrium, which releases blood and tissue breakdown products from the uterus to the outside through the vagina. When the flow ceases, at day 4 to 5 of the cycle, the endometrium begins to grow again; this is the proliferative phase. As the endometrium gradually thickens, the oocytes in both ovaries begin to develop further, eventually leading to ovulation at about 14 days after the beginning of the cycle, as already described.

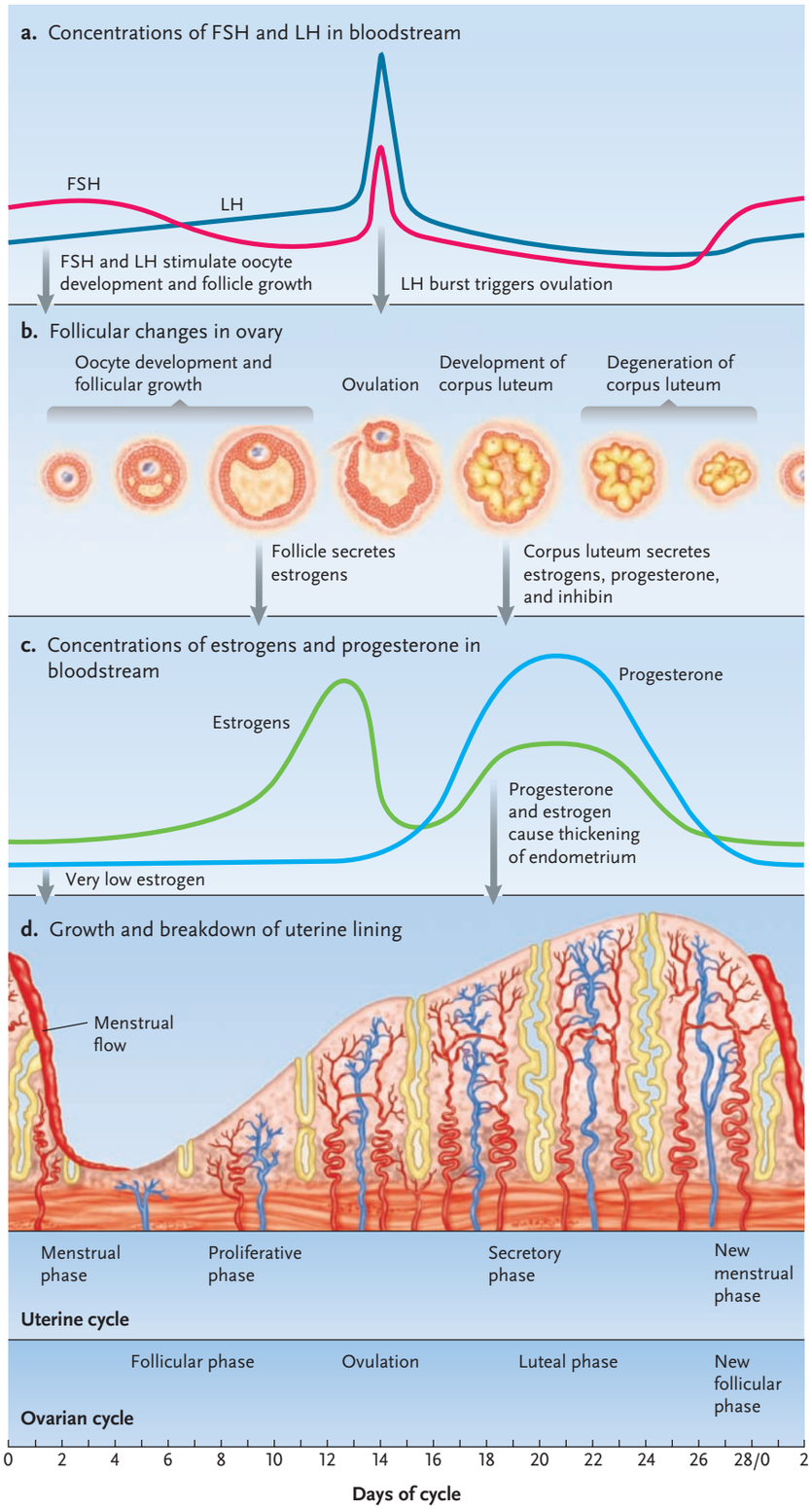


Figure 47.13

The ovarian and uterine (menstrual) cycles of a human female. **(a)** The changing concentrations of FSH and LH in the bloodstream, triggered by GnRH secretion by the hypothalamus. **(b)** The cycle of follicle development, ovulation, and formation of the corpus luteum in the ovary. **(c)** The concentrations of estrogens and progesterone in the bloodstream. **(d)** The growth and breakdown of the uterine lining. The days of the monthly cycle are given in the scale at the bottom of the diagram.

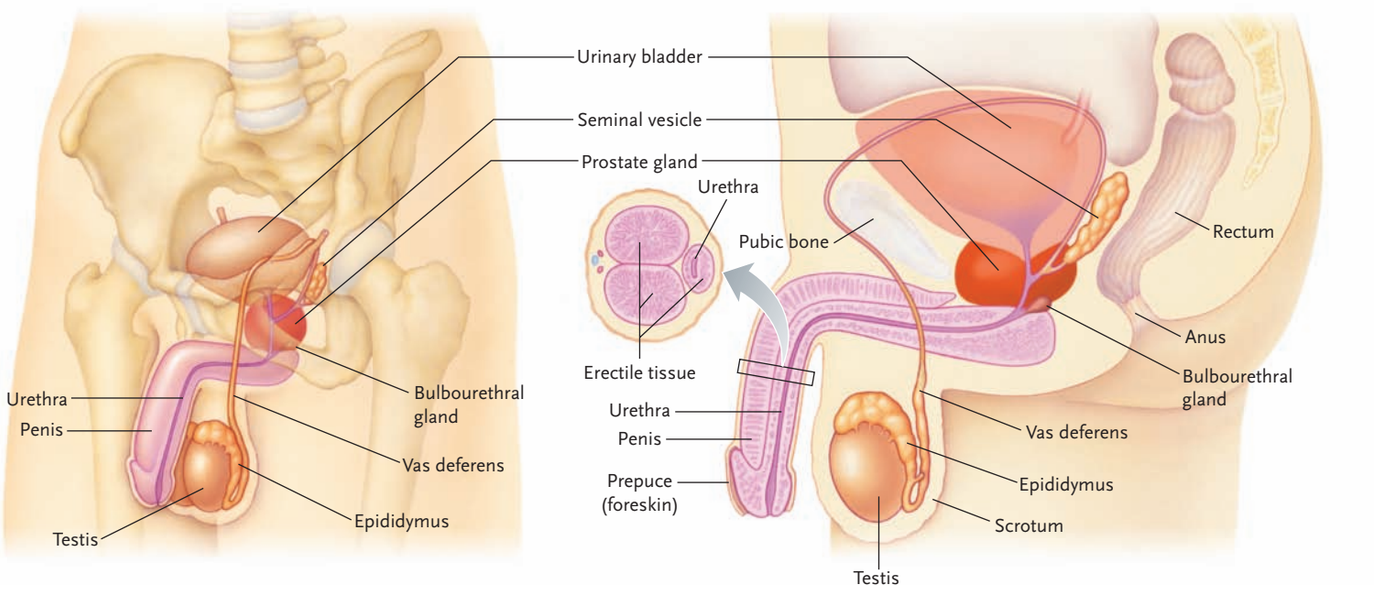


Figure 47.14
The reproductive organs of a human male.

