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CHAPTER 7

# Processes of Cell Division, Differentiation, and Specialization

**Read This Chapter to Learn About**

- Mitosis
- Meiosis
- Gametogenesis
- Embryogenesis

## MITOSIS

**Mitosis** is the process of normal cell division in eukaryotic cells. It occurs in most cells with the exception of gametes as well as mature nerve and muscle cells in animals. It begins with a single parent cell that replicates all components within the cell, divides the components into two piles, and then splits to form two genetically identical daughter cells. The most critical components for replication and division are the chromosomes, so particular care will be taken to ensure an equal distribution of chromosomes to each daughter cell.

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## Chromosomes

**Chromosomes** occur in homologous pairs as can be seen in the karyotype in Figure 7-1. For each pair of chromosomes found in an individual, one member of the pair came from the maternal parent and the other member of the pair came from the paternal parent. Recall the genetic inheritance of two alleles per trait—one allele per trait from each parent.

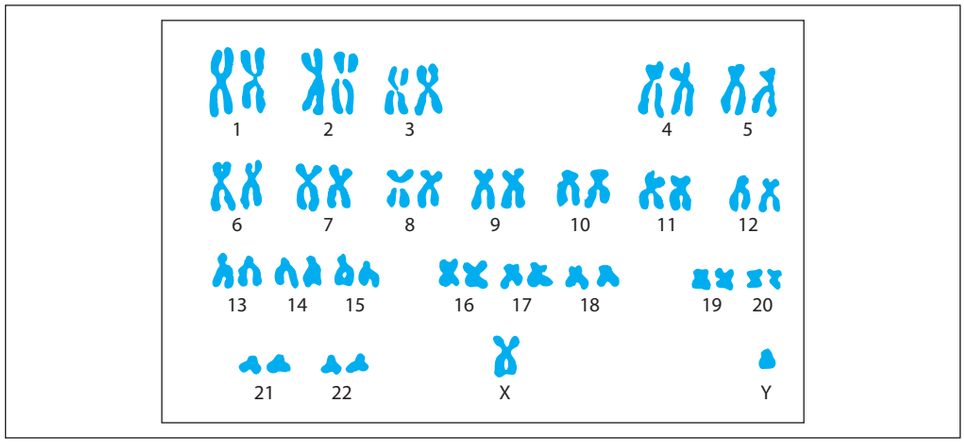


FIGURE 7-1 A karyotype. Chromosomes from a single cell are arranged in pairs to construct a karyotype. This karyotype is from a male. *Source:* From Eldon D. Enger, Frederick C. Ross, and David B. Bailey, *Concepts in Biology*, 11th ed., McGraw-Hill, 2005; reproduced with permission of The McGraw-Hill Companies.

The total number of chromosomes found in an individual is called the **diploid (2N) number**. When individuals reproduce, this number must be cut in half to produce **haploid (N) gametes**. The human diploid number is 46, and the human haploid number is 23. The process of mitosis begins with 1 diploid cell and ends with 2 identical diploid cells. In the process of meiosis, a diploid cell begins the process and produces 4 haploid gametes.

When a cell is not dividing, each chromosome exists in single copy called a **chromatid**. However, when the cell is preparing to divide, each chromosome must be replicated so that it contains 2 chromatids, sometimes called **sister chromatids**. Each chromosome has a compressed region called the **centromere**, and when the chromosomes replicate, the sister chromatids stay attached to each other at the centromere. Figure 7-2 shows the difference between an unreplicated and a replicated chromosome.

## The Cell Cycle

Mitosis is used for the growth of organisms because it takes an increased number of cells for an organism to get bigger. When an individual has stopped growing, mitosis is only needed to replace cells that have died or been injured. For this reason, mitosis

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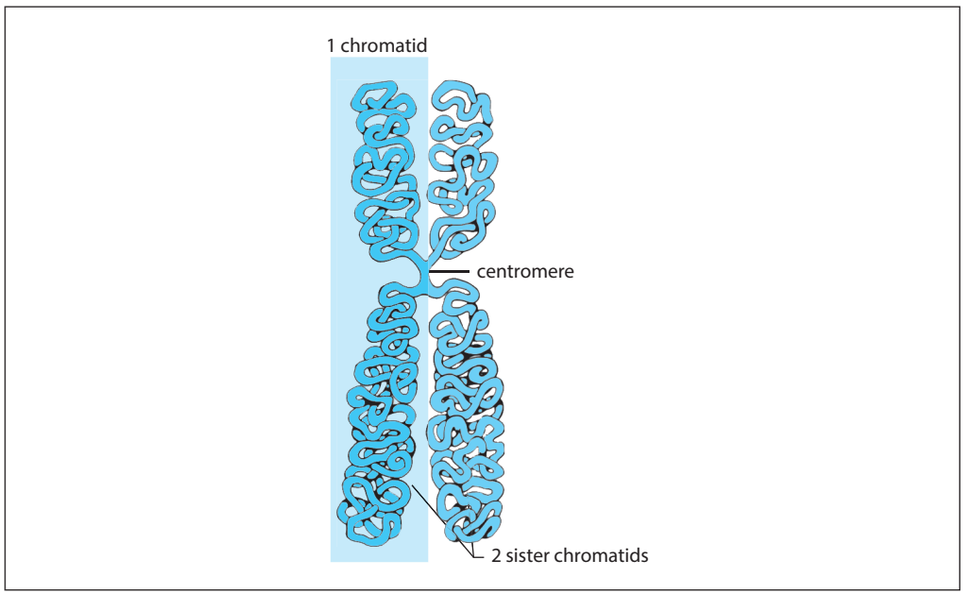


