Citric Acid Cycle

The **citric acid cycle** is a cyclical metabolic pathway located in the matrix of mitochondria (Fig. 8.7). The citric acid cycle is also known as the Krebs cycle, after Hans Krebs, the chemist who worked out the fundamentals of the process in the 1930s.

At the start of the citric acid cycle, the (C_2) acetyl group carried by CoA joins with a C_4 molecule, and a C_6 citrate molecule results. During the cycle, oxidation occurs when electrons are accepted by NAD^+ in three instances and by FAD in one instance. Therefore, three NADH and one $FADH_2$ are formed as a result of the citric acid cycle. Also, the acetyl group received from the prep reaction is oxidized to two CO_2 molecules. Substrate-level ATP synthesis is also an important event of the citric acid cycle. In substrate-level ATP synthesis, you will recall, an enzyme passes a high-energy phosphate to ADP, and ATP results.

Because the citric acid cycle turns twice for each original glucose molecule, the inputs and outputs of the citric acid cycle per glucose molecule are as follows:

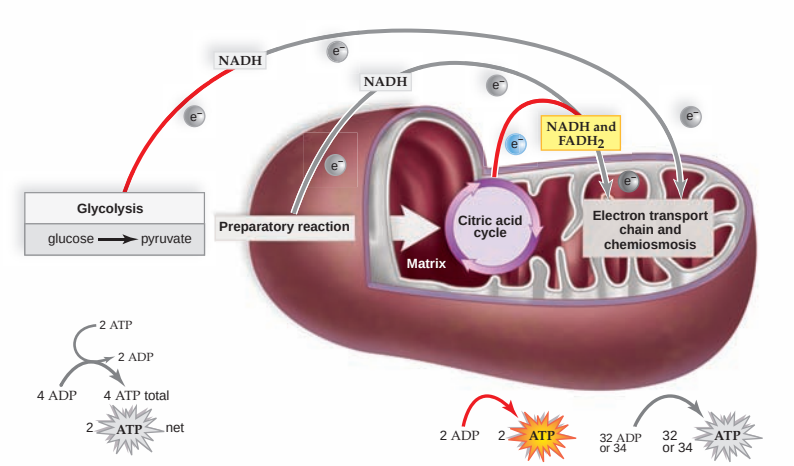
Citric acid cycle

inputs	outputs
2 acetyl groups	4 CO_2
6 NAD^+	6 NADH
2 FAD	2 $FADH_2$
2 ADP + 2 P	2 ATP

Production of CO_2

The six carbon atoms originally located in a glucose molecule have now become CO_2. The prep reaction produces two CO_2, and the citric acid cycle produces four CO_2 per glucose molecule. We have already mentioned that this is the CO_2 humans and other animals breathe out.

Thus far, we have broken down glucose to CO_2 and hydrogen atoms. NADH and $FADH_2$ are in the process of carrying high-energy electrons to the electron transport chain, as discussed next.



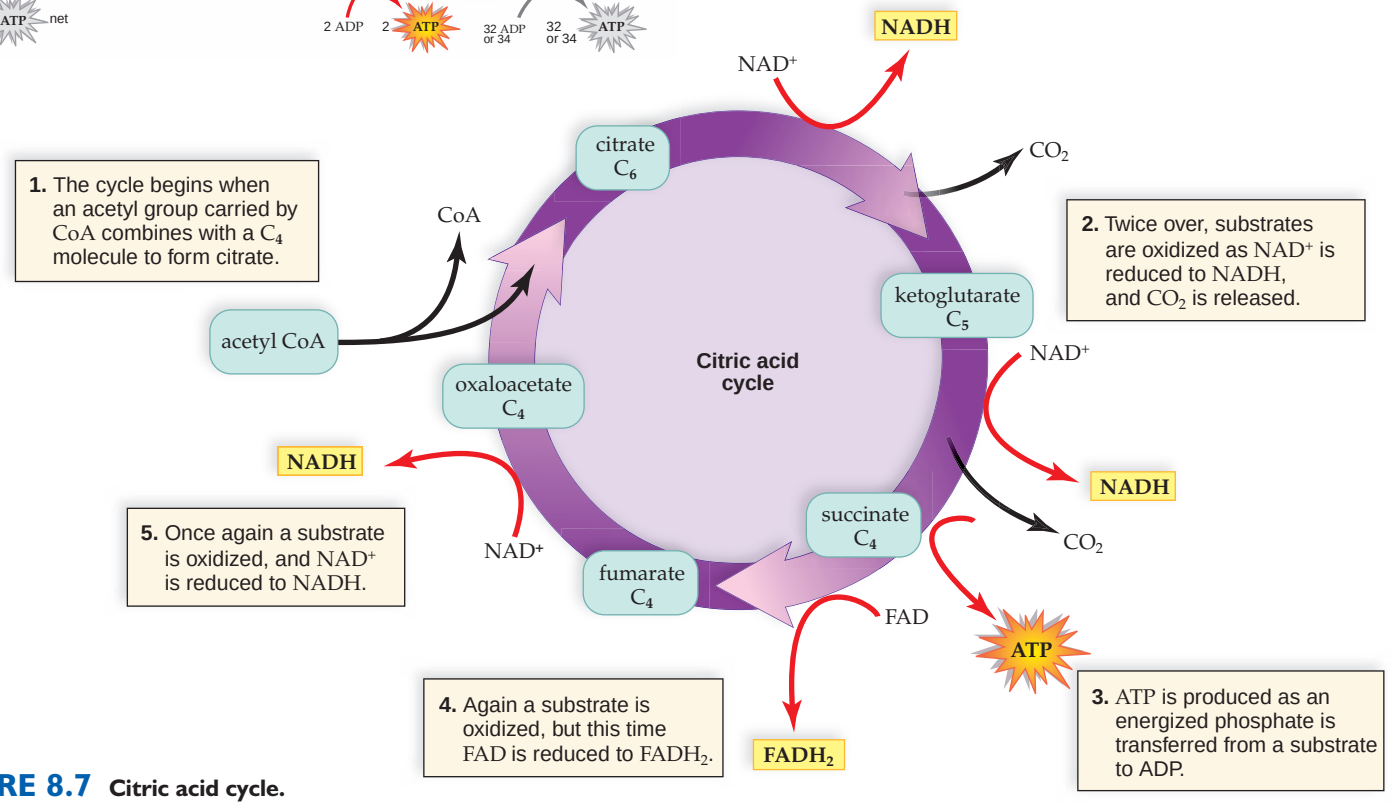


FIGURE 8.7 Citric acid cycle.

Citric acid cycle turns twice per glucose molecule.

Electron Transport Chain

The **electron transport chain (ETC)** located in the cristae of the mitochondria and the plasma membrane of aerobic prokaryotes is a series of carriers that pass electrons from one to the other. The electrons that enter the electron transport chain are carried by NADH and $FADH_2$. Figure 8.8 is arranged to show that high-energy electrons enter the chain, and low-energy electrons leave the chain.

Members of the Chain

When NADH gives up its electrons, it becomes NAD^+, and when $FADH_2$ gives up its electrons, it becomes FAD. The next carrier gains the electrons and is reduced. This oxidation-reduction reaction starts the process, and each of the carriers, in turn, becomes reduced and then oxidized as the electrons move down the chain.

Many of the carriers are cytochrome molecules. A **cytochrome** is a protein that has a tightly bound heme group with a central atom of iron, the same as hemoglobin does. When the iron accepts electrons, it becomes reduced, and when iron gives them up, it becomes oxidized. A number of poisons, such as cyanide, cause death by binding to and blocking the function of cytochromes. As the pair of electrons is passed from carrier to carrier, energy is captured and eventually used to form ATP molecules.

What is the role of oxygen in cellular respiration and the reason we breathe to take in oxygen? Oxygen is the final acceptor of electrons from the electron transport chain. Oxygen receives the energy-spent electrons from the last of the carriers (i.e., cytochrome oxidase). After receiving electrons, oxygen combines with hydrogen ions, and water forms:

$$\tfrac{1}{2}O_2 + 2e^- + 2H^+ \longrightarrow H_2O$$

The critical role of oxygen as the final acceptor of electrons during cellular respiration is exemplified by noting that if oxygen is not present, the chain does not function, and no ATP is produced by mitochondria. The limited capacity of the body to form ATP in a way that does not involve the electron transport chain means that death eventually results if oxygen is not available.

Cycling of Carriers

When NADH delivers electrons to the first carrier of the electron transport chain, enough energy is captured by the time the electrons are received by O_2 to permit the production of three ATP molecules. When $FADH_2$ delivers electrons to the electron transport chain, only two ATP are produced.

Once NADH has delivered electrons to the electron transport chain, it is "free" to return and pick up more hydrogen atoms. The reuse of coenzymes increases cellular efficiency since it does away with the necessity to synthesize them anew.

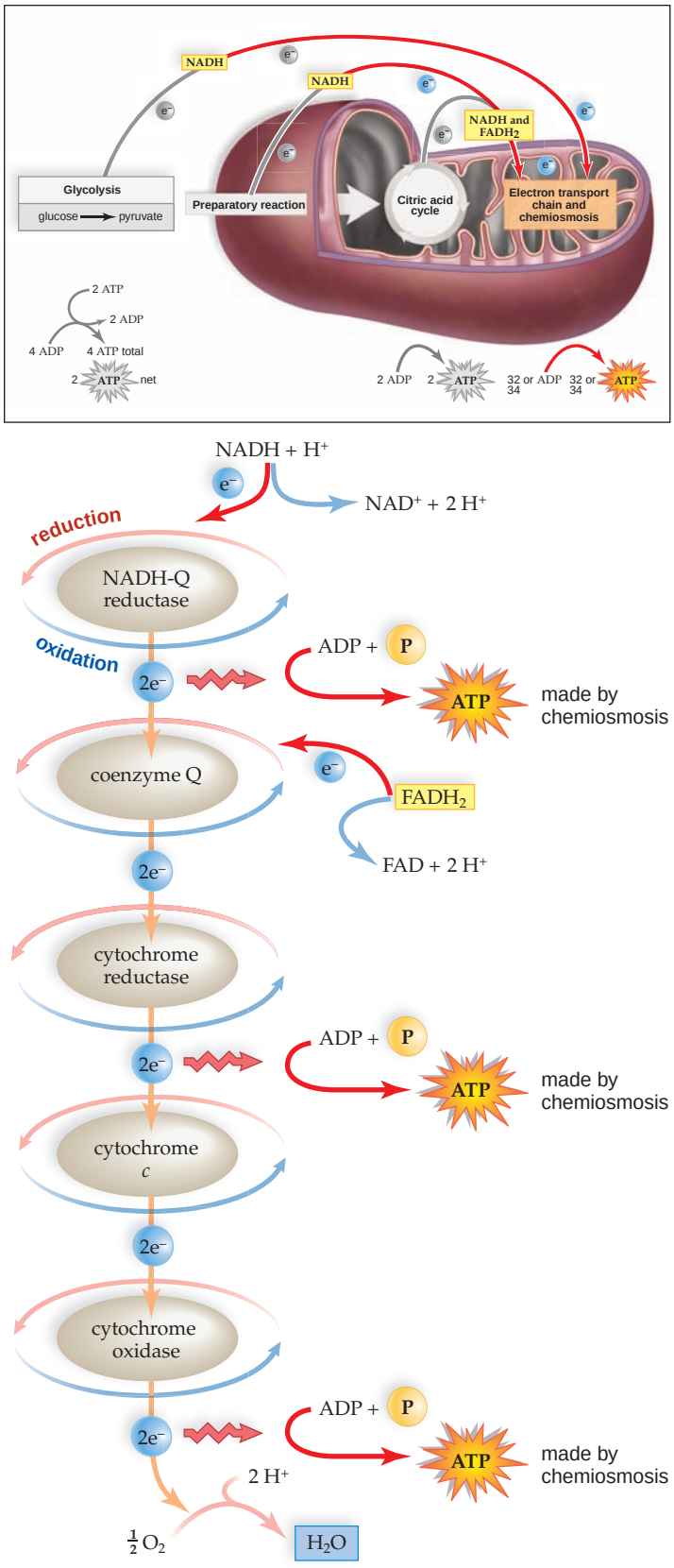


FIGURE 8.8 The electron transport chain (ETC).

NADH and $FADH_2$ bring electrons to the electron transport chain. As the electrons move down the chain, energy is captured and used to form ATP. For every pair of electrons that enters by way of NADH, three ATP result. For every pair of electrons that enters by way of $FADH_2$, two ATP result. Oxygen, the final acceptor of the electrons, becomes a part of water.