If fertilization does not take place, the uterine lining continues to grow for another 14 days after ovulation; this is the secretory phase. At the end of that time, the absence of progesterone results in the contraction of arteries supplying blood to the uterine lining, shutting down the blood supply and causing the lining to disintegrate. The menstrual flow begins. Contractions of the uterus, no longer inhibited by progesterone, help expel the debris. Prostaglandins released by the degenerating endometrium add to the uterine contractions, making them severe enough to be felt as the pain of "cramps," and also sometimes causing other effects such as nausea, vomiting, and headaches.

Menstruation—the menstrual flow—occurs only in human females and our closest primate relatives, gorillas and chimpanzees. In other mammals, the uterine lining is completely reabsorbed if a fertilized egg does not implant during the period of reproductive activity. The uterine cycle in those mammals is called the *estrous* cycle.

Human Male Sexual Organs Function in Sperm Production and Delivery

Organs that produce and deliver sperm make up the male reproductive system **(Figure 47.14).** The testes are located outside the abdominal cavity; sperm produced by the testes pass through tubules that enter the abdominal cavity and join with the urethra, the duct that carries urine from the bladder to an opening at the tip of the penis.

Male Reproductive Structures. Human males have a pair of testes, suspended in the baglike **scrotum.** Suspension in the scrotum keeps the testes cooler than the body core, at a temperature that provides an optimal environment for sperm development. Some land mammals such as elephants and monotremes have relatively low body temperatures and have internal testes, that is, testes carried within the body. Marine mammals such as whales and dolphins also have internal testes despite relatively high body temperatures. In these animals particular blood vessel networks serve to lower the temperature in the testes to allow for normal function. A testis is packed with about 125 meters of **seminiferous tubules,** in which sperm proceed through all the stages of spermatogenesis **(Figure 47.15).** The entire process, from spermatogonium to sperm, takes about 9 to 10 weeks. The testes produce about 130 million sperm each day.

Supportive cells called **Sertoli cells** completely surround the developing spermatocytes in the seminiferous tubules. They supply nutrients to the spermatocytes and seal them off from the body's blood supply. Other cells located in the tissue surrounding the developing spermatocytes, the **Leydig cells,** produce the male sex hormones, known as **androgens,** particularly **testosterone** (see Figure 47.15).

Mature sperm flow from the seminiferous tubules into the **epididymis,** a coiled storage tubule attached to the surface of each testis. Rhythmic muscular contractions of the epididymis move the sperm into a thick-walled, muscular tube, the **vas deferens** (plural, *vasa deferentia*), which leads into the abdominal cavity. Just below the bladder, the vasa deferentia empty into the urethra. During ejaculation, muscular contractions force the sperm into the urethra and out of the penis. The sperm are activated and become motile as they come in contact with alkaline secretions added to the ejaculated fluid by accessory glands.

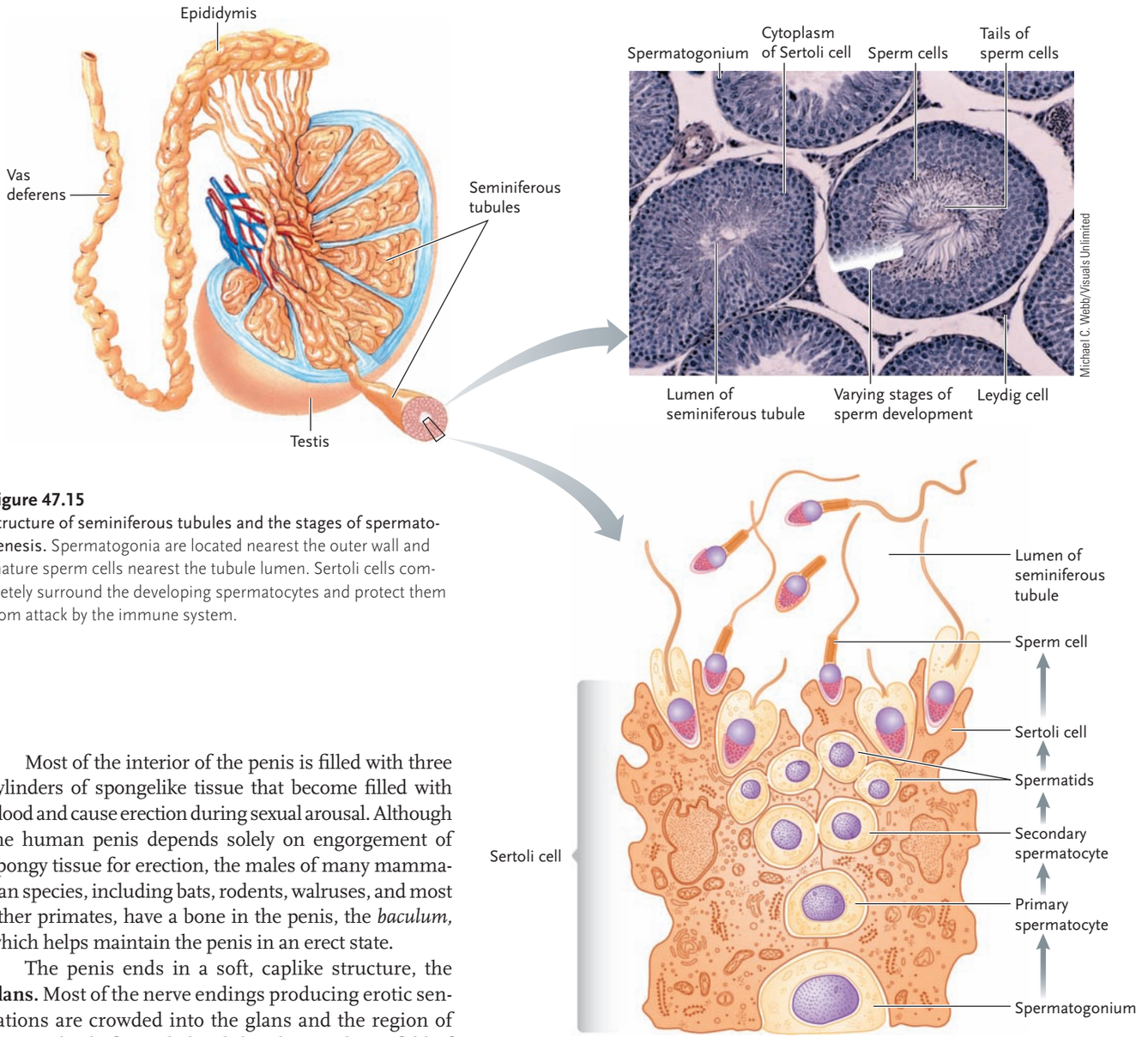


Figure 47.15
Structure of seminiferous tubules and the stages of spermatogenesis. Spermatogonia are located nearest the outer wall and mature sperm cells nearest the tubule lumen. Sertoli cells completely surround the developing spermatocytes and protect them from attack by the immune system.