**FIGURE 7-2** Chromosome structure. A replicated chromosome consists of 2 sister chromatids attached to each other at the centromere. *Source:* From Sylvia S. Mader, *Biology*, 8th ed., McGraw-Hill, 2004; reproduced with permission of The McGraw-Hill Companies.

needs to be a regulated process that occurs only when new cells are needed. The **cell cycle** is used to regulate the process of cell division in each individual cell. A normal cell cycle has the following stages that can be seen in Figure 7-3:

- **$G_1$.** This is the first gap phase of the cell cycle. In this stage, the parent cell is growing larger, adding additional cytoplasm, and replicating organelles.
- **S.** During this phase of DNA synthesis, the chromosomes are all being replicated. Once this stage is complete, each chromosome consists of 2 sister chromatids connected at the centromere.
- **$G_2$.** This is the second gap phase. The cell continues to grow in size and make final preparations for cell division.
- **M.** During the **M phase**, mitosis actually occurs. The replicated chromosomes and other cellular components are divided to ensure that each daughter cell receives equal distributions. The division of the cytoplasm at the end of the M phase is referred to as **cytokinesis**.

The first three phases of the cell cycle, $G_1$, S, and $G_2$, are collectively called **interphase**. Interphase simply means preparation for cell division. The actual cell division occurs during the M phase of the cycle.

Some cells lose the ability to progress through the cell cycle and are thus unable to divide. Mature human nerve and muscle cells are an example. Cells without the ability to divide are considered to be in the $G_0$ phase of the cell cycle where division never resumes.

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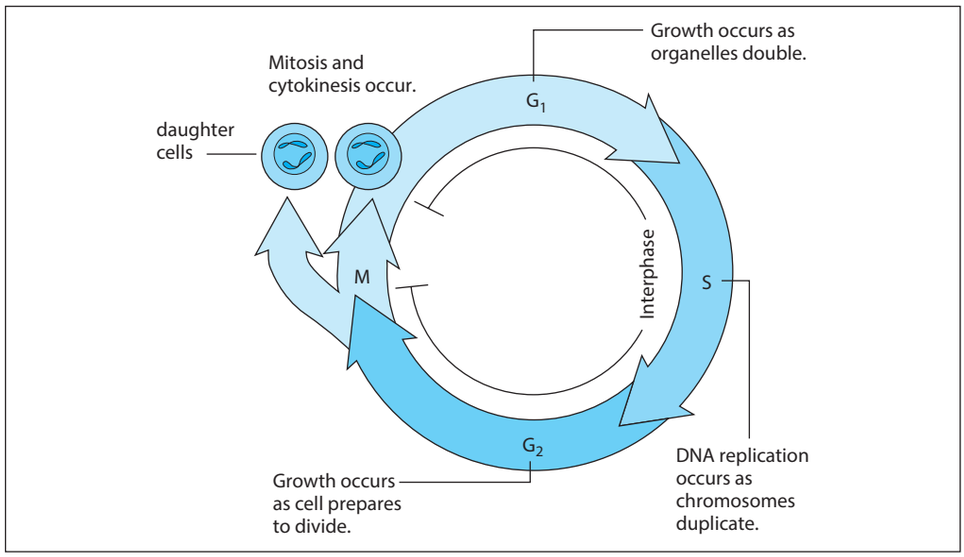


**FIGURE 7-3** The cell cycle. Cells go through a cycle that regulates their division. Interphase is preparation for cell division and consists of the $G_1$, S, and $G_2$ phases of the cycle. The M phase is where the cells actually divide. *Source:* From Sylvia S. Mader, *Biology*, 8th ed., McGraw-Hill, 2004; reproduced with permission of The McGraw-Hill Companies.