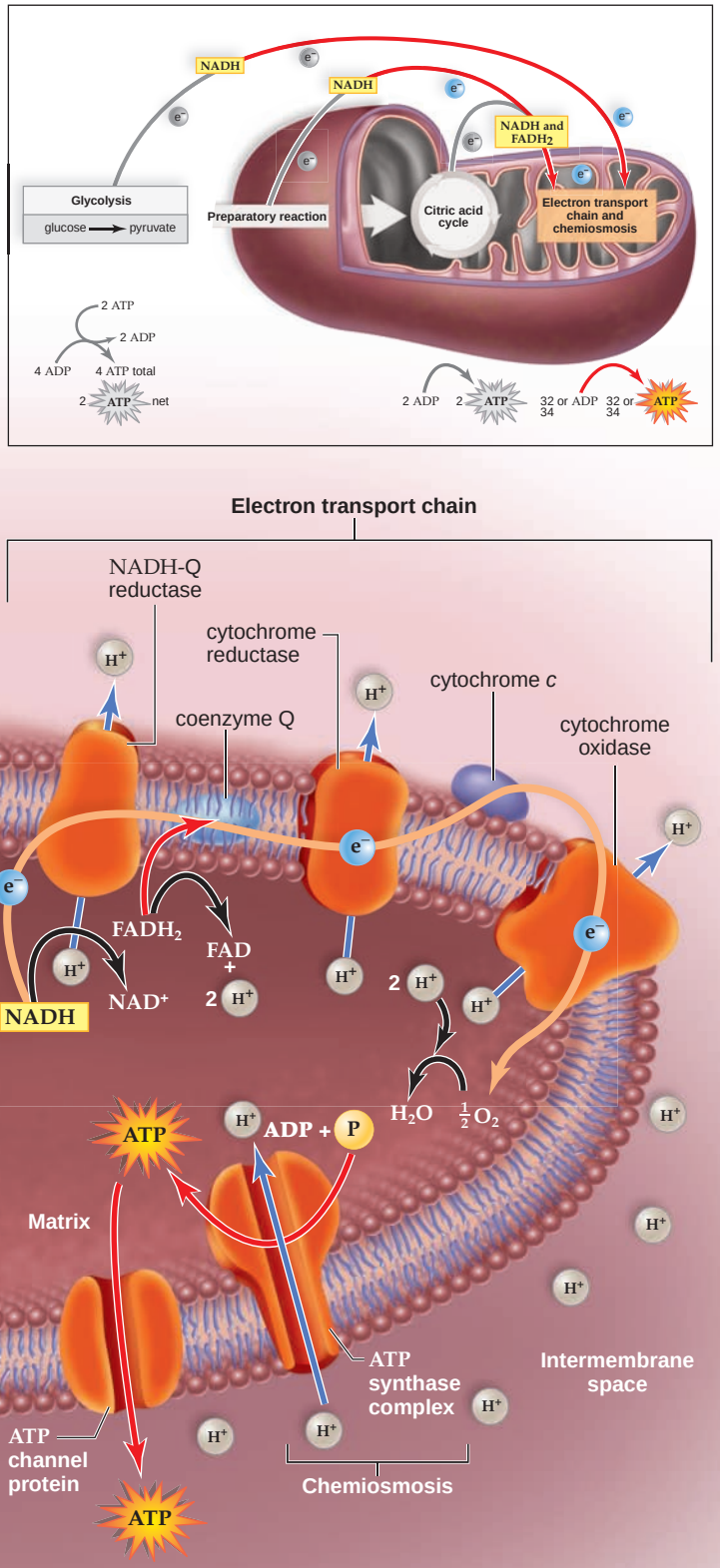


FIGURE 8.9 **Organization and function of cristae.**

The electron transport chain is located in the cristae. As electrons move from one protein complex to the other, hydrogen ions (H^+) are pumped from the matrix into the intermembrane space. As hydrogen ions flow down a concentration gradient from the intermembrane space into the mitochondrial matrix, ATP is synthesized by the enzyme ATP synthase. ATP leaves the matrix by way of a channel protein.

The Cristae of a Mitochondrion and Chemiosmosis

The carriers of the electron transport chain and the proteins concerned with ATP synthesis are spatially arranged on the cristae of mitochondria. Their arrangement on the cristae allows the production of ATP to occur.

The ETC Pumps Hydrogen Ions Essentially, the electron transport chain consists of three protein complexes and two carriers. The three protein complexes include NADH-Q reductase complex, the cytochrome reductase complex, and cytochrome oxidase complex. The two other carriers that transport electrons between the complexes are coenzyme Q and cytochrome *c* (Fig. 8.9).

We have already seen that the members of the electron transport chain accept electrons, which they pass from one to the other. What happens to the hydrogen ions (H^+) carried by NADH and $FADH_2$? The complexes of the electron transport chain use the released energy to pump these hydrogen ions from the matrix into the intermembrane space of a mitochondrion. The vertical arrows in Figure 8.9 show that all the protein complexes of the electron transport chain all pump H^+ into the intermembrane space. Just as the walls of a dam hold back water, allowing it to collect, so do cristae hold back hydrogen ions. Eventually, a strong electrochemical gradient develops; there are about ten times as many H^+ in the intermembrane space as there are in the matrix.

The ATP Synthase Complex Produces ATP The ATP synthase complex can be likened to the gates of a dam. When the gates of a hydroelectric dam are opened, water rushes through, and electricity (energy) is produced. Similarly, when H^+ flows down a gradient from the intermembrane space into the matrix, the enzyme ATP synthase synthesizes ATP from ADP + Ⓟ. This process is called **chemiosmosis** because ATP production is tied to the establishment of an H^+ gradient.

Once formed, ATP moves out of mitochondria and is used to perform cellular work, during which it breaks down to ADP and Ⓟ. Then these molecules are returned to mitochondria for recycling. At any given time, the amount of ATP in a human would sustain life for only about a minute; therefore, ATP synthase must constantly produce ATP. It is estimated that mitochondria produce our body weight in ATP every day.

Active Tissues Contain Mitochondria Active tissues, such as muscles, require greater amounts of ATP and have more mitochondria than less active cells. When a burst of energy is required, however, muscles still ferment.

As an example of the relative amounts of ATP, consider that the dark meat of chickens, the legs, contains more mitochondria than the white meat of the breast. This suggests that chickens mainly walk or run, rather than fly about the barnyard.

Energy Yield from Glucose Metabolism

Figure 8.10 calculates the ATP yield for the complete breakdown of glucose to CO_2 and H_2O during cellular respiration. Notice that the diagram includes the number of ATP produced directly by glycolysis and the citric acid cycle (to the left), as well as the number produced as a result of electrons passing down the electron transport chain (to the right). Thirty-two or 34 ATP molecules are produced by the electron transport chain.

Substrate-Level ATP Synthesis

Per glucose molecule, there is a net gain of two ATP from glycolysis, which takes place in the cytoplasm. The citric acid cycle, which occurs in the matrix of mitochondria, accounts for two ATP per glucose molecule. This means that a total of four ATP are formed by substrate-level ATP synthesis outside the electron transport chain.

ETC and Chemiosmosis

Most ATP is produced by the electron transport chain and chemiosmosis. Per glucose molecule, ten NADH and two $FADH_2$ take electrons to the electron transport chain. For each NADH formed *inside* the mitochondria by the citric acid cycle, three ATP result, but for each $FADH_2$, only two ATP are produced. Figure 8.8 explains the reason for this difference: $FADH_2$ delivers its electrons to the transport chain after NADH, and therefore these electrons cannot account for as much ATP production.

What about the ATP yield per NADH generated *outside* the mitochondria by the glycolytic pathway? In some cells, NADH cannot cross mitochondrial membranes, but a "shuttle" mechanism allows its electrons to be delivered to the electron transport chain inside the mitochondria. The cost to the cell is one ATP for each NADH that is shuttled to the ETC. This reduces the overall count of ATP produced as a result of glycolysis, in some cells, to four instead of six ATP.

Efficiency of Cellular Respiration

It is interesting to calculate how much of the energy in a glucose molecule eventually becomes available to the cell. The difference in energy content between the reactants (glucose and O_2) and the products (CO_2 and H_2O) is 686 kcal. An ATP phosphate bond has an energy content of 7.3 kcal, and 36 of these are usually produced during glucose breakdown; 36 phosphates are equivalent to a total of 263 kcal. Therefore, 263/686, or 39%, of the available energy is usually transferred from glucose to ATP. The rest of the energy is lost in the form of heat.

This concludes our discussion of the phases of cellular respiration, and in the next part of the chapter, we consider how cellular respiration fits into metabolism as a whole.

Check Your Progress 8.4

1. A C_2 acetyl group enters the citric acid cycle. Where does it come from?
2. What are the products of the citric acid cycle per glucose breakdown?
3. Compare the function of the mitochondrial inner molecule to a hydroelectric dam.

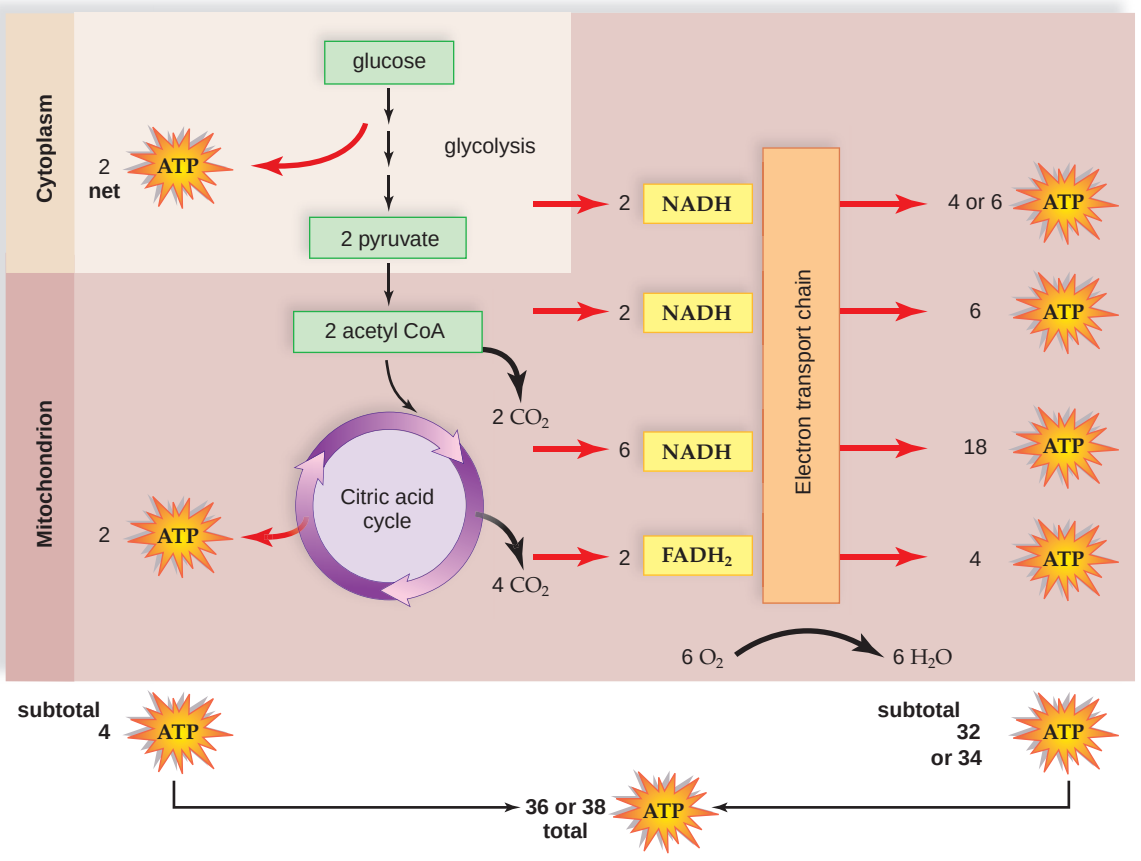


FIGURE 8.10

Accounting of energy yield per glucose molecule breakdown.

Substrate-level ATP synthesis during glycolysis and the citric acid cycle accounts for 4 ATP. The electron transport chain accounts for 32 or 34 ATP, and the grand total of ATP is therefore 36 or 38 ATP. Cells differ as to the delivery of the electrons from NADH generated outside the mitochondria. If they are delivered by a shuttle mechanism to the start of the electron transport chain, 6 ATP result; otherwise, 4 ATP result.

8.5 Metabolic Pool

Certain substrates recur in various key metabolic pathways, and therefore they form a **metabolic pool.** In the metabolic pool, these substrates serve as entry points for the degradation or synthesis of larger molecules (Fig. 8.11). Degradative reactions break down molecules and collectively participate in **catabolism.** The cellular respiration pathways make a significant contribution to catabolism. Synthetic reactions are to be contrasted with catabolic reactions because they build up molecules and collectively participate in anabolism.

Catabolism

We already know that glucose is broken down during cellular respiration. However, other molecules can also undergo catabolism. When a fat is used as an energy source, it breaks down to glycerol and three fatty acids. As Figure 8.11 indicates, glycerol can enter glycolysis. The fatty acids are converted to acetyl CoA, and the acetyl group enters the citric acid cycle. An 18-carbon fatty acid results in nine acetyl CoA molecules. Calculation shows that respiration of these can produce a total of 108 ATP molecules. For this reason, fats are an efficient form of stored energy—there are three long fatty acid chains per fat molecule.

The carbon skeleton of amino acids can enter glycolysis, be converted to acetyl group, or enter the citric acid cycle at some other juncture. The carbon skeleton is produced in the liver when an amino acid undergoes **deamination,** or the removal of the amino group. The amino group becomes ammonia (NH_3), which enters the urea cycle and becomes part of urea, the primary excretory product of humans. Just where the carbon skeleton begins degradation depends on the length of the *R* group, since this determines the number of carbons left after deamination.

Anabolism

We have already mentioned that the ATP produced during catabolism drives anabolism. But catabolism is also related to anabolism in another way. The substrates making up the pathways in Figure 8.11 can be used as starting materials for synthetic reactions. In other words, compounds that enter the pathways are oxidized to substrates that can be used for biosynthesis. This is the cell's metabolic pool, in which one type of molecule can be converted to another. In this way, carbohydrate intake can result in the formation of fat. G3P from glycolysis can be converted to glycerol, and acetyl groups from glycolysis can be joined to form fatty acids. Fat synthesis follows. This explains why you gain weight from eating too much candy, ice cream, or cake.

Some substrates of the citric acid cycle can be converted to amino acids through transamination—the transfer of an amino group to an organic acid, forming a different amino acid. Plants are able to synthesize all of the amino acids they need. Animals, however, lack some of the enzymes necessary for synthesis of all amino acids. Adult humans, for example, can synthesize 11 of the common amino acids, but they cannot synthesize the other 9. The amino acids that cannot be synthesized must be supplied by the diet; they are called the essential amino acids. (The amino acids that can be synthesized are called nonessential.) It is quite possible for animals to suffer from protein deficiency if their diets do not contain adequate quantities of all the essential amino acids.