Most of the interior of the penis is filled with three cylinders of spongelike tissue that become filled with blood and cause erection during sexual arousal. Although the human penis depends solely on engorgement of spongy tissue for erection, the males of many mammalian species, including bats, rodents, walruses, and most other primates, have a bone in the penis, the *baculum,* which helps maintain the penis in an erect state.

The penis ends in a soft, caplike structure, the **glans.** Most of the nerve endings producing erotic sensations are crowded into the glans and the region of the penile shaft just behind the glans. A loose fold of skin, the **prepuce** or **foreskin,** covers the glans (see Figure 47.14). In many cultures the prepuce is removed for hygienic, religious, or other ritualistic reasons by the procedure called **circumcision** ("around cut"). In 2007, the World Health Organization stated that male circumcision is an important strategy to prevent heterosexually acquired HIV infection in males.

Accessory Glands and the Semen. About 150 million to 350 million sperm are released in a single ejaculation. Before they leave the body, these cells are mixed with the secretions of several accessory glands, forming the fluid known as **semen.** In humans, about two-thirds of the volume is produced by a pair of **seminal vesicles,** which secrete a thick, viscous liquid, the **seminal fluid,** into the vasa deferentia near the point where they join with the urethra. The seminal fluid contains prostaglandins that, when ejaculated into the female, trigger contractions of the female reproductive tract that help move the sperm into and through the uterus.

The large **prostate gland,** which surrounds the region where the vasa deferentia empty into the urethra, adds a thin, milky fluid to the semen. The alkaline prostate secretion, which makes up about one-third of the volume of the semen, raises the pH of the semen, and of the vagina, to about pH 6, the level of acidity best tolerated by sperm. The raised pH also activates motility of the sperm. As part of the prostate secretion, a fast-acting enzyme converts the semen to a thick gel when it is first ejaculated. The thickened

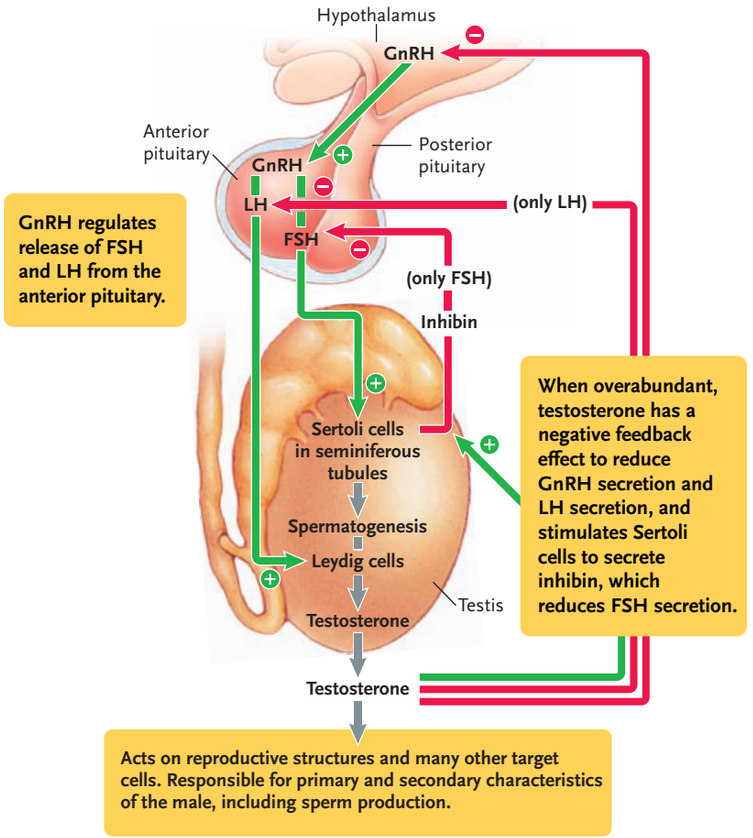


Figure 47.16
Hormonal regulation of reproduction in the male, and the negative feedback systems controlling hormone levels.

consistency helps keep the semen from draining from the vagina when the penis is withdrawn. A second, slower-acting enzyme in the prostate secretion then gradually breaks down the semen clot and releases the sperm to swim freely in the female reproductive tract.

Finally, a pair of **bulbourethral glands** secretes a clear, mucus-rich fluid into the urethra before and during ejaculation. This fluid lubricates the tip of the penis and neutralizes the acidity of any residual urine in the urethra. In total, the secretions of the accessory glands make up more than 95% of the volume of semen; less than 5% is sperm.

Hormones Also Regulate Male Reproductive Functions

Many of the hormones regulating the menstrual cycle, including GnRH, FSH, LH, and inhibin, also regulate male reproductive functions. Testosterone, secreted by the Leydig cells in the testes, also plays a key role **(Figure 47.16).**

In sexually mature males, the hypothalamus secretes GnRH in brief pulses every 1 to 2 hours. The GnRH, in turn, stimulates the pituitary to secrete LH and FSH. LH stimulates the Leydig cells to secrete testosterone, which stimulates sperm production and controls the growth and function of male reproductive structures. FSH stimulates Sertoli cells to secrete a protein and other molecules that are required for spermatogenesis.

The concentrations of these hormones are maintained by negative feedback mechanisms. If the concentration of testosterone falls in the bloodstream, the hypothalamus responds by increasing GnRH secretion. If the concentration of testosterone rises too high, the overabundance inhibits GnRH secretion by the hypothalamus and LH secretion by the anterior pituitary. An overabundance of testosterone also stimulates Sertoli cells to secrete inhibin, which inhibits FSH secretion by the anterior pituitary. As a result, testosterone secretion by the Leydig cells drops off, returning the concentration to optimal levels in the bloodstream.

Human Copulation Follows a Typical Mammalian Pattern

When the male is sexually aroused, sphincter muscles controlling the flow of blood to the spongy erectile tissue of the penis relax, allowing the tissue to become engorged with blood. (The penis is a hydrostatic skeleton structure; see Section 41.2.) As the spongy tissue swells, it maintains the pressure by compressing and almost shutting off the veins draining blood from the penis. The engorgement produces an erection in which the penis lengthens, stiffens, and enlarges. During continued sexual arousal, lubricating fluid secreted by the bulbourethral glands may be released from the tip of the penis.