## M PHASE

The M phase of the cell cycle is subdivided into four stages: prophase, metaphase, anaphase, and telophase. The primary concern in these stages is alignment and splitting of sister chromatids to ensure that each daughter cell receives an equal contribution of chromosomes from the parent cell. A visual summary of the events of the M phase can be seen in Figure 7-4.

***Prophase.*** Chromosomes are located in the nucleus. Prior to division, the chromosomes are not condensed and thus are not visible. Leaving the chromosomes in an uncondensed state makes it easier to copy the DNA but makes the chromosomes very stringy and fragile. Once the DNA is replicated, the chromosomes must condense so that they are not broken as they are divided up into the two daughter cells.

Another major event of **prophase** is a breakdown of the nuclear membrane releasing the chromosomes into the cytoplasm of the cell. The centrioles present in the cell replicate and move to opposite ends of the cell. Once they have migrated to the poles of the cell, they begin to produce a spindle apparatus consisting of spindle fibers that radiate outward forming asters. The spindle fibers are composed of microtubules that will ultimately attach to each chromosome at the kinetochore. The **kinetochore** appears at the centromere of each chromosome.

***Metaphase.*** In **metaphase**, each chromosome is attached to a spindle fiber at the kinetochore. The chromosomes are aligned down the center of the cell at the metaphase plate.

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***Anaphase.*** During **anaphase**, the centromere splits, allowing each chromatid to have its own centromere. At this point, the chromatids can be separated from each other and are pulled toward opposite poles of the cell separating the chromosomes into two distinct piles, one for each daughter cell.

***Telophase.*** Now that the chromosomes have been divided into two groups, the spindle apparatus is no longer needed and disappears during **telophase**. A new nuclear membrane forms around each set of chromosomes, and the chromosomes uncoil back to their original state.

Finally, **cytokinesis** occurs where the cytoplasm is divided between the cells. A cleavage furrow forms, which pinches the cells apart from each other. The end result is 2 daughter cells ready to begin interphase of their cell cycles.