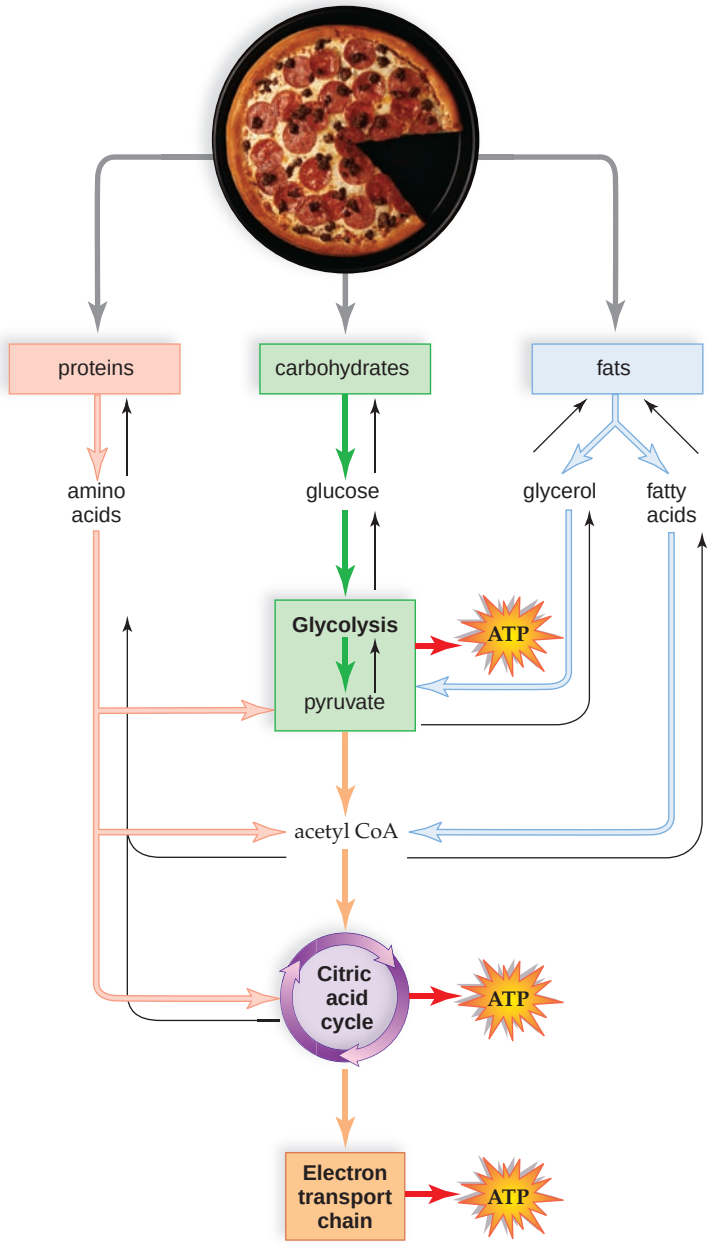


FIGURE 8.11 The metabolic pool concept.

Carbohydrates, fats, and proteins can be used as energy sources, and their monomers (carbohydrates and proteins) or subunits (fats) enter degradative pathways at specific points. Catabolism produces molecules that can also be used for anabolism of other compounds.

The Energy Organelles Revisited

The equation for photosynthesis in a chloroplast is opposite to that of cellular respiration in a mitochondrion (Fig. 8.12):

$$\text{energy} + 6\,CO_2 + 6\,H_2O \underset{\text{cellular respiration}}{\overset{\text{photosynthesis}}{\rightleftharpoons}} C_6H_{12}O_6 + 6\,O_2$$

Even so, while you were studying photosynthesis and cellular respiration, you may have noticed a remarkable similarity in the organization of chloroplasts and mitochondria. Through evolution, all organisms are related, and the similar organization of these organelles suggests that they may be related also. This list summarizes the likeness of the two organelles as they carry out opposite processes:

1. Use of membrane. In a chloroplast, an inner membrane forms the thylakoids of the grana. In a mitochondrion, an inner membrane forms the convoluted cristae.
2. Electron transport chain (ETC). An ETC is located on the thylakoid membrane of chloroplasts and the cristae of mitochondria. In chloroplasts, the electrons passed down the ETC have been energized by the sun; in mitochondria, energized electrons have been removed from glucose and glucose products. In both, the ETC establishes an electrochemical gradient of H^+ with subsequence ATP production by chemiosmosis.
3. Enzymes. In a chloroplast, the stroma contains the enzymes of the Calvin cycle and in mitochondria, the matrix contains the enzymes of the citric acid cycle. In the Calvin cycle, NADPH and ATP are used to reduce carbon dioxide to a carbohydrate. In the citric acid cycle, the oxidation of glucose products occurs as NADH and ATP are produced.

Flow of Energy

The ultimate source of energy for producing a carbohydrate in chloroplasts is the sun; the ultimate goal of cellular respiration in a mitochondrion is the conversion of carbohydrate energy into that of ATP molecules. Therefore, there is a flow of energy through chloroplasts to carbohydrates and then through mitochondria to ATP molecules.

This flow of energy maintains biological organization at all levels from molecules, organisms, and the biosphere. In keeping with the energy laws, useful energy is lost with each chemical transformation: as carbohydrate is made and as food is captured and used by all members of food chains. Eventually, the solar energy captured by plants is lost in the form of heat. Therefore, living things are dependent on a continual input of solar energy.

Although energy flows through organisms, chemicals cycle. All living things utilize the carbohydrate and oxygen produced by chloroplasts, but they return to chloroplasts, and the carbon dioxide produced by mitochondria return to chloroplasts. Therefore, chloroplasts and mitochondria are instrumental in not only allowing a flow of energy through living things, they also permit a cycling of chemicals.

Check Your Progress 8.5

1. In Chapter 3, you learned the terms dehydration reaction and hydrolytic reaction. **a.** Which type of reaction is catabolic? Anabolic? **b.** Which term could be associated with ATP breakdown?
2. Compare the structure and function of chloroplasts and mitochondria.

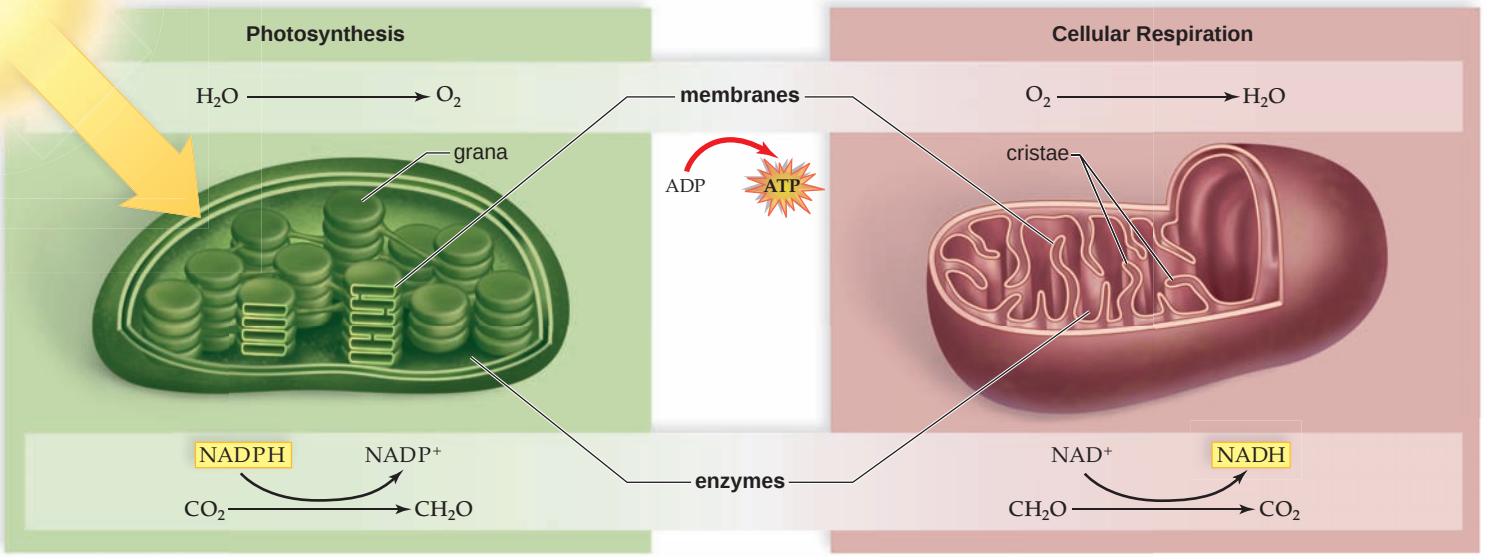


FIGURE 8.12 Photosynthesis versus cellular respiration.

Above: In photosynthesis, water is oxidized and oxygen is released; in cellular respiration, oxygen is reduced to water. *Middle:* Both processes have an electron transport chain located within membranes (the grana of chloroplasts and the cristae of mitochondria), where ATP is produced by chemiosmosis. *Below:* Both have enzyme-catalyzed reactions within the semifluid interior. In photosynthesis, CO_2 is reduced to a carbohydrate; in cellular respiration, a carbohydrate is oxidized to CO_2.

Connecting the Concepts

Chloroplasts and mitochondria play a significant role in metabolism and their enzyme-requiring pathways permit a flow of energy through all living things. The energy transformations that take place in these organelles results in a loss of energy in the form of heat. Therefore, all organisms are in need of a constant supply of energy, which they get from their food. Food is ultimately produced by plants, which have the ability to capture solar energy.

"Structure suits function" is a concept well exemplified by chloroplasts and mitochondria. Their membranous structure is well suited to the isolation of enzymatic reactions in the interior from complexes located on the membrane. As high-energy electrons make energy available, these complexes pump H^+ ions into the thylakoid space of chloroplasts and the intermembrane space of mitochondria. When H^+ flows down its concentration gradient through ATP synthase complexes, ATP synthesis results. ATP production in mitochondria is traceable back to the ability of chloroplasts to capture solar energy.

In the next part of the text, we depart from metabolism briefly to learn certain laws of genetics. Mendelian genetics will allow you to predict chances an offspring will have particular traits, including genetic disorders. Such disorders stem from a faulty genetic code that results in malformed proteins, including enzymes. The twentieth century was the age of genetics, during which scientists discovered that the genes are on the chromosomes housed in the nucleus. These scientists defined genes as a sequence of nitrogen-containing bases that code for a sequence of amino acids in a protein. When we study the details of protein synthesis, we are once again studying metabolism. Scientists of the twenty-first century are in the process of redefining genes as a result of analyzing the data gathered from the Human Genome Project.

summary

8.1 Cellular Respiration

Cellular respiration, during which glucose is completely broken down to CO_2 and H_2O, consists of four phases: glycolysis, the prep reaction, the citric acid cycle, and the passage of electrons along the electron transport chain. Oxidation of substrates involves the removal of hydrogen atoms ($H^+ + e^-$), usually by redox coenzymes. NAD^+ becomes NADH, and FAD becomes $FADH_2$.

8.2 Outside the Mitochondria: Glycolysis

Glycolysis, the breakdown of glucose to two molecules of pyruvate, is a series of enzymatic reactions that occur in the cytoplasm and is anaerobic. Breakdown releases enough energy to immediately give a net gain of two ATP by substrate-level ATP synthesis and the production of 2 NADH.

8.3 Fermentation

Fermentation involves glycolysis followed by the reduction of pyruvate by NADH either to lactate (animals) or to alcohol and carbon dioxide (CO_2) (yeast). The reduction process "frees" NAD^+ so that it can accept more hydrogen atoms from glycolysis.

Although fermentation results in only two ATP molecules, it still serves a purpose. Many of the products of fermentation are used in the baking and brewing industries. In vertebrates, it provides a quick burst of ATP energy for short-term, strenuous muscular activity. The accumulation of lactate puts the individual in oxygen debt because oxygen is needed when lactate is completely metabolized to CO_2 and H_2O.

8.4 Inside the Mitochondria

When oxygen is available, pyruvate from glycolysis enters the mitochondrion, where the prep reaction takes place. During this reaction, oxidation occurs as CO_2 is removed from pyruvate. NAD^+ is reduced, and CoA receives the C_2 acetyl group that remains. Since the reaction must take place twice per glucose molecule, two NADH result.

The acetyl group enters the citric acid cycle, a cyclical series of reactions located in the mitochondrial matrix. Complete oxidation follows, as two CO_2 molecules, three NADH molecules, and one $FADH_2$ molecule are formed. The cycle also produces one ATP molecule. The entire cycle must turn twice per glucose molecule.

The final stage of glucose breakdown involves the electron transport chain located in the cristae of the mitochondria. The electrons received from NADH and $FADH_2$ are passed down a chain of carriers until they are finally received by oxygen, which combines with H^+ to produce water. As the electrons pass down the chain, energy is captured and stored for ATP production.

The cristae of mitochondria contain complexes of the electron transport chain that not only pass electrons from one to the other but also pump H^+ into the intermembrane space, setting up an electrochemical gradient. When H^+ flows down this gradient through an ATP synthase complex, energy is captured and used to form ATP molecules from ADP and Ⓟ. This is ATP synthesis by chemiosmosis.

Of the 36 or 38 ATP formed by complete glucose breakdown, four are the result of substrate-level ATP synthesis and the rest are produced as a result of the electron transport chain. For most NADH molecules that donate electrons to the electron transport chain, three ATP molecules are produced. However, in some cells, each NADH formed in the cytoplasm results in only two ATP molecules because a shuttle, rather than NADH, takes electrons through the mitochondrial membrane. $FADH_2$ results in the formation of only two ATP because its electrons enter the electron transport chain at a lower energy level.

8.5 Metabolic Pool

Carbohydrate, protein, and fat can be metabolized by entering the degradative pathways at different locations. These pathways also provide metabolites needed for the anabolism of various important substances. Therefore, catabolism and anabolism both use the same pools of metabolites.