Female sexual arousal results in enlargement and erection of the clitoris, in a process analogous to erection of the penis in males. The labia minora also become engorged with blood and swell in size, and lubricating fluid is secreted onto the surfaces of the vulva by the greater vestibular glands. In addition to these changes, the nipples become erect by contraction of smooth muscle cells, and the breasts swell due to engorgement with blood.

Insertion of the penis into the vagina and the thrusting movements of copulation lead to the reflex actions of ejaculation, including spasmodic contractions of muscles surrounding the vasa deferentia, accessory glands, and urethra. During ejaculation, the sphincter muscles controlling the exit from the bladder close tightly, preventing urine from being released from the bladder and mixing with the ejaculate. Ejaculation is usually accompanied by *orgasm,* a sensation of intense physical pleasure that is the peak—climax—of excitement for sexual intercourse, followed by feelings of relaxation and gratification.

The motions of copulation stretch the vagina and stimulate the clitoris. The stretching and stimulation can also induce orgasm in females. The vaginal stretching also stimulates the hypothalamus to secrete oxyto-

Insights from the Molecular Revolution

Egging on the Sperm

Whether human eggs release attractants to draw sperm near has long been a subject of speculation and research. Now molecular investigations by Marc Spehr and his colleagues at Ruhr University in Germany indicate that sperm can detect and swim toward attractant chemicals.

Other investigators had found that human sperm cells have receptors able to bind to chemical substances classified as odorants, aroma molecules that can be specifically recognized ("smelled"). In vertebrates, more than a thousand genes encode odorant receptors, most of them olfactory receptors associated with the senses of smell and taste. However, odorant receptors are also located on cell types that do not function in taste and smell, including sperm.

But do the odorant receptors function in sperm–egg attraction? The Spehr team began their investigation of this possibility by testing testicular tissue for odorant-receptor-gene activity, using probes for mRNAs with sequences typical of odorant receptor genes. Only two active odorant receptor genes were found in the testes: hOR17-2 (hOR = human olfactory receptor), which had been discovered by others; and hOR17-4, which was not previously known to be active.

The researchers molecularly cloned (see Section 18.1) the hOR17-4 gene of testicular cells and inserted the gene in a line of cultured human embryonic kidney (HEK) cells. Previous work had shown that when an odorant receptor combines with the chemical it recognizes, it triggers cytoplasmic reactions that lead to Ca^{2+} release in the cytoplasm (the IP_3 pathway, described in Section 7.4). Accordingly, the investigators tested the genetically engineered HEK cells for a Ca^{2+} response to any of the chemicals in a mixture containing 100 different chemicals. Only one of the chemicals, *cyclamal,* caused the HEK cells to respond. HEK cells that did not receive the hOR17-4 gene did not respond to cyclamal. The researchers then tested chemicals closely related in chemical structure to cyclamal and found that they also elicit a Ca^{2+} response in the engineered HEK cells. They used one of these chemicals, *bourgonal,* in further testing because it triggered a stronger response than cyclamal.

Next, the investigators tested human sperm cells to see if they would respond to bourgeonal. The sperm cells responded to the chemical by an increase in cytoplasmic Ca^{2+} concentration, indicating that the hOR17-4 gene was active during spermatogenesis, leading to synthesis and insertion of the hOR17-4 receptor in the sperm plasma membrane.

In a final experiment, human sperm cells were exposed to gradients of bourgeonal solutions in micropipettes. The sperm swam consistently toward the regions of highest concentration, and swam faster and more directly as the concentration increased.

These experiments indicate that human sperm can detect and respond to chemical attractants by swimming toward the source of the attractant. Whether human eggs actually release such attractants remains to be determined. If so, the egg attractant detected by the hOR17-4 receptor is likely to resemble cyclamal and bourgeonal in chemical structure, because odorant receptors are highly specific in their responses.

As part of their research, the Spehr team found that another chemical, *undecanal,* strongly inhibits the binding of the hOR17-4 receptor to cyclamal and bourgeonal. With chemicals at hand that can both stimulate and eliminate sperm attraction, the system might provide a method for either contraception or procreation.

cin, which induces contractions of the uterus. The contractions keep the sperm in suspension and aid their movement through the reproductive tract. Uterine contractions are also induced by the prostaglandins in the semen.

Sperm reach the site of fertilization in the oviducts within 30 minutes after their ejaculation into the vagina. Of the millions of sperm released in a single ejaculation, only a few hundred actually reach the oviducts. After orgasm, the penis, clitoris, and labia minora gradually return to their unstimulated size. Females can experience additional orgasms within minutes or even seconds of a first orgasm, but most males enter a *refractory period* that lasts for 15 minutes or longer before they can regain an erection and have another orgasm.

A Human Egg Can Be Fertilized Only in the Oviduct

A human egg can be fertilized only during its passage through the third of the oviduct nearest the ovary. If the egg is not fertilized during the 12- to 24-hour period that it is in this location, it disintegrates and dies. However, sperm do not swim randomly for a chance encounter with the egg. Rather, they first swim up the cervical canal to reach the oviduct, and then are propelled up the oviduct by contractions of the oviduct's smooth muscles. Further, researchers have found evidence that eggs release chemical attractant molecules that the sperm recognize, causing them to swim directly toward the egg. (*Insights from the Molecular Revolution* describes some of this research.)

To reach the egg, the fertilizing sperm must penetrate the layer of follicle cells surrounding the egg, and then pass through the zona pellucida coating the egg surface **(Figure 47.17).** Enzymes built into the plasma membrane of the sperm cells aid penetration through the follicle cells. Once through the follicle cells, the sperm binds to receptor molecules on the surface of the zona pellucida. The binding triggers the acrosome reaction in which hydrolytic enzymes are released from the acrosome and digest a pathway to the egg. As soon as the first sperm cell reaches the egg through the pathway digested by the released acrosomal enzymes, the sperm and egg plasma membranes fuse, and the sperm cell enters the cytoplasm of the egg. Although only one sperm fertilizes the egg, the combined release of acrosomal enzymes from many sperm greatly increases the chance that a complete channel will be opened through the zona pellucida. Partially for this reason, a low sperm count is often a source of male infertility. Low sperm count has a number of causes, including infection, heat, frequent intercourse, smoking, and excess alcohol consumption.