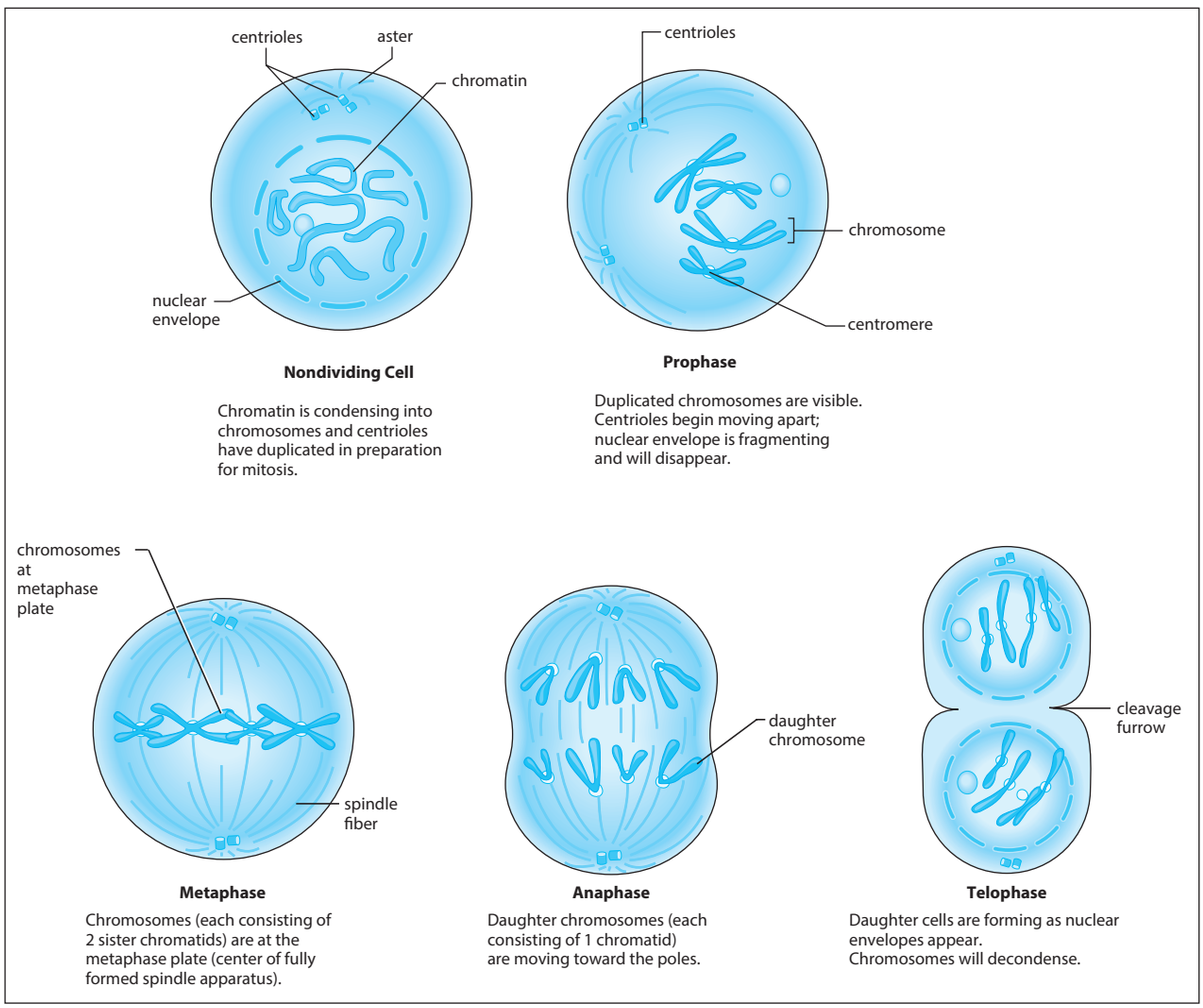


**FIGURE 7-4** Mitosis consists of four phases: prophase, metaphase, anaphase, and telophase. *Source:* From Sylvia S. Mader, *Biology*, 8th ed., McGraw-Hill, 2004; reproduced with permission of The McGraw-Hill Companies.

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## Failure of Cell Cycle Regulatory Mechanisms

A normal cell divides about 50 times before its telomeres shorten to the point where the chromosome is risking damage on subsequent divisions. Once the telomeres shorten to a threshold point, **apoptosis** (programmed cell death) occurs in the cell. Some cells have the ability to bypass cell death and thus become immortal. This is a key characteristic of cancer cells.

**Cancer** develops by a failure of a variety of mechanisms used to regulate progression through the cell cycle. Checkpoints exist throughout the cycle to ensure that cell division does not occur unless necessary. When these checkpoints are bypassed, cell division happens continually, ultimately producing a mass of unnecessary cells termed a **tumor**. The genetic mechanisms of cancer were discussed previously in Chapter 2.

One of the biggest challenges to cancer treatment is finding a way to kill cancerous cells without killing healthy cells. Many cancer therapies target cells as they divide. Since cancer cells divide quickly, they can be damaged by these therapies. However, other cells in the body that are dividing are also damaged. This is the cause of many of the side effects related to cancer therapies.

# MEIOSIS

Because mitosis produces genetically identical diploid daughter cells, it is not appropriate for sexual reproduction. If diploid cells were used for reproduction in humans, each egg would contain 46 chromosomes as would each sperm. This would result in embryos having 96 chromosomes. This number would double each generation if mitosis were used to produce gametes.

The process of **meiosis** begins with a diploid parent cell in the reproductive system that has completed interphase and then follows stages similar to mitosis, twice. The result is 4 haploid gametes that are genetically diverse. A summary of the events of meiosis can be seen in Figure 7-5.

## Meiosis I

**Meiosis I** encompasses stages similar to mitosis with two major changes. The first involves genetic recombination between homologous pairs, and the second involves the alignment of chromosome pairs during metaphase of meiosis I.

### PROPHASE I

During **prophase I** of meiosis, there are many similarities to prophase of mitosis. The chromosomes condense, the centrioles divide and move toward the poles of the cell, spindle fibers begin to form, and the nuclear membrane dissolves. The unique event seen in prophase I is crossing over, demonstrated in Figure 7-6.

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Homologous pairs of chromosomes associate and twist together in synapsis. This configuration consists of 2 replicated chromosomes, or a total of 4 chromatids, and is often called a **tetrad**. The synaptonemal complex assists in chromosome pairing, synapsis, and crossing over. At this point, crossing over can occur where pieces of one chromatid break off and exchange with another. Crossing over can occur in more than one location (double crossovers) and can unlink genes that were previously linked on the same chromosome. It is also an important source of genetic diversity, creating new combinations of alleles that were not seen previously.