Similar to the metabolic pool concept, photosynthesis and cellular respiration can be compared. For example, both utilize an ETC and chemiosmosis. As a result of the ETC in chloroplasts, water is split, while in mitochondria, water is formed. The enzymatic reactions in chloroplasts reduce CO_2 to a carbohydrate, while the enzymatic reactions in mitochondria oxidize carbohydrate with the release of CO_2.

understanding the terms

aerobic 135
anaerobic 135
catabolism 145
cellular respiration 134
chemiosmosis 143
citric acid cycle 135, 141
cytochrome 142
deamination 145
electron transport chain (ETC) 135, 142
FAD 134
fermentation 135, 138
glycolysis 135, 136
metabolic pool 145
mitochondrion 140
NAD^+ 134
oxygen debt 138
preparatory (prep) reaction 135, 140
pyruvate 135
substrate-level ATP synthesis 136

Match the terms to these definitions:

a. _____ A metabolic pathway that begins with glucose and ends with two molecules of pyruvate.
b. _____ Occurs due to the accumulation of lactate following vigorous exercise.
c. _____ Metabolic process that degrades molecules and tends to be exergonic.
d. _____ Metabolites that are the products of and/or the substrates for key reactions in cells.
e. _____ Uses a hydrogen ion gradient to drive ATP formation.

reviewing this chapter

1. What is the overall chemical equation for the complete breakdown of glucose to CO_2 and H_2O? Explain how this is an oxidation-reduction reaction. 134
2. What are NAD^+ and FAD? What are their functions? 134
3. Briefly describe the four phases of cellular respiration. 135
4. What are the main events of glycolysis? How is ATP formed? 136–37
5. What is fermentation, and how does it differ from glycolysis? Mention the benefit of pyruvate reduction during fermentation. What types of organisms carry out lactic acid fermentation, and what types carry out alcoholic fermentation? 138–39
6. Give the substrates and products of the prep reaction. Where does it take place? 140
7. What are the main events of the citric acid cycle? 141
8. What is the electron transport chain, and what are its functions? 142
9. Describe the organization of protein complexes within the cristae. Explain how the complexes are involved in ATP production. 143
10. Calculate the energy yield of glycolysis and complete glucose breakdown. Compare the yields from substrate-level ATP synthesis and from the electron transport chain. 144
11. Give examples to support the concept of the metabolic pool. 145
12. Compare the structure and function of chloroplasts and mitochondria. Explain the flow of energy concept. 146

testing yourself

Choose the best answer for each question.
For questions 1–8, identify the pathway involved by matching each description to the terms in the key.

KEY:
a. glycolysis
b. citric acid cycle
c. electron transport chain

1. carbon dioxide (CO_2) given off
2. water (H_2O) formed
3. G3P
4. NADH becomes NAD^+
5. pump H^+
6. cytochrome carriers
7. pyruvate
8. FAD becomes $FADH_2$
9. The prep reaction
   a. connects glycolysis to the citric acid cycle.
   b. gives off CO_2.
   c. uses NAD^+.
   d. results in an acetyl group.
   e. All of these are correct.
10. The greatest contributor of electrons to the electron transport chain is
    a. oxygen.
    b. glycolysis.
    c. the citric acid cycle.
    d. the prep reaction.
    e. fermentation.
11. Substrate-level ATP synthesis takes place in
    a. glycolysis and the citric acid cycle.
    b. the electron transport chain and the prep reaction.
    c. glycolysis and the electron transport chain.
    d. the citric acid cycle and the prep reaction.
    e. Both b and d are correct.
12. Which of these is not true of fermentation?
    a. net gain of only two ATP
    b. occurs in cytoplasm
    c. NADH donates electrons to electron transport chain
    d. begins with glucose
    e. carried on by yeast
13. Fatty acids are broken down to
    a. pyruvate molecules, which take electrons to the electron transport chain.
    b. acetyl groups, which enter the citric acid cycle.
    c. amino acids, which excrete ammonia.
    d. glycerol, which is found in fats.
    e. All of these are correct.
14. How many ATP molecules are usually produced per NADH?
    a. 1 c. 36
    b. 3 d. 10
15. How many NADH molecules are produced during the complete breakdown of one molecule of glucose?
    a. 5 c. 10
    b. 30 d. 6

16. What is the name of the process that adds the third phosphate to an ADP molecule using the flow of hydrogen ions?
    a. substrate-level ATP synthesis
    b. fermentation
    c. reduction
    d. chemiosmosis

17. Which are possible products of fermentation?
    a. lactic acid
    b. alcohol
    c. CO_2
    d. All of these are possible.

18. The metabolic process that produces the most ATP molecules is
    a. glycolysis.
    b. citric acid cycle.
    c. electron transport chain.
    d. fermentation.

19. Which of these is not true of the citric acid cycle? The citric acid cycle
    a. includes the prep reaction.
    b. produces ATP by substrate-level ATP synthesis.
    c. occurs in the mitochondria.
    d. is a metabolic pathway, as is glycolysis.

20. Which of these is not true of the electron transport chain? The electron transport chain
    a. is located on the cristae.
    b. produces more NADH than any metabolic pathway.
    c. contains cytochrome molecules.
    d. ends when oxygen accepts electrons.

21. Which of these is not true of the prep reaction? The prep reaction
    a. begins with pyruvate and ends with acetyl CoA.
    b. produces more NADH than does glycolysis.
    c. occurs in the mitochondria.
    d. occurs after glycolysis and before the citric acid cycle.

22. The oxygen required by cellular respiration is reduced and becomes part of which molecule?
    a. ATP
    b. H_2O
    c. pyruvate
    d. CO_2

For questions 23–26, match each pathway to metabolite in the key. Choose more than one if correct.

KEY:
    a. pyruvate
    b. acetyl CoA
    c. G3P
    d. NADH
    e. None of these are correct.

23. electron transport chain

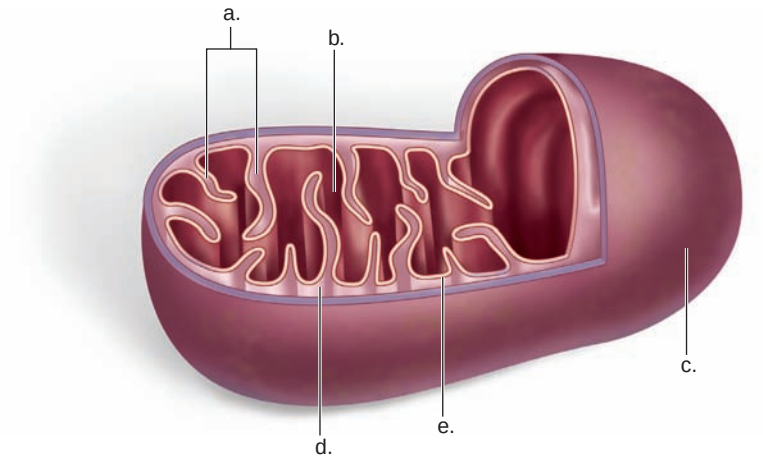
24. glycolysis

25. citric acid cycle

26. prep reaction

27. Which of these is not true of glycolysis? Glycolysis
    a. is anaerobic.
    b. occurs in the cytoplasm.
    c. is a part of fermentation.
    d. evolved after the citric acid cycle.

28. Label this diagram of a mitochondrion, and state a function for each portion indicated.



thinking scientifically

1. You are able to extract mitochondria from the cell and remove the outer membrane. You want to show that the mitochondria can still produce ATP if placed in the right solution. The solution should be isotonic, but at what pH? Why?
2. You are working with acetyl CoA molecules that contain only radioactive carbon. They are incubated with all the components of the citric acid cycle long enough for one turn of the cycle. Examine Figure 8.7 and explain why the carbon dioxide given off is radioactive.

bioethical issue

Alternative Medicine

Feeling tired and run-down? Want to jump-start your mitochondria? If you seem to have no specific ailment, you might be tempted to turn to what is now called alternative medicine. Alternative medicine includes such nonconventional therapies as herbal supplements, acupuncture, chiropractic therapy, homeopathy, osteopathy, and therapeutic touch (e.g., laying on of hands).

Advocates of alternative medicine have made some headway in having alternative medicine practices accepted by almost anyone. For example, Congress has established the National Center for Complementary and Alternative Medicine. It has also passed the Dietary Supplement Health and Education Act, which allows vitamins, minerals, and herbs to be marketed without first being approved by the Food and Drug Administration (FDA).

But is this a mistake? Many physicians believe control studies are needed to test the efficacy of alternative medications and practices. Do you agree, or is word of mouth good enough?

Biology website

The companion website for *Biology* provides a wealth of information organized and integrated by chapter. You will find practice tests, animations, videos, and much more that will complement your learning and understanding of general biology.

http://www.mhhe.com/maderbiology10

part II

Genetic Basis of Life

This part gives you a wonderful opportunity to become acquainted with the basics of Mendelian and molecular genetics. Mendelian genetics can help you predict your chances of having a child with a genetic disorder, and DNA technology can suggest possible procedures to prevent such an occurrence. The potential to cure genetic diseases has expanded greatly now that the human genome has been sequenced, and we know the order of the base pairs in our DNA. Yet, genetic advances are fraught with ethical decisions, such as whether the cloning of humans should be permissible or how far to go in shaping the traits of our children.

The field of genetics is making progress in other areas too. We are beginning to understand how cell division is regulated by various genes. Improper regulation of cell division leads to cancer, and therefore we need to know as much as possible about proper regulation if cancer is to be prevented. At every turn, it is clear that you can't be a part of the happenings of the twenty-first century without a knowledge of genetics, and this is your chance to become a part of the action.

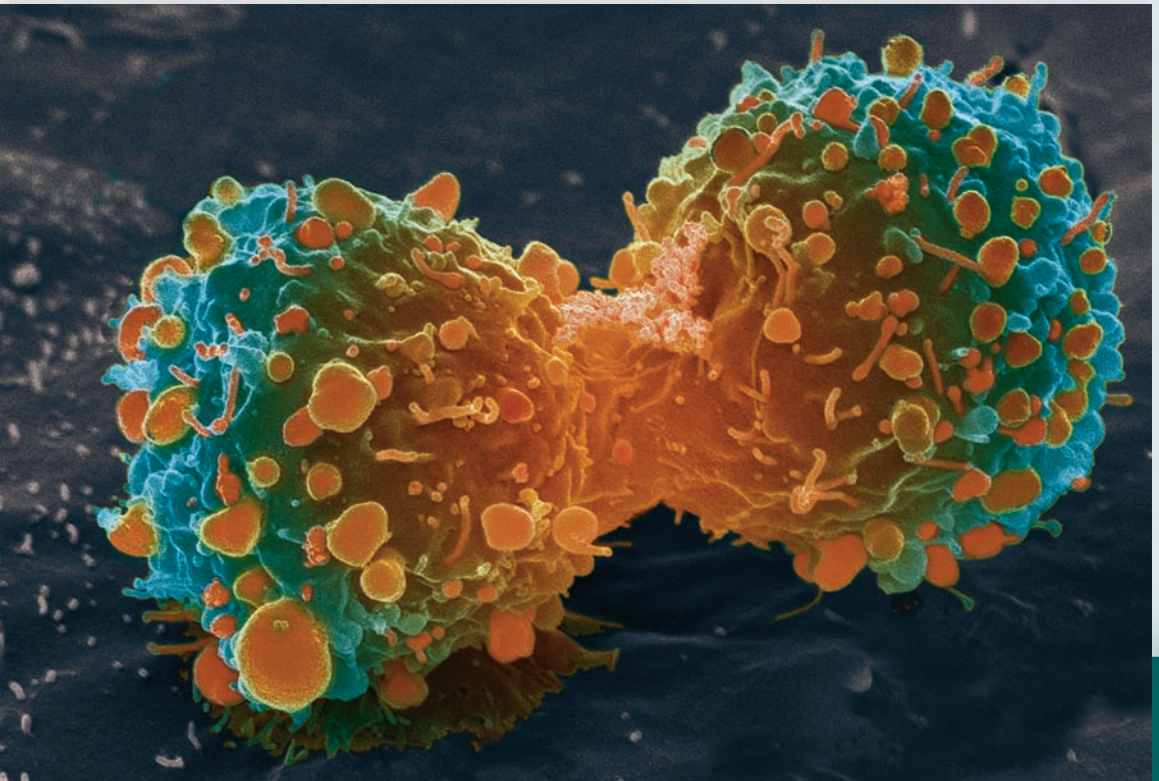
9

The Cell Cycle and Cellular Reproduction

Consider the development of a human being. A new life begins as one cell—an egg fertilized by a sperm. Yet in nine short months, a human becomes a complex organism consisting of trillions of cells. How is such a feat possible? Cell division enables a single cell to eventually produce many cells, allowing an organism to grow and develop. Cell division also occurs when repair is needed and worn-out tissues have to be replaced. Adult humans have over 200 different types of specialized cells working together in harmony.

Genes code for signaling molecules that turn on and off the process of cell division. During the first part of an organism's life, all cells divide. When adulthood is reached, however, only specific cells—human blood and skin cells, for example—continue to divide daily. Other cells, such as nerve cells, no longer routinely divide and produce new cells. Cancer results when the genes that code for signaling proteins mutate and cell division occurs nonstop. The following chapter describes the process of cell division, how it is regulated, and how cancer may develop when regulatory mechanisms malfunction.

Cancer cell dividing.



concepts

9.1 THE CELL CYCLE

- The cell cycle is a repeating sequence of growth, replication of DNA, and cell division. 152–53
- The cell cycle is tightly controlled; it can stop at three different checkpoints if conditions are not normal. 152–53
- Most cells are permanently arrested and will not complete the cell cycle without proper signals from nearby or distant tissues. 153
- The cell cycle, which leads to an increase in cell number, is opposed by apoptosis, which is programmed cell death. 153

9.2 MITOSIS AND CYTOKINESIS

- Cell division consists of mitosis and cytokinesis. Mitosis is nuclear division, and cytokinesis is division of the cytoplasm. 155–59
- Following mitosis, each daughter nucleus has the same number of chromosomes as the parent cell. 155–58
- Once cytokinesis has occurred following mitosis, two daughter cells are present. 158–59

9.3 THE CELL CYCLE AND CANCER

- Cancer develops when mutations lead to a loss of cell cycle control. 161–63
- Cancer cells develop characteristics that can be associated with their ability to divide uncontrollably. 161–63

9.4 PROKARYOTIC CELL DIVISION

- Binary fission is a type of cell division that ensures each new prokaryotic cell has a single circular chromosome. 164
- In prokaryotes, binary fission is a form of asexual reproduction. In eukaryotes, mitosis permits renewal and repair. 164–65

9.1 The Cell Cycle

The **cell cycle** is an orderly set of stages that take place between the time a eukaryotic cell divides and the time the resulting daughter cells also divide. When a cell is going to divide, it grows larger, the number of organelles doubles, and the amount of DNA doubles as DNA replication occurs. The two portions of the cell cycle are interphase, which includes a number of stages, and the mitotic stage when mitosis and cytokinesis occur.