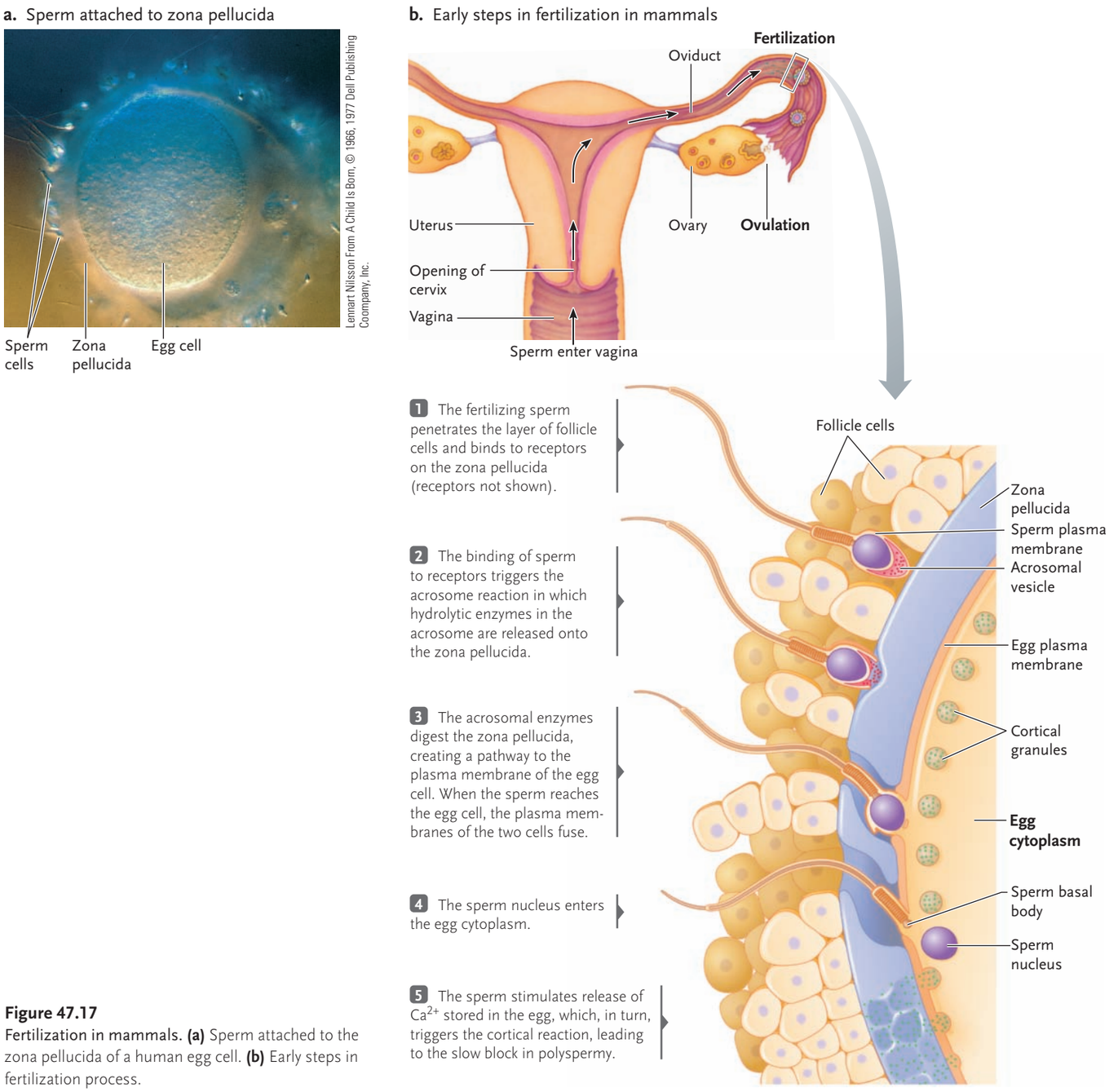


Figure 47.17
Fertilization in mammals. **(a)** Sperm attached to the zona pellucida of a human egg cell. **(b)** Early steps in fertilization process.

The membrane fusion activates the egg. The sperm that has entered the egg releases nitric oxide, which stimulates the release of stored Ca^{2+} in the egg. The Ca^{2+} triggers cortical granule release to the outside of the egg. Enzymes from the cortical granules crosslink molecules in the zona pellucida, hardening it and sealing the channels opened by acrosomal enzymes. The enzymes also destroy the receptors that bind sperm to the surface of the zona pellucida. As a result, no further sperm can bind to the zona or reach the plasma membrane of the egg. The Ca^{2+} also triggers the completion of meiosis of the egg (recall that, up to that point, it is a secondary oocyte arrested in metaphase of meiosis II). The sperm and egg nuclei then fuse and the cell is now the zygote. Mitotic divisions of the zygote soon initiate embryonic development.

The first cell divisions of embryonic development take place while the fertilized egg is still in the oviduct. By about 7 days after ovulation, the embryo passes from the oviduct and implants in the uterine lining. During and after implantation, cells associated with the embryo secrete **human chorionic gonadotropin (hCG)**, a hormone that keeps the corpus luteum in the ovary from breaking down. Excess hCG is excreted in the urine; its presence in urine or blood provides the basis of pregnancy tests.

The continued activity of the corpus luteum keeps estrogen and progesterone secretion at high levels, maintaining the uterine lining and preventing menstruation. The high progesterone level also thickens the mucus secreted by the uterus, forming a plug that seals the opening of the cervix from the vagina. The plug keeps bacteria, viruses, and sperm cells from further copulation from entering the uterus.

Later in development, about 10 weeks after implantation, the placenta takes over the secretion of progesterone, hCG secretion drops off, and the corpus luteum regresses. However, the corpus luteum continues to secrete the hormone *relaxin,* which inhibits contraction of the uterus until the time of birth is near.

Study Break

Outline the roles of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in the ovarian cycle of a human female.

47.4 Methods for Preventing Pregnancy: Contraception

In human society, pregnancy can be a blessing or a disaster. An unwanted pregnancy can be inconvenient at the least, or at the worst can have serious physical and social repercussions, particularly for the mother. Many methods exist for achieving contraception—the prevention of pregnancy—some old and others relatively new.

Table 47.1 **Pregnancy Rates for Birth Control Methods**

Method	Lowest Expected Rate of Pregnancy[a]	Typical-Use Rate of Pregnancy[b]
Rhythm method	1%–9%	25%
Withdrawal	4%	19%
Condom (male)	3%	14%
Condom (female)	5%	21%
Diaphragm and spermicidal jelly	6%	20%
Vasectomy (male sterilization)	0.1%	0.15%
Tubal ligation (female sterilization)	0.5%	0.5%
Contraceptive pill (combination estrogen/progestin)	0.1%	5%
Contraceptive pill (progestin only)	0.5%	5%
Implant (progestin)	0.09%	0.09%
Intrauterine device (IUD) (copper T)	0.6%	0.8%

[a]Rate of pregnancy when the birth control method was used correctly every time.
[b]Rate of pregnancy when the method was used typically, meaning that it may not have been always used correctly every time.
Source: U.S. Food and Drug Administration, http://www.fda.gov/fdac/features/1997/conceptbl.html. Data reported in 1997 for effectiveness of methods in a 1-year period.