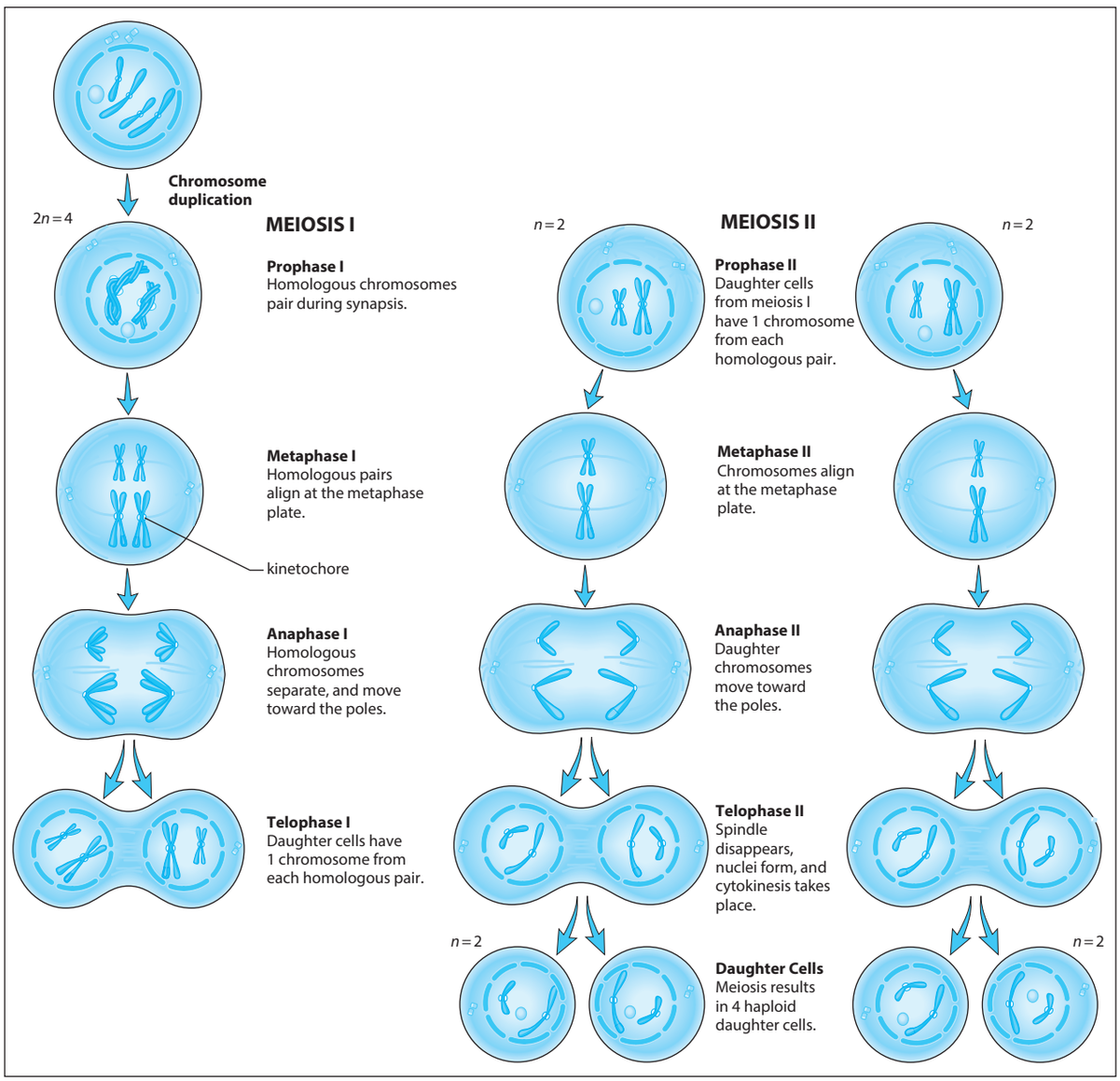


**FIGURE 7-5** Meiosis consists of two rounds of cell division. *Source:* From Sylvia S. Mader, *Biology*, 8th ed., McGraw-Hill, 2004; reproduced with permission of The McGraw-Hill Companies.

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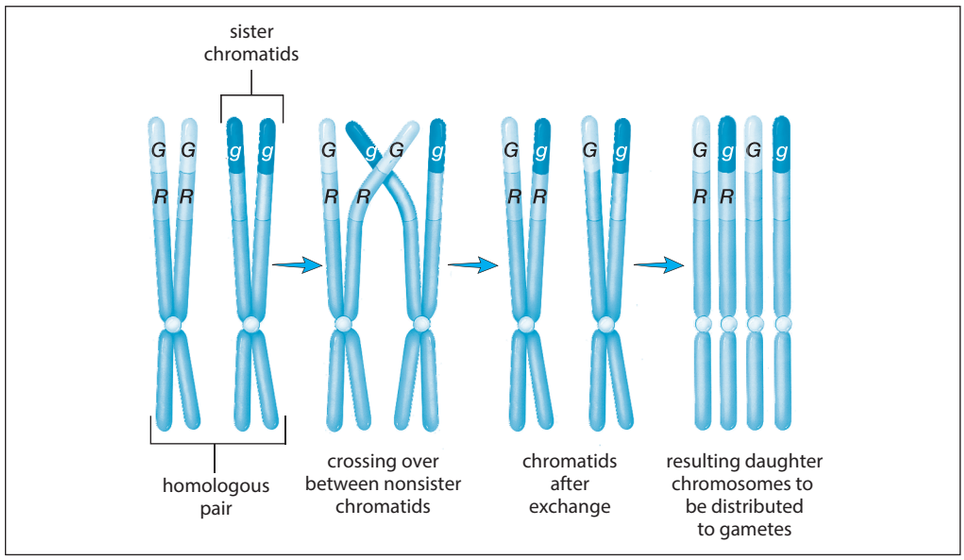


**FIGURE 7-6** Crossing over during meiosis results in genetic diversity. *Source:* From Sylvia S. Mader, *Biology*, 8th ed., McGraw-Hill, 2004; reproduced with permission of The McGraw-Hill Companies.