Interphase

As Figure 9.1 shows, most of the cell cycle is spent in **interphase.** This is the time when a cell performs its usual functions, depending on its location in the body. The amount of time the cell takes for interphase varies widely. Embryonic cells complete the entire cell cycle in just a few hours. For adult mammalian cells, interphase lasts for about 20 hours, which is 90% of the cell cycle. In the past, interphase was known as the resting stage. However, today it is known that interphase is very busy, and that preparations are being made for mitosis. Interphase consists of three stages, referred to as G_1, S, and G_2.

G_1 Stage

Cell biologists named the stage before DNA replication G_1, and they named the stage after DNA replication G_2. G stood for "gap," but now that we know how metabolically active the cell is, it is better to think of G as standing for "growth." During G_1, the cell recovers from the previous division. Then, the cell increases in size, doubles its organelles (such as mitochondria and ribosomes), and accumulates materials that will be used for DNA synthesis. Otherwise, during G_1, cells are constantly performing their normal daily functions, including communicating with other cells, secreting substances, and carrying out cellular respiration.

Some cells, such as nerve and muscle cells, typically do not complete the cell cycle and are permanently arrested. These cells are said to have entered a G_0 stage. While the cells continue to perform normal everyday processes, there are no preparations being made for cell division, and cells may not leave G_0 stage without proper signals from other cells and other parts of the body. Thus, completion of the cell cycle is very tightly controlled.

S Stage

Following G_1, the cell enters the S stage, when DNA synthesis or replication occurs. At the beginning of the S stage, each chromosome is composed of one DNA double helix. Following DNA replication, each chromosome is composed of two identical DNA double helix molecules. Each double helix is called a **chromatid.** Another way of expressing these events is to say that DNA replication has resulted in duplicated chromosomes, and the two chromatids will remain attached until they are separated during mitosis.

G_2 Stage

Following the S stage, G_2 is the stage from the completion of DNA replication to the onset of mitosis. During this stage, the cell synthesizes proteins that will assist cell division. For example, it makes the proteins that form microtubules. Microtubules are used during the mitotic stage to form the mitotic spindle.

M (Mitotic) Stage

Following interphase, the cell enters the M (for mitotic) stage. This cell division stage includes **mitosis** (nuclear division) and **cytokinesis** (division of the cytoplasm). During mitosis, daughter chromosomes are distributed by the **mitotic spindle** to two daughter nuclei. When division of the cytoplasm is complete, two daughter cells are present.

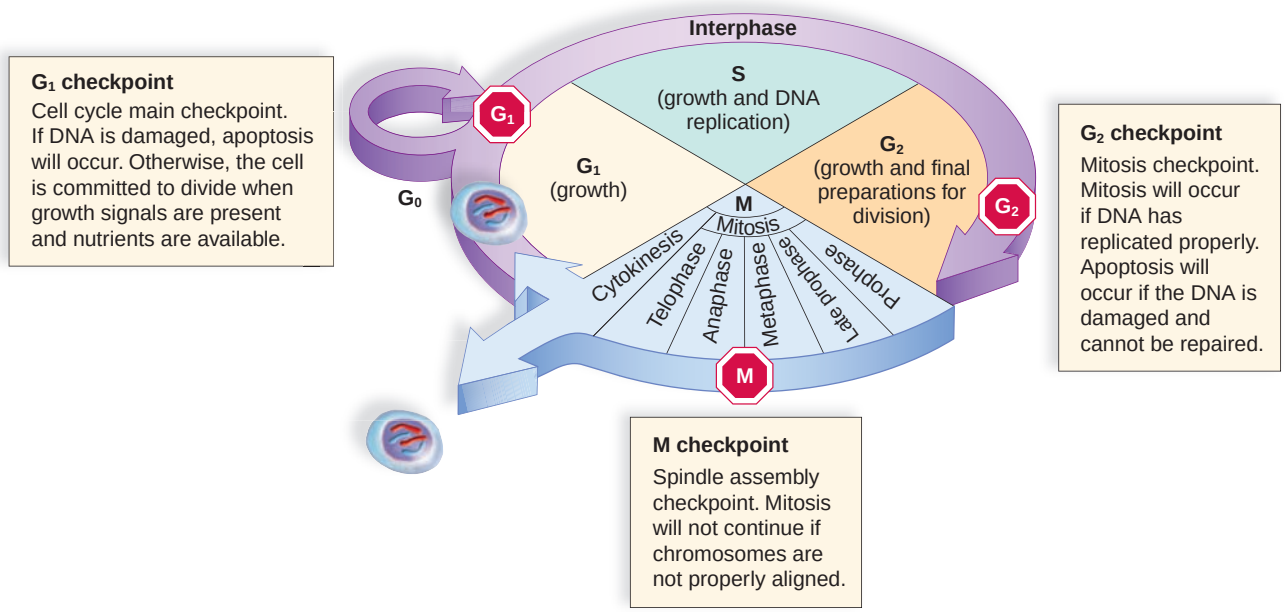


FIGURE 9.1 The cell cycle.

Cells go through a cycle that consists of four stages: G_1, S, G_2, and M. The major activities and checkpoints for each stage are given.

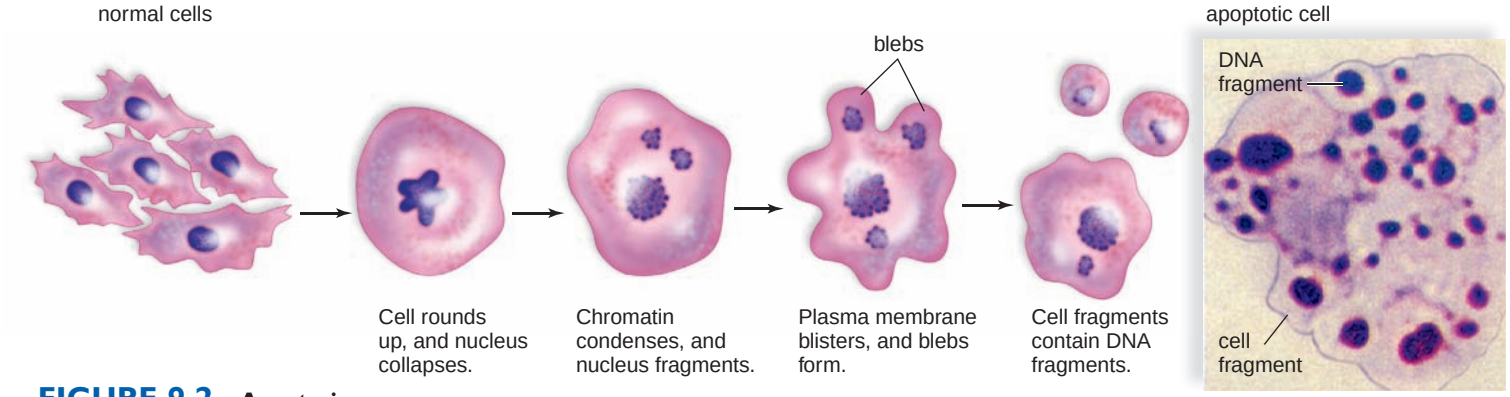


FIGURE 9.2 Apoptosis.

Apoptosis is a sequence of events that results in a fragmented cell. The fragments are phagocytized (engulfed) by white blood cells and neighboring tissue cells.

Control of the Cell Cycle

A **signal** is an agent that influences the activities of a cell. **Growth factors** are signaling proteins received at the plasma membrane. Even cells arrested in G_0 will finish the cell cycle if stimulated to do so by growth factors. In general, signals ensure that the cell cycle stages follow one another in the normal sequence.

Cell Cycle Checkpoints

The red barriers in Figure 9.1 represent three checkpoints when the cell cycle either stops or continues on, depending on the internal signal it receives. Researchers have identified a family of internal signaling proteins called **cyclins** that increase and decrease as the cell cycle continues. Specific cyclins must be present for the cell to proceed from the G_1 stage to the S stage and for the cell to proceed from the G_2 stage to the M stage.

As discussed in the Science Focus on the next page, the primary checkpoint of the cell cycle is the G_1 checkpoint. In mammalian cells, the signaling protein **p53** (p stands for *p*rotein and 53 stands for a molecular weight of 53,000 g) stops the cycle at the G_1 checkpoint when DNA is damaged. First, p53 attempts to initiate DNA repair, but rising levels bring about **apoptosis,** which is programmed cell death (Fig. 9.2). Another protein, called **RB,** is responsible for interpreting growth signals and also nutrient availability signals. RB stands for *r*etino*b*lastoma, a cancer of the retina that occurs when the *RB* gene undergoes a mutation.

The cell cycle may also stop at the G_2 checkpoint if DNA has not finished replicating. This prevents the initiation of the M stage before completion of the S stage. If DNA is physically damaged, such as from exposure to solar radiation or X-rays, the G_2 checkpoint also offers the opportunity for DNA to be repaired.

Another cell cycle checkpoint occurs during the mitotic stage. The cycle stops if the chromosomes are not properly attached to the mitotic spindle. Normally, the mitotic spindle ensures that the chromosomes are distributed accurately to the daughter cells.

Apoptosis

Apoptosis is often defined as programmed cell death because the cell progresses through a usual series of events that bring about its destruction (Fig. 9.2). The cell rounds up, causing it to lose contact with its neighbors. The nucleus fragments, and the plasma membrane develops blisters. Finally, the cell fragments are engulfed by white blood cells and/or neighboring cells. A remarkable finding of the past few years is that the enzymes that bring about apoptosis, called **caspases,** are always present in the cell. The enzymes are ordinarily held in check by inhibitors but can be unleashed by either internal or external signals.

Apoptosis and Cell Division. In living systems, opposing events keep the body in balance and maintain homeostasis. For now, consider that some carrier proteins transport molecules into the cell, and others transport molecules out of the cell. Some hormones increase the level of blood glucose, and others decrease the level. Similarly, cell division and apoptosis are two opposing processes that keep the number of cells in the body at an appropriate level. Cell division increases and apoptosis decreases the number of **somatic** (body) **cells.** Both mitosis and apoptosis are normal parts of growth and development. An organism begins as a single cell that repeatedly divides to produce many cells, but eventually some cells must die for the organism to take shape. For example, when a tadpole becomes a frog, the tail disappears as apoptosis occurs. The fingers and toes of a human embryo are at first webbed, but then they are usually freed from one another as a result of apoptosis.

Cell division occurs during your entire life. Even now, your body is producing thousands of new red blood cells, skin cells, and cells that line your respiratory and digestive tracts. Also, if you suffer a cut, cell division repairs the injury. Apoptosis occurs all the time too, particularly if an abnormal cell that could become cancerous appears, or a cell becomes infected with a virus. Death through apoptosis prevents a tumor from developing and helps to limit the spread of viruses.

Check Your Progress 9.1

1. What are the four stages of the cell cycle? During which of these stages is the DNA replicated, and when does cell division occur?
2. What conditions might cause a cell to halt the cell cycle?

science focus

The G_1 Checkpoint

Cell division is very tightly regulated so that only certain cells in an adult body are actively dividing. After cell division occurs, cells enter the G_1 stage. Upon completing G_1, they will divide again, but before this happens they have to pass through the G_1 checkpoint. The G_1 checkpoint ensures that conditions are right for making the commitment to divide by evaluating the meaning of growth signals, determining the availability of nutrients, and assessing the integrity of DNA. Failure to meet any one of these criteria results in a cell halting the cell cycle and entering G_0 stage, or undergoing apoptosis if the problems are severe.

Evaluating Growth Signals

Multicellular organisms tightly control cell division so that it occurs only when needed. Signaling molecules, such as hormones, may be sent from nearby cells or distant tissues to encourage or discourage cells from entering the cell cycle. Such signals may cause a cell to enter a G_0 stage, or complete G_1 and enter the S stage. Growth signals that promote cell division cause a cyclin-dependent-kinase (CDK) to add a phosphate group to RB, a major regulator of the G_1 checkpoint.

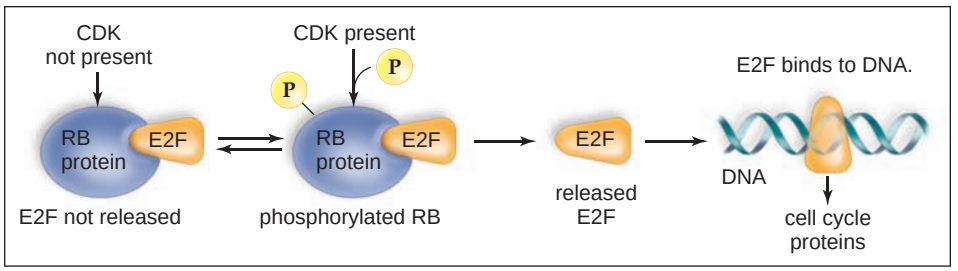
Ordinarily, a protein called E2F is bound to RB, but when RB is phosphorylated, its shape changes and it releases E2F. Now, E2F binds to DNA, activating certain genes whose products are needed to complete the cell cycle (Fig. 9A*a*). Likewise, growth signals prompt cells that are in G_0 stage to reenter the G_1 stage, complete it, and enter the S stage. If growth signals are sufficient, a cell passes through the G_1 checkpoint and cell division occurs.

Determining Nutrient Availability

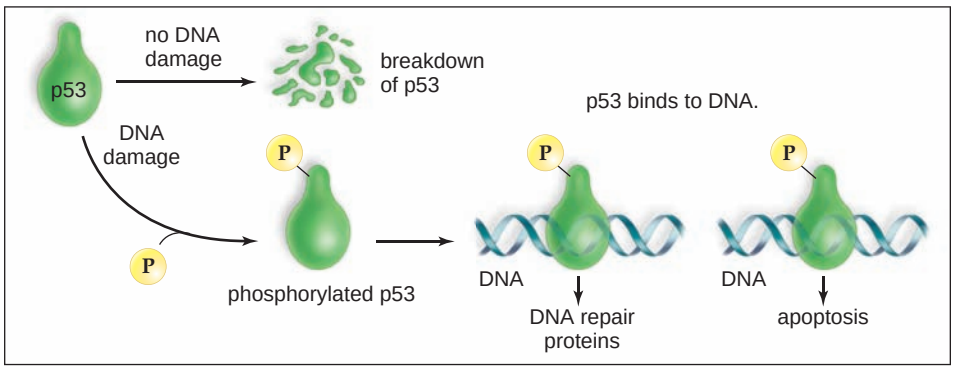
Much as an experienced hiker would ensure that she has sufficient food for her journey, a cell ensures that nutrient levels to support cell division are adequate before committing to it. For example, scientists know that starving cells in culture enter G_0. At that time, phosphate groups are removed from RB (see reverse arrows in Figure 9Aa); RB does not release E2F; and the proteins needed to complete the cell cycle are not produced. When, nutrients *become* available, CDKs bring about the phosphorylation of RB, which then releases E2F (see forward arrows in Figure 9A*a*). After E2F binds to DNA, proteins needed to complete the cell cycle are produced. As mentioned, growth signals prompt a cell that is in the G_0 stage to reenter the G_1 stage, complete it, and enter the S stage. Again, we can note that cells do not commit to divide until conditions are conducive for them to do so.