The oldest method of contraception is total abstinence from sex. Unfortunately, millions of years of animal evolution have stacked the cards against total abstinence by making the sex drive among the most powerful of compulsions. Literally millions of unwanted children attest to the failures of this method. Other methods of preventing pregnancy include techniques for (1) preventing the sperm from reaching the site of fertilization, (2) preventing ovulation, or (3) interfering with implantation if fertilization does occur. **Table 47.1** lists the most common contraceptive techniques and their reliability, based on 1 year of use. Two values are given: (1) the lowest expected rate of pregnancy, meaning the rate of pregnancy when the birth control method was used correctly every time; and (2) the typical use rate of pregnancy, meaning the rate of pregnancy when the method was used in a typical manner, meaning that it may not always have been used correctly every time.

Of Methods Preventing Fertilization, Vasectomy and Tubal Ligation Are Most Effective

A natural technique for preventing fertilization is the *rhythm method,* which consists of avoiding intercourse during the time of the month when the egg can be fertilized. Because sperm can survive for as long as 5 days

in the female reproductive tract, intercourse should be avoided from 5 days before ovulation and, for safety's sake, for another 4 or 5 days after ovulation. Although conceptually straightforward, the method is difficult to apply because of the unpredictability of the time of ovulation (and the power of the sex drive). The lowest expected rate of pregnancy for this method is 1% to 9%, while the typical rate is 25%.

Another natural method to prevent fertilization is *withdrawal*—starting sexual intercourse, but withdrawing the penis before ejaculation. Unfortunately, once ejaculation begins, it proceeds as a series of reflexes that is extremely difficult to interrupt; in addition, some sperm may be present in lubrication produced prior to ejaculation. The lowest expected rate of pregnancy for this method is 4%, while the typical rate is 19%.

The *condom,* a thin, close-fitting sheath of latex, lambskin, or polyurethane worn over the penis, is one of the traditional methods of preventing ejaculated sperm from entering the vagina. Condoms made from latex may also provide a barrier to the transmission of disease between sexual partners (condoms made from natural skin do not block viruses such as HIV). Pouchlike "female condoms," inserted into the vagina, prevent ejaculated sperm from entering the uterus. The lowest rate of pregnancy for male condoms is 3%, while the typical rate is 14%. The lowest and typical rates for female condoms are 5% and 21%, respectively.

The *diaphragm* is a cuplike rubber device that blocks the cervix in females. (The similar *cervical cap* is smaller and fits more closely over the cervix.) Typically a spermicidal jelly or cream is also used. To be most effective, a diaphragm and the spermicidal jelly must be inserted no more than an hour before intercourse, and left in place for the recommended time afterward. The lowest rate of pregnancy for a diaphragm used with a spermicide is 6%, while the typical rate is 20%.

Fertilization can also be prevented surgically, by cutting and closing off either the vasa deferentia in males or the oviducts in females. In *vasectomy,* the procedure carried out in males, an incision is made in the scrotum and each vas deferens is severed and tied off. After vasectomy, the seminal fluid is still produced and ejaculated, but it does not contain sperm. In *tubal ligation,* the procedure for females, the oviducts are cut and tied off, or seared with heat (cauterized) to close them. The ligation prevents eggs from being fertilized or reaching the uterus. Neither vasectomy nor tubal ligation interferes with the production of sex hormones by the ovaries or testes, or results in any change in sexual behavior. Both operations are highly effective in preventing pregnancy. Although they can be reversed, the procedures are difficult and not always successful. The lowest rate of pregnancy for vasectomy is 0.1%, while the typical rate is 0.15%. The lowest and typical rates for tubal ligation are both 0.5%.

Of Methods Preventing Ovulation, the Oral Contraceptive Pill Is Most Effective

The primary method used to prevent ovulation is the *oral contraceptive pill,* or simply "the pill," containing a combination of estrogen and *progestin* (a synthetic form of progesterone) or progestin alone. In this highly effective method, the pill is taken daily for 20 to 21 days after the end of the menstrual flow and then stopped (actually, placebo pills are taken for the remaining days of the cycle to maintain the routine of pill taking) to allow menstruation; then the next month's course is begun. If pregnancy is desired, the pill is simply not taken after the menstrual flow.

The pill works by inhibiting the secretion of FSH and LH by the pituitary; without these hormones, ovulation does not occur. When the pill is stopped after 20 to 21 days, the resulting drop in progestin concentration causes the uterine lining to break down and initiates the menstrual flow. Since ovulation does not occur, fertilization and pregnancy are not possible.

The lowest rate of pregnancy for the estrogen/progestin pill is 0.1%, while the typical rate is 5%. The lowest and typical rates for the progestin pill are 0.5% and 5%, respectively. Most pregnancies among women taking the pill result from failure to take it on schedule—often simply by forgetting to take the pill for a day or two at the wrong time of the month. Some women, about one in four, experience unpleasant side effects, such as nausea, tenderness of the breasts, irritability, nervousness, or changes in skin color or texture. Modern versions of the pill have almost eliminated the more serious side effects, such as increased incidence of breast cancer and formation of blood clots. However, cigarette smoking significantly increases the risk of heart attacks and strokes for women taking the pill. This risk increases with age and with the number of cigarettes smoked per day.

As an alternative to the pill, progestin is also injected in a time-release form that prevents ovulation throughout the period of release. In one method, plastic tubes containing progestin are implanted under the skin, usually in the upper arm. The tubes release progestin for up to 5 years, making the method effective for women in countries or situations in which obtaining and taking the pill on a daily basis is impractical. The lowest rate and the typical rate of pregnancy for the implant are both 0.09%.

The IUD and the Morning-After Pill Are Effective in Preventing Implantation

A commonly used method for preventing implantation if fertilization occurs is insertion of an *intrauterine device (IUD),* a small plastic or copper device, into the uterus just inside the cervix. The IUD remains in place

as a long-term preventive measure; depending on the type, a single IUD is approved for 5 to 10 years of use. It is not clear how the IUD works; presumably, it causes a mild inflammation of the uterine lining that makes it unreceptive to implantation. The IUD is a refinement of a method used by women since ancient times, in which small pebbles were inserted in the uterus to prevent conception.

The IUD is effective as long as it is not deflected from its correct position in the uterus; unfortunately, this may happen without warning or the user's awareness. A few women also experience unpleasant side effects from the IUD such as cramps, uterine infections, or excessive menstrual bleeding. The lowest rate of pregnancy for the copper T types of IUD is 0.6%, while the typical rate is 0.8%.

Whatever the method of birth control, its effectiveness is improved if sex partners are highly motivated and careful in its use. The effectiveness of condoms, for example, is greatly improved if the penis is withdrawn immediately after ejaculation (before the semen has time to spread under the condom and leak into the vagina) and is not reinserted, with or without a condom, for several hours. Similarly, high motivation in use of the rhythm method, which might require abstaining from intercourse for most of the month except for a few days just after the menstrual flow, considerably improves the percentage of success with this method.