### METAPHASE I

In metaphase of mitosis, chromosomes align single file along the center of the cell. In **metaphase I** of meiosis, the chromosomes align as pairs along the center of the cell. This alignment of pairs is the critical factor in creating haploid daughter cells. Recall from genetics **the law of independent assortment**. The alignment of each member of the homologous pair during metaphase I is random, so each daughter cell will have a unique combination of maternal and paternal alleles.

### ANAPHASE I

The homologous pairs separate from each other during **anaphase I** and are pulled to the poles of the cells. This separation is referred to as **disjunction**.

### TELOPHASE I

The events of **telophase I** are similar to those of telophase of mitosis. The spindle apparatus dissolves, nuclear membranes form around each set of chromosomes, and cytokinesis occurs to form the 2 daughter cells. At this point, each daughter cell is genetically unique and contains half the number of chromosomes of the parent cell. However, these chromosomes are still in their replicated form, consisting of 2 chromatids each.

## Meiosis II

**Meiosis II** is only necessary to split the chromatids present in the daughter cells produced during meiosis I. There is no interphase between meiosis I and II, because the chromosomes are already replicated. The events of meiosis II are as follows:

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- **Prophase II.** Centrioles replicate and move toward the poles of the cell, chromosomes condense, and the nuclear membrane dissolves.
- **Metaphase II.** Chromosomes align along the center of the cell.
- **Anaphase II.** Sister chromatids are separated and move toward the poles of the cell.
- **Telophase II.** Nuclear membranes re-form, and cytokinesis occurs to produce daughter cells.

At the end of meiosis II, there are 4 daughter cells. Each is haploid with a single copy of each chromosome. Each cell is genetically diverse as a result of crossing over and independent assortment.

## GAMETOGENESIS

Meiosis results in 4 gametes. In men, all four of these gametes will become sperm. In women, only one of these gametes will become a functional oocyte that will be released once every 28 days during ovulation. If all 4 gametes became functional oocytes and were released each cycle, there would be the potential for 4 embryos. The three gametes that do not become functional oocytes in women are termed **polar bodies**. Some of the major differences between meiosis in men (spermatogenesis) and women (oogenesis) are described in the following table.

**TABLE 7-1** Differences between Spermatogenesis and Oogenesis

| Characteristic | Spermatogenesis | Oogenesis |
|---|---|---|
| Time at which the process begins | At puberty | Before a female is born (during development) |
| Time at which the process ends | Never | At menopause |
| Time needed to complete meiosis | 65–75 days | Many years |
| Number of gametes made | Unlimited numbers are possible | The number of potential oocytes is set at birth in females |
| Fates of the daughter cells | All 4 are sperm | One is the oocyte and the other 3 are polar bodies |
| Age of the gametes | Not applicable—old sperm are degraded | Women are born with a set number of follicles so that eggs are the same age as the woman |
| Presence of arresting stages in meiosis | No | Yes. Meiosis I starts before birth and then arrests. Meiosis I resumes only after puberty. Only one cell is selected to complete meiosis I per month. Meiosis II only happens if fertilization occurs. |

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# EMBRYOGENESIS

As the haploid nucleus of a sperm cell is contributed to an egg cell (also containing a haploid nucleus) during fertilization, the resulting cell is termed a **zygote**. The zygote begins cell division by mitosis. This produces a ball of identical cells that is the **embryo**. In humans, the first 8 weeks of development constitute embryonic development and all development after 8 weeks constitutes fetal development. The human gestation (development) period is 266 days, or about 9 months. These 9 months are divided into trimesters. Embryonic development is complete within the first trimester.

## Fertilization

Sperm have the ability to survive about 48 hours in the female reproductive system, whereas an oocyte only survives about 24 hours. Sperm deposited prior to or right after ovulation are capable of fertilizing the egg, which should happen in the upper third of a **fallopian tube**. Whereas 200 to 500 million sperm are typically released during ejaculation, only about 200 will make it to the oocyte.