Assessing DNA Integrity

For cell division to occur, DNA must be free of errors and damage. The p53 protein is involved in this quality control function. Ordinarily, p53 is broken down because it has no job to do. In response to DNA damage, CDK phosphorylates p53 (Fig. 9A*b*). Now, the molecule will not be broken down as usual, and instead its level in the nucleus begins to rise. Phosphorylated p53 binds to DNA; certain genes are activated; and DNA repair proteins are produced. If the DNA damage cannot be repaired, p53 levels continue to rise, and apoptosis is triggered. If the damage is successfully repaired, p53 levels fall, and the cell is allowed to complete G_1 stage as long as growth signals and nutrients are present, for example. Actually, there are many criteria that must be met in order for a cell to commit to cell division, and the failure to meet any one of them may cause the cell cycle to be halted and/or apoptosis to be initiated. The G_1 checkpoint is currently an area of intense research because understanding it holds the key to possibly curing cancer and for unleashing the power of normal, healthy cells to regenerate tissues that could be used to cure many other human conditions.



a.



b.

FIGURE 9A Regulation of the G1 checkpoint.
a. *When CDK (cyclin-dependent-kinase) is not present, RB retains E2F. When CDK is present, a phosphorylated RB releases E2F, and after it binds to DNA, proteins necessary to completing cell division are produced.* ***b.*** *If DNA is damaged, p53 is not broken down, and instead is involved in the production of DNA repair enzymes and in triggering apoptosis when repair is impossible.*

9.2 Mitosis and Cytokinesis

As mentioned, cell division in eukaryotes involves mitosis, which is nuclear division, and cytokinesis, which is division of the cytoplasm. During mitosis, chromosomes are distributed to two daughter cells.

Eukaryotic Chromosomes

The DNA in the chromosomes of eukaryotes is associated with various proteins, including **histones** that are especially involved in organizing chromosomes. When a eukaryotic cell is not undergoing division, the DNA (and associated proteins) are located within **chromatin** which has the appearance of a tangled mass of thin threads. Before mitosis begins, chromatin becomes highly coiled and condensed, and it is easy to see the individual chromosomes.

When the chromosomes are visible, it is possible to photograph and count them. Each species has a characteristic chromosome number (Table 9.1). This is the full or **diploid (2n) number** [Gk. *diplos,* twofold, and *-eides,* like] of chromosomes that is found in all cells of the individual. The diploid number includes two chromosomes of each kind. Half the diploid number, called the **haploid (n) number** [Gk. *haplos,* single, and *-eides,* like] of chromosomes, contains only one chromosome of each kind. Typically, only sperm and eggs have the haploid number of chromosomes in the life cycle of animals.

Preparations for Mitosis

During interphase, a cell must make preparations for cell division. These arrangements include replicating the chromosomes and duplicating most cellular organelles, including the centrosome, which will organize the spindle apparatus necessary for movement of chromosomes.

Chromosome Duplication

During mitosis, a 2n nucleus divides to produce daughter nuclei that are also 2n. The dividing cell is called the *parent cell,* and the resulting cells are called the *daughter cells*. Before nuclear division takes place, DNA replicates, duplicating the chromosomes in the parent cell. This occurs during S stage of interphase. Now each chromosome has two identical double helical molecules. Each double helix is a chromatid, and the two identical chromatids are called **sister chromatids** (Fig. 9.3). Sister chromatids are constricted and attached to each other at a region called the **centromere.** Protein complexes called **kinetochores** develop on either side of the centromere during cell division.

During nuclear division, the two sister chromatids separate at the centromere, and in this way each duplicated chromosome gives rise to two daughter chromosomes. Each daughter chromosome has only one double helix molecule. The daughter chromosomes are distributed equally to the daughter cells. In this way, each daughter nucleus gets a copy of each chromosome that was in the parent cell.

TABLE 9.1

Diploid Chromosome Numbers of Some Eukaryotes

Type of Organism	*Name of Chromosome*	*Chromosome Number*
Fungi	*Saccharomyces cerevisiae* (yeast)	32
Plants	*Pisum sativum* (garden pea)	14
	Solanum tuberosum (potato)	48
	Ophioglossum vulgatum (Southern adder's tongue fern)	1,320
Animals	*Drosophila melanogaster* (fruit fly)	8
	Homo sapiens (human)	46
	Carassius auratus (goldfish)	94

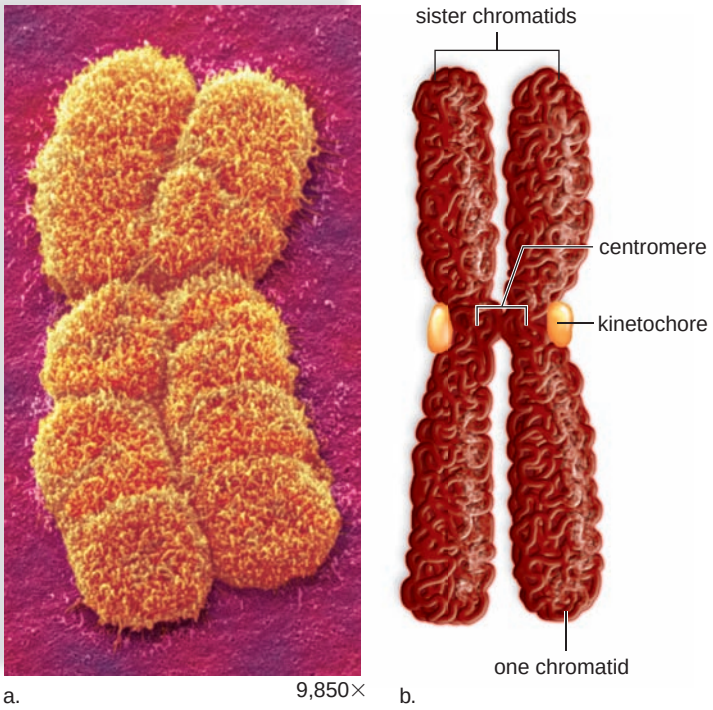


FIGURE 9.3 Duplicated chromosomes.

A duplicated chromosome contains two sister chromatids, each with a copy of the same genes. **a.** Electron micrograph of a highly coiled and condensed chromosome, typical of a nucleus about to divide. **b.** Diagrammatic drawing of a condensed chromosome. The chromatids are held together at a region called the centromere.

Division of the Centrosome

The **centrosome** [Gk. *centrum,* center, and *soma,* body], the main microtubule-organizing center of the cell, also divides before mitosis begins. Each centrosome in an animal cell—but not a plant cell—contains a pair of barrel-shaped organelles called **centrioles.**

The centrosomes organize the mitotic spindle, which contains many fibers, each composed of a bundle of microtubules. Microtubules are hollow cylinders made up of the protein tubulin. They assemble when tubulin subunits join, and when they disassemble, tubulin subunits become free once more. The microtubules of the cytoskeleton disassemble when spindle fibers begin forming. Most likely, this provides tubulin for the formation of the spindle fibers, or may allow the cell to change shape as needed for cell division.

Phases of Mitosis

Mitosis is a continuous process that is arbitrarily divided into five phases for convenience of description: prophase, prometaphase, metaphase, anaphase, and telophase (Fig. 9.4).

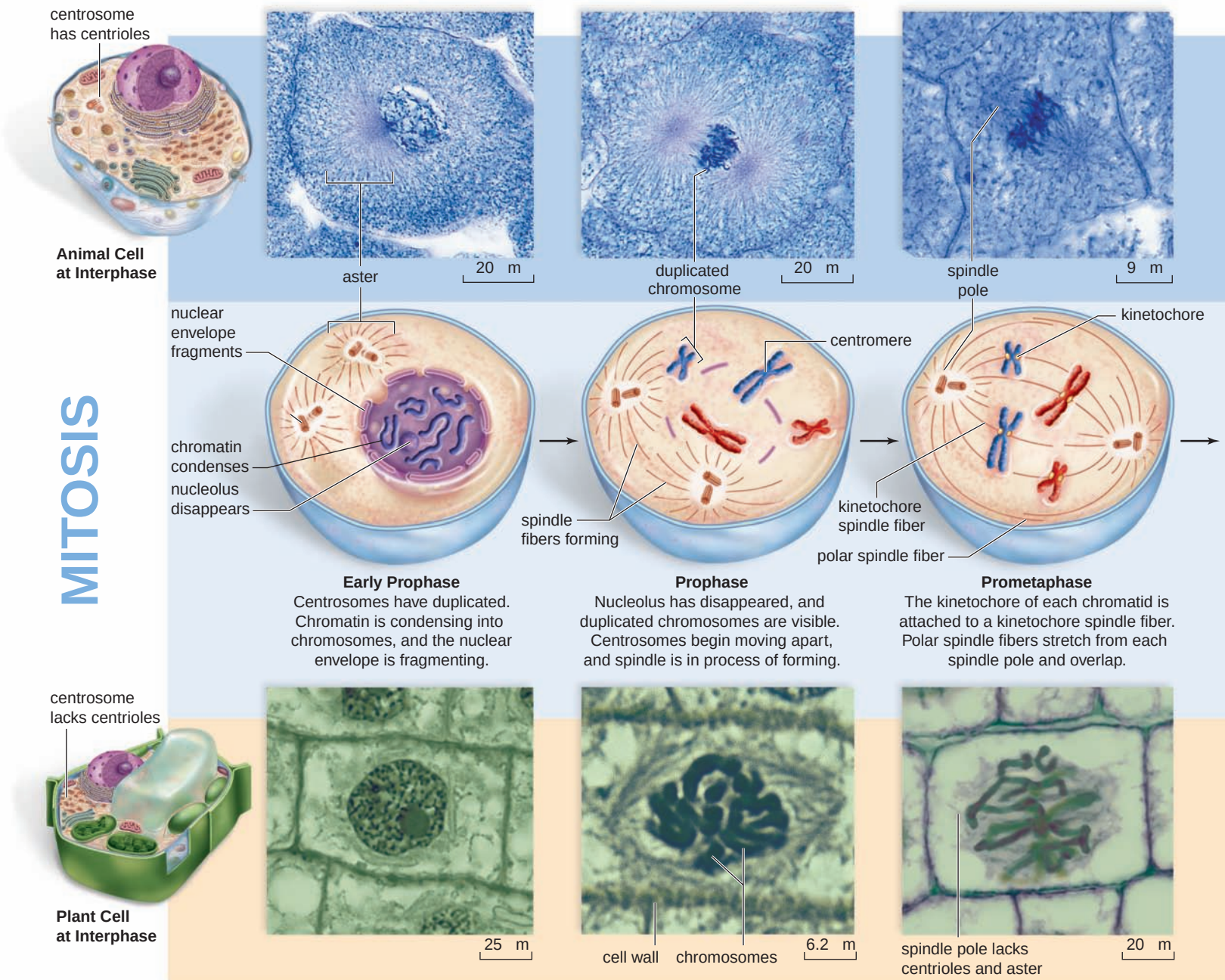
Prophase

It is apparent during **prophase** that nuclear division is about to occur because chromatin has condensed and the chromosomes are visible. Recall that DNA replication occurred during interphase, and therefore the *parental chromosomes are already duplicated and composed of two sister chromatids held together at a centromere.* Counting the number of centromeres in diagrammatic drawings gives the number of chromosomes for the cell depicted.

During prophase, the nucleolus disappears and the nuclear envelope fragments. The spindle begins to assemble as the two centrosomes migrate away from one another. In animal cells, an array of microtubules radiates toward the plasma membrane from the centrosomes. These structures are called **asters.** It is thought that asters serve to brace the centrioles during later stages of cell division. Notice that the chromosomes have no particular orientation because the spindle has not yet formed.

FIGURE 9.4 **Phases of mitosis in animal and plant cells.**

The blue chromosomes were inherited from one parent and the red from the other parent.