Another method used to prevent pregnancy is the so-called *emergency contraception pill,* commonly referred to as the "morning-after pill." These pills are administered after intercourse has occurred as a means to prevent pregnancy. A high dosage synthetic progestin emergency contraception pill called Plan B is available in the United States without prescription to women who are 18 or older. This pill is highly effective if taken within 72 hours after unprotected sexual intercourse. Pregnancy tests do not work until significantly after this time. Research data show that Plan B works by blocking ovulation; there is no effect of the hormone on implantation of a fertilized egg. But, because sperm can survive in the female reproductive tract for a few days, blocking ovulation can obviously be effective in preventing pregnancy.

Another emergency contraception pill is *mifepristone (RU-486),* which contains a molecule that binds to and blocks progesterone receptors in the uterine lining. The blockage prevents the lining from responding to progesterone and causes it to break down (that is, a menstrual period is initiated), taking with it any embryo that may have implanted. Mifepristone is approved in the United States for terminating pregnancies up to 49 days post-conception; the time period is

Unanswered Questions

Why do male mammals have "female" hormones?

Given the paramount importance of reproduction in biology, there is a surprising lack of knowledge regarding even its basic features. For example, both sexes make the same set of reproductive hormones, but for some of these, we are only beginning to understand their roles in males. For example, oxytocin, released by the pituitary, has long been known to control labor and milk ejection in females. But oxytocin is also found in semen, where it may boost sperm counts and aid sperm transport in the female reproductive tract. And it may also have a role in social behavior. Several studies have shown a role for oxytocin in male–female and mother–child bonding; and recently research groups led by Markus Heinrichs at the University of Zurich, Switzerland, and Ernst Fehr at Collegium Helveticum, Zurich, reported that men who sniffed a nasal spray with oxytocin in the laboratory were much more likely to trust other males in engaging in risky financial transactions. Thus oxytocin has been dubbed the "trust hormone." However, its roles (and how it is regulated) in real social interactions are not known.

Prolactin, also from the pituitary gland, stimulates milk production in females. Tillmann Krüger and colleagues at the Swiss Federal Institute of Technology have found that prolactin levels surge during orgasms in both sexes and that prolactin is associated with a feeling of relaxation and satisfaction. In males, it may also inhibit erection during post-coitus recovery. In 2006, Stuart Brody of the University of Paisley in Scotland and Dr. Krüger found the surge to be much higher after intercourse than masturbation, which may explain why the latter is generally less satisfying. They suggest that excessive prolactin could play a role in male impotence, a possibility now being investigated.

What is the anatomy of the human clitoris?

There is also surprising ignorance on basic reproductive anatomy. Diagrams of the human clitoris are quite misleading, showing it simply as a small external bulb in the female vulva. However, dissections and magnetic resonance images in studies led by Dr. Helen O'Connell, an Australian urology surgeon, revealed the clitoris to be much larger, rivaling the penis. Most of the clitoral tissue consists of large, highly vascular internal bulbs that surround the urethra and vagina. The role of these bulbs is uncertain, but they engorge during intercourse, perhaps to squeeze the urethra closed to prevent infections, to support the vaginal wall during penile penetration, and/or to increase pleasure signaling. Knowledge of this anatomy is crucial for performing safe pelvic surgeries on women.

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longer in some foreign countries. It is available only by prescription.

In this chapter we have focused on animal reproduction up to the point of the fertilized egg. In the next chapter, we address the final stage of reproduction in sexually reproducing organisms, the development of a new individual from the fertilized egg.

Study Break

How does the oral contraceptive pill prevent pregnancy?

Review

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47.1 Animal Reproductive Modes: Asexual and Sexual Reproduction

- In asexual reproduction, a single parent gives rise to offspring without genetic input from another individual. In sexual reproduction, offspring are produced by the union of gametes—eggs and sperm—from two parents.
- Asexual reproduction involving mitosis occurs in animals by fission, budding, or fragmentation (Figure 47.2). In parthenogenesis, a form of asexual reproduction, females produce eggs that develop without being fertilized.
- In sexual reproduction, genetic variability is produced by the meiotic processes of genetic recombination and independent assortment.

47.2 Cellular Mechanisms of Sexual Reproduction

- Sexual reproduction includes two cellular processes, gametogenesis and fertilization, and a whole-organism process, mating. Gametogenesis is the formation of male and female gametes by meiotic cell division, followed by differentiation of the gametes; fertilization is the union of gametes that initiates development of new individuals (Figure 47.3).
- Gametogenesis takes place in the testes of males and in the ovaries of females. Sperm and eggs are delivered to the site of fertilization by sperm ducts in males and oviducts in females. External reproductive structures aid the delivery in many species.
- In male gametogenesis—spermatogenesis—each cell entering meiosis produces four haploid motile sperm cells. In female gametogenesis—oogenesis—each cell entering meiosis produces one haploid egg cell. The meiotic divisions of oogenesis concentrate almost all the cytoplasm in the single egg cell; the other division products are nonfunctional polar bodies (Figures 47.3–47.5).
- The egg contains stored nutrients and information required for at least the early stages of embryonic development. It is covered by one or more protective coats, and it has a mechanism that blocks additional sperm from entering after fertilization (Figure 47.5).
- Fertilization, which follows mating in most animals, may be external or internal. In external fertilization, sperm and eggs are shed into the surrounding water. In internal fertilization, sperm are released close to or inside the female reproductive ducts via copulation (Figure 47.6).
- When a sperm and egg touch during fertilization, their plasma membranes fuse, introducing the sperm nucleus into the egg cytoplasm. The sperm and egg nuclei then fuse to form a diploid zygote nucleus and initiate embryonic development (Figure 47.8).
- Oviparous animals lay eggs in which development of new individuals takes place outside the female's body. In viviparous animals, development takes place inside the female's body. In ovoviviparous animals, fertilized eggs are retained within the body while the embryo develops, the eggs hatch within the mother, and the young are then released from the body.
- In hermaphroditism, single individuals produce both mature egg-producing tissue and mature sperm-producing tissue (Figure 47.10).