Secretions from the female system change the membrane composition of the sperm near its **acrosome**. This membrane instability causes the release of acrosomal contents. This allows the sperm to penetrate the **corona radiata** (outer layer) of the oocyte. Now the sperm must pass through the next layer of the oocyte, the **zona pellucida**. Then the first sperm to pass through the zona pellucida passes its nucleus into the oocyte. This causes a depolarization in the membrane of the oocyte, which makes it impenetrable to fertilization by other sperm. The nuclei of the oocyte and sperm fuse, creating the zygote.

## Embryonic Development

About 1 day after fertilization, the zygote performs its first mitotic division, becoming an embryo. This initiates **cleavage**, which is the rapid cell division characteristic of early embryonic development. Within about 4 days, the embryo reaches the **morula stage** that consists of a ball of hollow cells. During early cleavage, the embryo may split into two, resulting in identical twins. By about 6 days, the center of the embryo hollows out and becomes fluid filled. The embryo is now termed a **blastula** or **blastocyst**.

The outer cells of the blastocyst are the **trophoblast** and aid in implantation and the development of extraembryonic membranes and the placenta. The inner cell mass of the blastocyst will continue development as the embryo and is the source of embryonic stem cells, which have the ability to differentiate into any cell type. Implantation of the embryo begins about 1 week after fertilization and completes by the second week. The events of early embryonic development can be seen in Figure 7-7.

The blastocyst produces a critical hormone that is important in the maintenance of pregnancy. **Human chorionic gonadotropin (HCG)** is the signal to the **corpus luteum**

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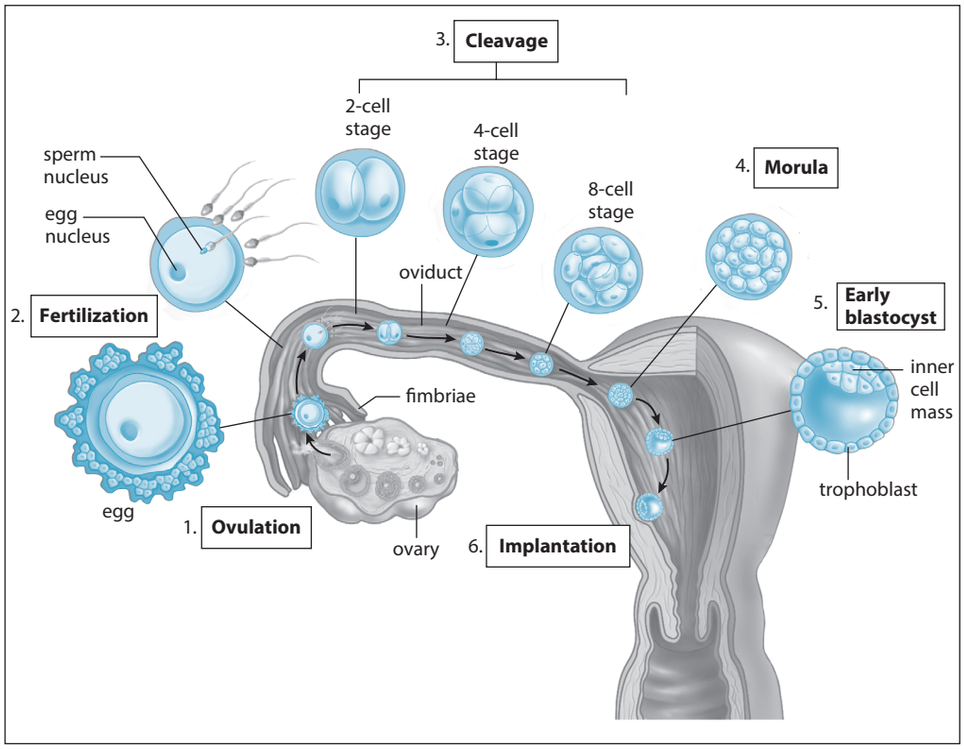


**FIGURE 7-7** Early embryonic development. Fertilization occurs in the fallopian tube. The developing embryo moves down the tube to eventually implant in the endometrium of the uterus at the blastocyst stage of development. *Source:* From Sylvia S. Mader, *Biology*, 8th ed., McGraw-Hill, 2004; reproduced with permission of The McGraw-Hill Companies.

in the ovary to not degrade. Normally, the degradation of the corpus luteum causes a decline of **estrogen** and **progesterone** and triggers menstruation. At this point in development, **menstruation** would mean a loss of the embryo or spontaneous abortion. HCG ensures that the corpus luteum continues to secrete estrogen and progesterone so that menstruation is delayed.