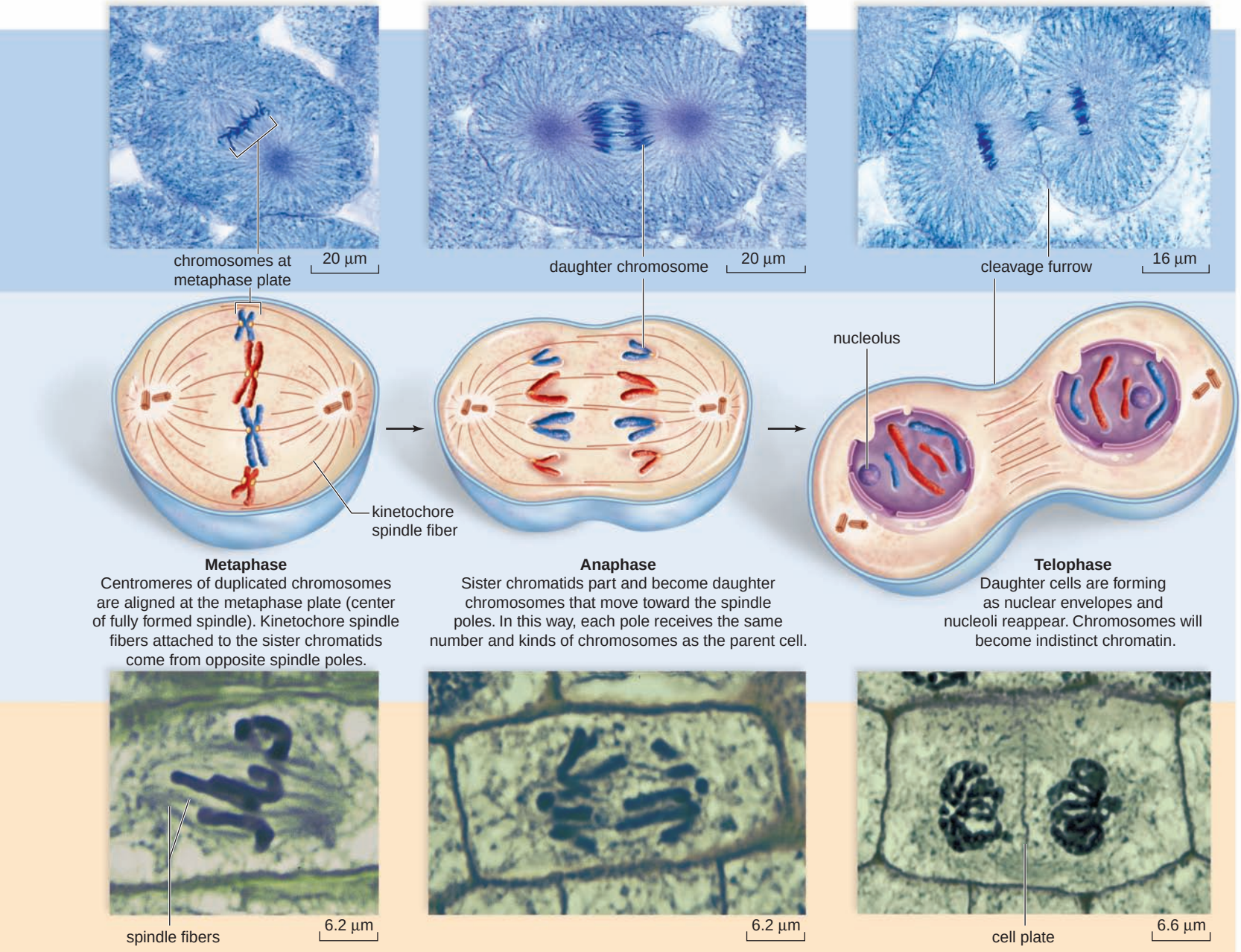
Prometaphase (Late Prophase)

During **prometaphase,** preparations for sister chromatid separation are evident. Kinetochores appear on each side of the centromere, and these attach sister chromatids to the so-called kinetochore spindle fibers. These fibers extend from the poles to the chromosomes, which will soon be located at the center of the spindle.

The kinetochore fibers attach the sister chromatids to opposite poles of the spindle, and the chromosomes are pulled first toward one pole and then toward the other before the chromosomes come into alignment. Notice that even though the chromosomes are attached to the spindle fibers in prometaphase, they are still not in alignment.

Metaphase

During **metaphase,** the centromeres of chromosomes are now in alignment on a single plane at the center of the cell. The chromosomes usually appear as a straight line across the middle of the cell when viewed under a light microscope. An imaginary plane that is perpendicular and passes through this circle is called the **metaphase plate.** It indicates the future axis of cell division. Several nonattached spindle fibers called *polar spindle fibers* reach beyond the metaphase plate and overlap. A cell cycle checkpoint, the M checkpoint, delays the start of anaphase until the kinetochores of each chromosome are attached properly to spindle fibers and the chromosomes are properly aligned along the metaphase plate.



Anaphase

At the start of **anaphase,** the two sister chromatids of each duplicated chromosome separate at the centromere, giving rise to two daughter chromosomes. Daughter chromosomes, each with a centromere and single chromatid composed of a single double helix, appear to move toward opposite poles. Actually, the daughter chromosomes are being pulled to the opposite poles as the kinetochore spindle fibers disassemble at the region of the kinetochores. Even as the daughter chromosomes move toward the spindle poles, the poles themselves are moving farther apart because the polar spindle fibers are sliding past one another. Microtubule-associated proteins such as the motor molecules kinesin and dynein are involved in the sliding process. Anaphase is the shortest phase of mitosis.

Telophase

During **telophase,** the spindle disappears as new nuclear envelopes form around the daughter chromosomes. Each daughter nucleus contains the same number and kinds of chromosomes as the original parent cell. Remnants of the polar spindle fibers are still visible between the two nuclei.

The chromosomes become more diffuse chromatin once again, and a nucleolus appears in each daughter nucleus. Division of the cytoplasm requires cytokinesis, which is discussed in the next section.

Cytokinesis in Animal and Plant Cells

As mentioned previously, cytokinesis is division of the cytoplasm. Cytokinesis accompanies mitosis in most cells but not all. When mitosis occurs but cytokinesis doesn't occur, the result is a multinucleated cell. For example, we will see that the embryo sac in flowering plants is multinucleated.

Division of the cytoplasm begins in anaphase, continues in telophase, but does not reach completion until the following interphase begins. By the end of mitosis each newly forming cell has received a share of the cytoplasmic organelles that duplicated during interphase. Cytokinesis proceeds differently in plant and animal cells because of differences in cell structure.

Cytokinesis in Animal Cells

In animal cells, a cleavage furrow, which is an indentation of the membrane between the two daughter nuclei, forms just as anaphase draws to a close. By that time, the newly forming cells have received a share of the cytoplasmic organelles that duplicated during the previous interphase.

The cleavage furrow deepens when a band of actin filaments, called the contractile ring, slowly forms a circular constriction between the two daughter cells. The action of the contractile ring can be likened to pulling a drawstring ever tighter about the middle of a balloon. As the drawstring is pulled tight, the balloon constricts in the middle as the material on either side of the constriction gathers in folds. These folds are represented by the longitudinal lines in Figure 9.5.

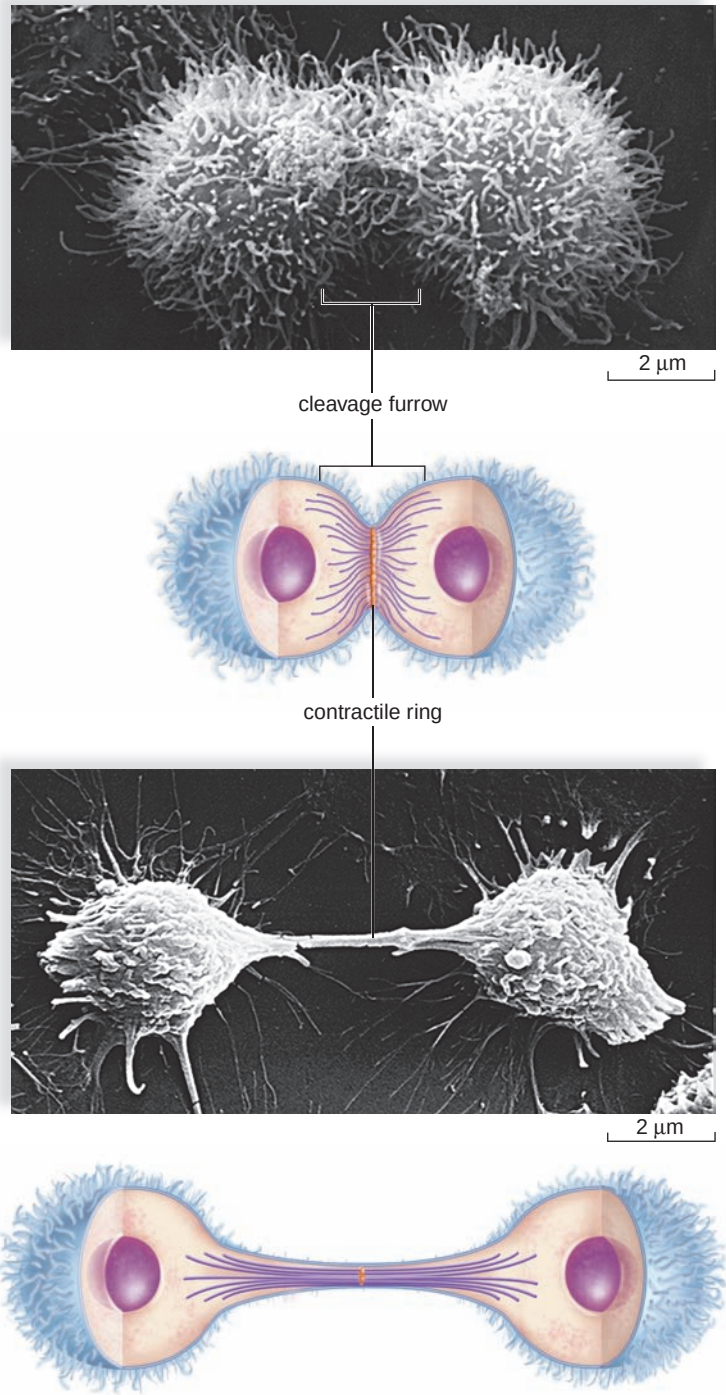


FIGURE 9.5 Cytokinesis in animal cells.

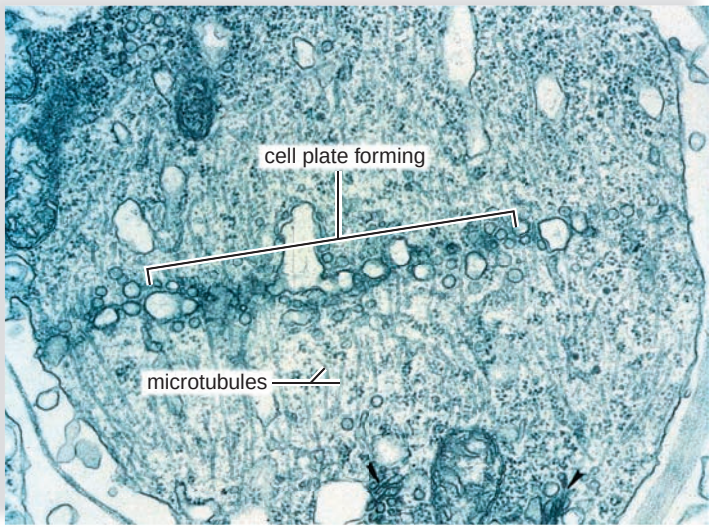
A single cell becomes two cells by a furrowing process. A contractile ring composed of actin filaments gradually gets smaller, and the cleavage furrow pinches the cell into two cells.

A narrow bridge between the two cells can be seen during telophase, and then the contractile ring continues to separate the cytoplasm until there are two independent daughter cells (Fig. 9.5).

Cytokinesis in Plant Cells

Cytokinesis in plant cells occurs by a process different from that seen in animal cells (Fig. 9.6). The rigid cell wall that surrounds plant cells does not permit cytokinesis by furrowing. Instead, cytokinesis in plant cells involves the building of new cell walls between the daughter cells.

Cytokinesis is apparent when a small, flattened disk appears between the two daughter plant cells near the site where the metaphase plate once was. In electron micrographs, it is possible to see that the disk is at right angles to a set of microtubules that radiate outward from the forming nuclei. The Golgi apparatus produces vesicles, which move along the microtubules to the region of the disk. As more vesicles arrive and fuse, a cell plate can be seen. The **cell plate** is simply newly formed plasma membrane that expands outward until it reaches the old plasma membrane and fuses with this membrane. The new membrane releases molecules that form the new plant cell walls. These cell walls, known as primary cell walls, are later strengthened by the addition of cellulose fibrils. The space between the daughter cells becomes filled with middle lamella, which cements the primary cell walls together.



Vesicles containing cell wall components fusing to form cell plate

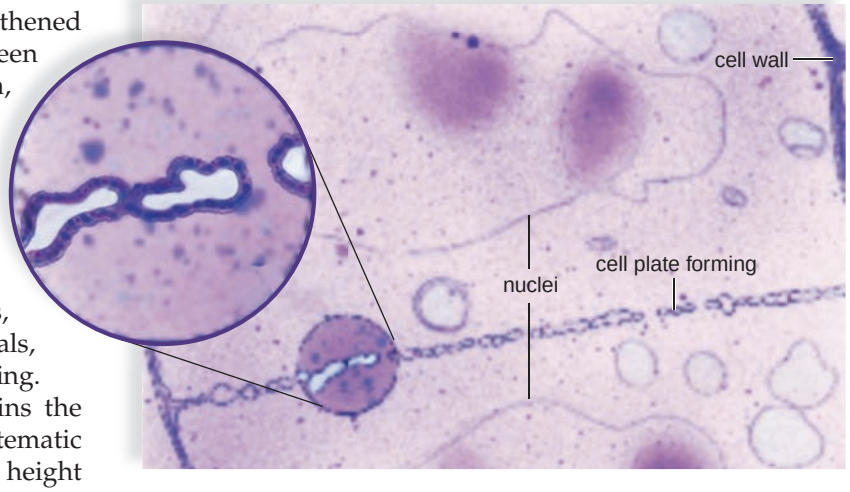


FIGURE 9.6 **Cytokinesis in plant cells.**

During cytokinesis in a plant cell, a cell plate forms midway between two daughter nuclei and extends to the plasma membrane.

The Functions of Mitosis

Mitosis permits growth and repair. In both plants and animals, mitosis is required during development as a single cell develops into an individual. In plants, the individual could be a fern or daisy, while in animals, the individual could be a grasshopper or a human being.

In flowering plants, meristematic tissue retains the ability to divide throughout the life of a plant. Meristematic tissue at the shoot tip accounts for an increase in the height of a plant for as long as it lives. Then, too, lateral meristem accounts for the ability of trees to increase their girth each growing season.

In human beings and other mammals, mitosis is necessary as a fertilized egg becomes an embryo and as the embryo becomes a fetus. Mitosis also occurs after birth as a child becomes an adult. Throughout life, mitosis allows a cut to heal or a broken bone to mend.

Stem Cells

Earlier, you learned that the cell cycle is tightly controlled, and that most cells of the body at adulthood are permanently arrested in G_0 stage. However, mitosis is needed to repair injuries, such as a cut or a broken bone. Many mammalian organs contain stem cells (often called adult stem cells) that retain the ability to divide. In the body, red bone marrow stem cells repeatedly divide to produce millions of cells that go on to become various types of blood cells. The possibility exists that researchers can learn to manipulate the production of various types of tissues from red bone marrow stem cells in the laboratory. If so, these tissues could be used to cure illnesses. As discussed in the Science Focus on page 160, **therapeutic cloning,** which is used to produce human tissues, can begin with either adult stem cells or embryonic stem cells. Embryonic stem cells can also be used for **reproductive cloning,** the production of a new individual.