Animation: Spermatogenesis

Animation: Fertilization

47.3 Sexual Reproduction in Humans

- In females, eggs released from the ovaries travel through the oviducts to the uterus. The uterus opens into the vagina, the entrance for sperm and the exit for offspring during birth (Figure 47.11).
- The ovarian cycle produces an egg. The cycle begins with the release of GnRH by the hypothalamus, which stimulates the release of FSH and LH from the anterior pituitary. FSH stimulates oocytes in the ovaries to begin meiosis. One oocyte typically develops to maturity surrounded by cells that form a follicle (Figures 47.12 and 47.13).
- The enlarging follicle secretes estrogens, causing a burst in FSH and LH release; at about 14 days, the LH stimulates ovulation, the bursting of the follicle and the release of the egg. The remainder of the follicle forms the corpus luteum, which secretes estrogens, progesterone, and inhibin (Figures 47.12 and 47.13).
- Day 0 of the monthly uterine (menstrual) cycle correlates with the beginning of follicular development in the ovary and the beginning of the menstrual flow. Secretion of estrogen from the developing follicle stimulates the growth of a new endometrium. If fertilization does not occur, progesterone and inhibin maintain the endometrium until the 28th day of the cycle, when the corpus luteum regresses. Without progesterone, the endometrium breaks down and is released as the menstrual flow (Figure 47.13).
- In males, sperm develop in seminiferous tubules in the testes and are released into the epididymis. When a male ejaculates, sperm travel from the epididymis to the vas deferens, and then through the urethra and the penis. The seminal vesicles, prostate gland, and bulbourethral glands add fluids to the sperm traveling to the outside (Figures 47.14 and 47.15).
- Sperm production in males is also controlled by LH and FSH. LH stimulates Leydig cells in the testes to secrete testosterone, which stimulates sperm production. FSH stimulates Sertoli cells in the testes to secrete molecules needed for spermatogenesis (Figure 47.16).
- During copulation, sperm are ejaculated into the vagina of the female. The sperm then swim through the female reproductive tract, aided by contractions of the oviduct and guided by molecules released by the egg. Upon contact with the egg in the oviduct, the acrosomes of sperm release enzymes that digest a path through the egg coats. As the fertilizing sperm contacts the egg, the sperm and egg plasma membranes fuse, releasing the sperm nucleus into the egg cytoplasm and activating the egg.

The egg completes meiosis, and the sperm and egg nuclei fuse, producing the zygote (Figure 47.17).

- As the embryo implants, the hormone hCG sustains the corpus luteum, which continues to secrete estrogen and progesterone at high levels. These hormones maintain the uterine lining and prevent menstruation.

Animation: Male reproductive system

Animation: Route sperm travel

Animation: Hormonal control of sperm production

Animation: Female reproductive system

Animation: Ovarian function

Animation: Hormones and the menstrual cycle

Animation: Menstrual cycle summary

47.4 Methods for Preventing Pregnancy: Contraception

- Methods of contraception work by preventing sperm from reaching the site of fertilization, by preventing ovulation, or by interfering with implantation (Table 47.1).
- Methods for preventing the sperm from reaching the site of fertilization include the condom, the diaphragm or cervical cap, and the rhythm method, as well as vasectomy or tubal ligation.
- The oral contraceptive pill prevents ovulation. It contains a combination of estrogen and the progesterone-like progestin, which inhibiting the secretion of FSH and LH and follicle formation.
- Methods for preventing implantation include the IUD and the morning-after pill.

Questions

Self-Test Questions

1. Asexual reproduction is most successful in:
   a. changing environments.
   b. sessile animals.
   c. densely settled populations.
   d. land animals.
   e. genetically varied individuals.
2. Which of the following processes does *not* increase genetic diversity?
   a. parthenogenesis.
   b. random DNA mutations.
   c. genetic recombination.
   d. independent assortment.
   e. random combinations of paternal and maternal chromosomes.
3. Gametogenesis has parallel stages in egg and sperm formation. The stage in eggs that is equivalent to spermatids is the:
   a. primary oocyte.
   b. oogonium.
   c. ovum.
   d. ootid and polar bodies.
   e. secondary oocyte and polar body.
4. The animal group that exhibits external fertilization is the:
   a. amphibians.
   b. birds.
   c. sharks.
   d. reptiles.
   e. mammals.
5. The slow block to polyspermy:
   a. is caused by a change in membrane potential from negative to positive.
   b. triggers the movement of Ca^{2+} from the cytosol to the endoplasmic reticulum.
   c. triggers a decrease in egg oxidation and protein synthesis.
   d. describes the fusion of egg and sperm nuclei.
   e. includes the fusion of cortical granules with the egg's plasma membrane.
6. Some placental animals provide nutrients to their embryos from an attached membranous yolk-containing sac. They are called:
   a. oviparous animals.
   b. ovoviviparous animals.
   c. metatherians.
   d. eutherians.
   e. mammals.
7. Which activity is a step in the ovarian cycle?
   a. FSH stimulates the pituitary to release GnRH.
   b. When FSH and LH levels fall, the corpus luteum shrinks and the uterine lining breaks down.
   c. Luteinizing hormone stimulates the uterus to make progesterone.
   d. Estrogen levels initially have a positive feedback effect on the pituitary, which is followed by higher estrogen levels causing negative feedback.
   e. A fully developed corpus luteum inhibits uterine lining growth.
8. During spermatogenesis in mammals, sperm travels from the:
   a. Sertoli cells past the epididymis and urethra, through the vas deferens to the prepuce.
   b. seminal vesicles past the prostate gland, through the glans and prepuce to the bulbourethral glands.
   c. vestibular glands past the Leydig cells, through the accessory glands and epididymis to the vas deferens.
   d. labia past the bulbourethral glands, through the vas deferens and urethra to the epididymis.
   e. seminiferous tubules past the Leydig cells, through the epididymis and vas deferens to the urethra.
9. The human egg is fertilized in the:
   a. uterus.
   b. vagina.
   c. oviduct.
   d. cervical canal.
   e. ovary.
10. The most effective method to prevent fertilization is:
    a. the oral contraceptive.
    b. the IUD.
    c. the morning-after pill.
    d. vasectomy and tubal ligation.
    e. the rhythm method.

Questions for Discussion

1. Currently under development is an "anti-pregnancy vaccine" that stimulates a woman's immune system to develop antibodies against human chorionic gonadotropin (hCG). How would this method prevent pregnancy?
2. Men sometimes have reduced fertility because of *testicular varioceles*, varicose veins in the testes in which blood pools. Based on what you now know of the conditions under which sperm develop properly, how do think this condition might impair sperm development?
3. Spermatogenesis produces four sperm for each spermatocyte, but oogenesis produces only one egg for each oocyte. Why might these different outcomes be adaptive?
4. Sertoli cells protect spermatocytes from attack by antibodies during their development in the human male. What structures

might protect the oocyte and egg from attack by antibodies in the human female?

5. Compare the advantages and disadvantages of sexual and asexual reproduction for an aphid and a parasitic worm.
6. It may be possible to develop a birth control drug that would prevent conception by interfering with fertilization. Outline the design for such a drug and explain exactly how it would work. (There may be more than one design that, in theory, would be effective.)

Experimental Analysis

Design experiments to determine if, and at what dose, vitamin E can decrease menstrual cramping significantly.

Evolution Link

The nematode species *Caenorhabditis elegans* and *Caenorhabditis briggsae* are both hermaphroditic. Phylogenetic evidence indicates that the last common ancestor of these two species had a normal male-female mechanism of reproduction. What does this evidence suggest about their hermaphroditism?

How Would You Vote?

Fertility drugs induce multiple ovulations at the same time and increase the likelihood of high-risk multiple pregnancies. Should the use of such drugs be restricted to conditions that limit the number of embryos formed? Go to www.thomsonedu.com/login to investigate both sides of the issue and then vote.