The next event of embryonic development is the **gastrula stage**. During gastrulation, three primary germ layers are formed as the cells in the embryo shift into layers as seen in Figure 7-8. Once a cell enters a germ layer, its ability to differentiate into specific cell types is limited. The three germ layers and the fates of cells in these layers are as follows:

- **Ectoderm.** Cells in this layer express the genes needed to become skin cells and cells of the nervous system.
- **Mesoderm.** Cells in this layer express the genes needed to become muscles, bones, and most internal organs.
- **Endoderm.** Cells in this layer express the genes needed to become the lining of internal body cavities as well as the linings of the respiratory, digestive, urinary, and reproductive tracts.

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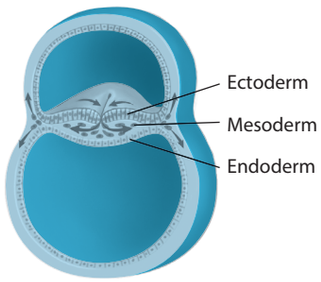


**FIGURE 7-8** During gastrulation, embryonic cells shift into the primary germ layers. *Source:* From George B. Johnson, *The Living World*, 3rd ed., McGraw-Hill, 2003; reproduced with permission of The McGraw-Hill Companies.

Once the germ layers are complete, neuralization occurs to begin the development of the nervous system. Mesoderm cells form the notochord. Ectoderm above the notochord starts to thicken and folds inward to form neural folds that continue to deepen and fuse to produce a neural tube, which eventually develops into the central nervous system. At this point, a head and tail region have been established in the embryo.

## GENE EXPRESSION IN EMBRYOGENESIS

Gene expression in embryos is regulated by a variety of factors. Gametes contain many **epigenetic markers** and when those gametes come together, the embryo inherits those markers. Through a process called **reprogramming**, most of the epigenetic markers inherited from the gametes are erased, although some of the markers remain. This reprogramming step is important because it allows the reprogrammed cells to have **pluripotency**, the potential to differentiate into any cell type, which is necessary during embryogenesis. These reprogrammed cells are referred to as **embryonic stem cells**. As embryogenesis progresses and cells differentiate, the cells begin to acquire new epigenetic markers. These epigenetic markers have considerable influence on further gene expression and differentiation.

As differentiation continues, certain cells can influence the gene expression of other cells in the process of induction via chemical messengers. Communication between cells is also used to establish positional information in the embryo that is critical to the formation of internal organs as well as the limbs. **Homeobox genes** produce proteins that are essential for guiding the development of the shape of the embryo. The proteins produced by the homeoboxes are transcription factors that serve to turn on specific genes within cells at specific times.

**Induction** helps ensure that the right structures occur in the right places. An additional process that is necessary during embryonic development is **apoptosis** of certain cells. While it seems odd to talk about cell death during development, it is necessary. For example, the separation of fingers and toes is the result of apoptosis of the cells that at one time joined the structures.

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The remainder of embryonic development deals with organogenesis and refining the shape of the embryo. Organ systems are developed on an as-needed basis with the most critical organs being produced first. By the fourth week, the heart is working and limbs are established. By the end of embryonic development (the eighth week), all major organs are established and most are functioning.

### EXTRAEMBRYONIC MEMBRANES

While the embryo is in the process of implanting into the endometrium, four membranes will be formed outside of the embryo. They are as follows:

- The **amnion**. It surrounds the embryo in a fluid-filled sac, which serves a protective function and provides cushioning for the embryo and fetus.
- The **allantois**. It is a membrane that will ultimately form the umbilical cord, which is the connection between the embryo and the placenta (the organ that will deliver nutrients and oxygen and remove carbon dioxide and wastes).
- The **yolk sac**. It is where the first blood cells develop. In other species, it serves as a source of nutrients.
- The **chorion**. It will eventually become the embryo's side of the placenta.

### THE PLACENTA

The **placenta** develops from the chorion and grows in size during development. It provides nutrients and oxygen to the embryo and removes wastes. Recall that fetal hemoglobin has a greater affinity for oxygen than adult hemoglobin. The placenta produces HCG, estrogen, and progesterone to maintain the pregnancy. It also produces the hormone relaxin to release the ligaments that attach the pubic bones to provide more space in the birth canal. It takes about 3 months for the placenta to fully develop.

## Fetal Development

**Fetal development** is primarily a refinement of the organ systems that are already established during embryonic development. The fetus enlarges in size and the organ systems are refined, so that they are all functioning, or are capable of functioning at the end of gestation.

## Birth

Labor is triggered by the hormone oxytocin that is produced by the posterior pituitary gland. **Oxytocin** causes contractions of the uterus, which intensify with time. Initially,

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the cervix must dilate, which can take hours. The amnion usually ruptures during the dilation stage. Once the cervix is dilated, contractions continue, which lead to expulsion of the baby. After the baby is delivered, the umbilical cord is clamped and cut, which severs the connection to the placenta. Finally, the placenta is delivered at the end of labor.