Check Your Progress 9.2

1. What are the major events that occur during prophase, and why are these events important to the process of cell division?
2. How does cytokinesis differ between animal and plant cells? Why is this difference necessary?

science focus

Reproductive and Therapeutic Cloning

Our knowledge of how the cell cycle is controlled has yielded major technological breakthroughs, including reproductive cloning—the ability to clone an adult animal from a normal body cell, and therapeutic cloning, which allows the rapid production of mature cells of a specific type. Both types of cloning are a direct result of recent discoveries about how the cell cycle is controlled.

Reproductive cloning, or the cloning of adult animals, was once thought to be impossible because investigators found it difficult to have the nucleus of an adult cell "start over" with the cell cycle, even when it was placed in an egg cell that had its own nucleus removed.

In 1997, Dolly the sheep demonstrated that reproductive cloning is indeed possible. The donor cells were starved before the cell's nucleus was placed in an enucleated egg. This caused them to stop dividing and go into a G_0 (resting) stage, and this made the nuclei amenable to cytoplasmic signals for initiation of development (Fig. 9B*a*). This advance has made it possible to clone all sorts of farm animals that have desirable traits and even to clone rare animals that might otherwise become extinct. Despite the encouraging results, however, there are still obstacles to be overcome, and a ban on the use of federal funds in experiments to clone human beings remains firmly in place.

In therapeutic cloning, however, the objective is to produce mature cells of various cell types rather than an individual organism. The purpose of therapeutic cloning is (1) to learn more about how specialization of cells occurs and (2) to provide cells and tissues that could be used to treat human illnesses, such as diabetes, or major injuries like strokes or spinal cord injuries. There are two possible ways to carry out therapeutic cloning. The first way is to use the exact same procedure as reproductive cloning, except embryonic cells, called *embryonic stem cells,* are separated and each is subjected to a treatment that causes it to develop into a particular type of cell, such as red blood cells, muscle cells, or nerve cells (Fig. 9B*b*). Some have ethical concerns about this type of therapeutic cloning, which is still experimental, because if the embryo were allowed to continue development, it would become an individual.

The second way to carry out therapeutic cloning is to use *adult stem cells.* Stem cells are found in many organs of the adult's body; for example, the bone marrow has stem cells that produce new blood cells. However, adult stem cells are limited in the possible number of cell types that they may become. Nevertheless, a recent advance shows promise in overcoming this obstacle. By adding just four genes to adult skin stem cells, Japanese scientists were able to coax the cells, called fibroblasts, into becoming very similar to embryonic stem cells. The researchers were then able to create heart and brain cells from the adult stem cells. Ultimately, this technique may provide a way to make tissues and organs for transplantation that carry no risk of rejection. In the future, this new technology promises to overcome current limitations and alleviate ethical concerns.

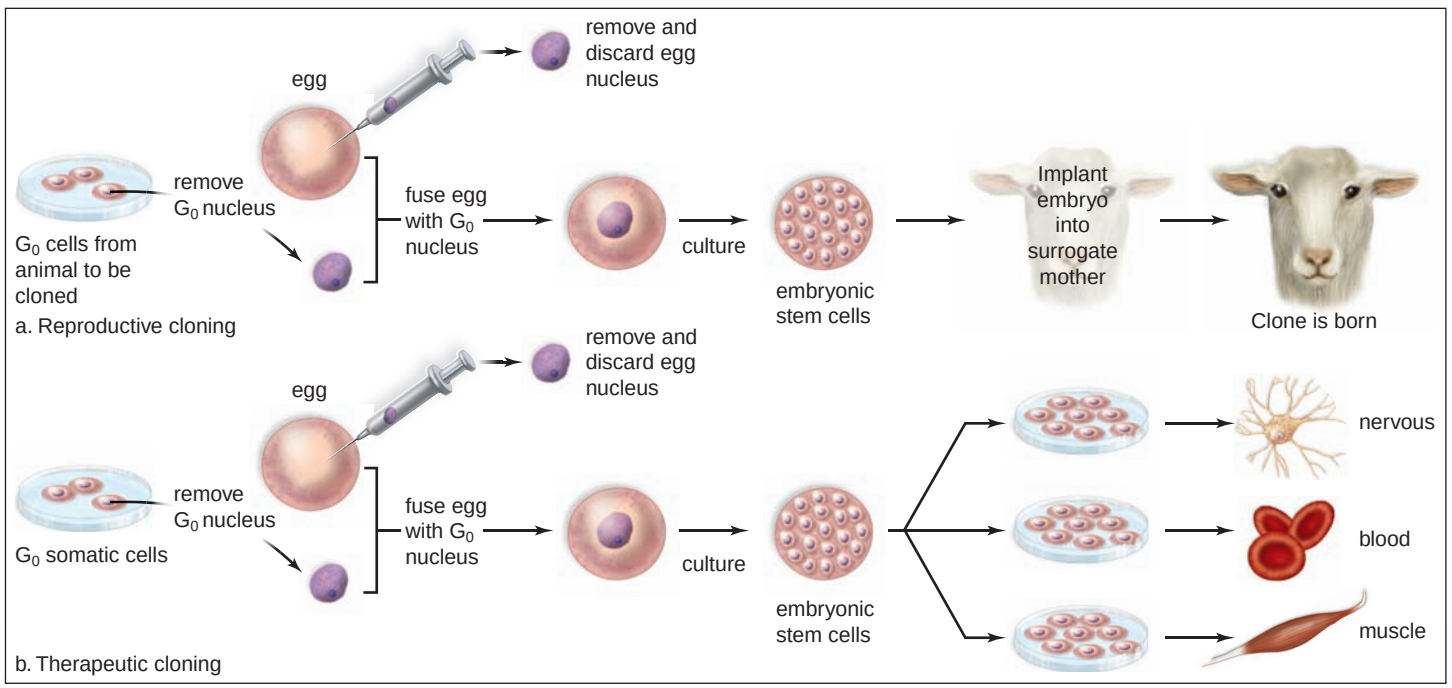


FIGURE 9B Two types of cloning. ***a.*** *The purpose of somatic cell cloning is to produce an individual that is genetically identical to the one that donated a nucleus. The nucleus is placed in an enucleated egg, and, after several mitotic divisions, the embryo is implanted into a surrogate mother for further development.* ***b.*** *The purpose of therapeutic cloning is to produce specialized tissue cells. A nucleus is placed in an enucleated egg, and, after several mitotic divisions, the embryonic cells (called embryonic stem cells) are separated and treated to become specialized cells.*

9.3 The Cell Cycle and Cancer

Cancer is a cellular growth disorder that occurs when cells divide uncontrollably. Although causes widely differ, most cancers are the result of accumulating mutations that ultimately cause a loss of control of the cell cycle.

Although cancers vary greatly, they usually follow a common multistep progression (Fig. 9.7). Most cancers begin as an abnormal cell growth that is **benign,** or not cancerous, and usually does not grow larger. However, additional mutations may occur, causing the abnormal cells to fail to respond to inhibiting signals that control the cell cycle. When this occurs, the growth becomes **malignant,** meaning that it is cancerous and possesses the ability to spread.

Characteristics of Cancer Cells

The development of cancer is gradual. A mutation in a cell may cause it to become precancerous, but many other regulatory processes within the body prevent it from becoming cancerous. In fact, it may be decades before a cell possesses most or all of the characteristics of a cancer cell (Table 9.2 and Fig. 9.7). Although cancers vary greatly, cells that possess the following characteristics are generally recognized as cancerous:

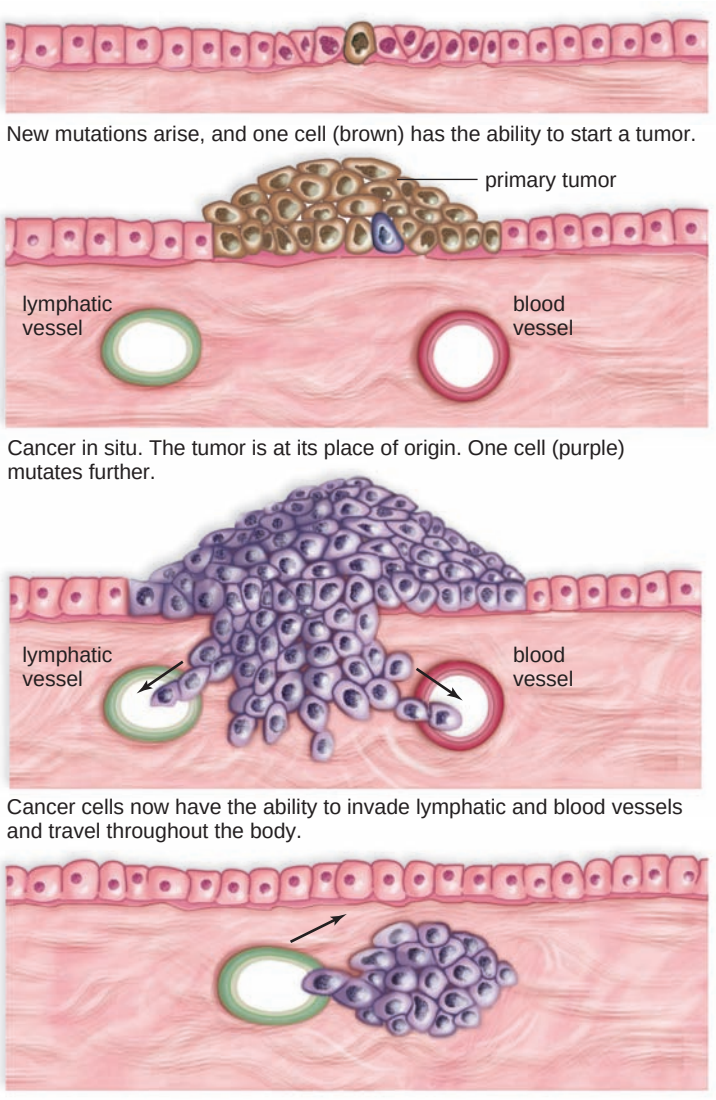
Cancer cells lack differentiation. Cancer cells are not specialized and do not contribute to the functioning of a tissue. Although cancer cells may still possess many of the characteristics of surrounding normal cells, they usually look distinctly abnormal. Normal cells can enter the cell cycle about 50 times before they are incapable of dividing again. Cancer cells can enter the cell cycle repeatedly, and in this way seem immortal.

Cancer cells have abnormal nuclei. The nuclei of cancer cells are enlarged and may contain an abnormal number of chromosomes. Often, extra copies of one or more chromosomes may be present. Often, there are also duplicated portions of some chromosomes present, which causes gene amplification, or extra copies of specific genes. Some chromosomes may also possess deleted portions.

Cancer cells do not undergo apoptosis. Ordinarily, cells with damaged DNA undergo apoptosis, or programmed cell death. The immune system can also recognize abnormal cells and trigger apoptosis, which normally prevents tumors from developing. Cancer cells fail to undergo apoptosis even though they are abnormal cells.

Cancer cells form tumors. Normal cells anchor themselves to a substratum and/or adhere to their neighbors. They exhibit contact inhibition—in other words, when they come in contact with a neighbor, they stop dividing. Cancer cells have lost all restraint and do not exhibit contact inhibition. The abnormal cancer cells pile on top of one another and grow in multiple layers, forming a **tumor.** During carcinogenesis, the most aggressive cell becomes the dominant cell of the tumor.

Cancer cells undergo metastasis and angiogenesis. Additional mutations may cause a benign tumor, which is usually contained within a capsule and cannot invade adjacent tissue,



New mutations arise, and one cell (brown) has the ability to start a tumor.

Cancer in situ. The tumor is at its place of origin. One cell (purple) mutates further.

Cancer cells now have the ability to invade lymphatic and blood vessels and travel throughout the body.

New metastatic tumors are found some distance from the primary tumor.

FIGURE 9.7 Progression of cancer.

The development of cancer requires a series of mutations leading first to a localized tumor and then to metastatic tumors. With each successive step toward cancer, the most genetically altered and aggressive cell becomes the dominant type of tumor. The cells take on characteristics of embryonic cells; they are not differentiated, they can divide uncontrollably; and they are able to metastasize and spread to other tissues.

TABLE 9.2

Cancer Cells Versus Normal Cells

Cancer Cells	*Normal Cells*
Nondifferentiated cells	Differentiated cells
Abnormal nuclei	Normal nuclei
Do not undergo apoptosis	Undergo apoptosis
No contact inhibition	Contact inhibition
Disorganized, multilayered	One organized layer
Undergo metastasis and angiogenesis	

to become malignant, and spread throughout the body, forming new tumors distant from the primary tumor. These cells now produce enzymes that they normally do not express, allowing tumor cells to invade underlying tissues. Then, they travel through the blood and lymph, to start tumors elsewhere in the body. This process is known as **metastasis.**

Tumors that are actively growing soon encounter another obstacle—the blood vessels supplying nutrients to the tumor cells become insufficient to support the sudden growth of the tumor. In order to grow further, the cells of the tumor must receive additional nutrition. Thus, the formation of new blood vessels is required to bring nutrients and oxygen to support further growth. Additional mutations occurring in tumor cells allow them to direct the growth of new blood vessels into the tumor in a process called **angiogenesis.** Some modes of cancer treatment are aimed at preventing angiogenesis from occurring.

Origin of Cancer

Normal growth and maintenance of body tissues depend on a balance between signals that promote and inhibit cell division. When this balance is upset, conditions such as cancer may occur. Thus, cancer is usually caused by mutations affecting genes that directly or indirectly affect this balance, such as those shown in Figure 9.8. These two types of genes are usually affected:

1. **Proto-oncogenes** code for proteins that promote the cell cycle and prevent apoptosis. They are often likened to the gas pedal of a car because they cause the cell cycle to go or speed up.
2. **Tumor suppressor genes** code for proteins that inhibit the cell cycle and promote apoptosis. They are often likened to the brakes of a car because they cause the cell cycle to go more slowly or even stop.

Proto-oncogenes Become Oncogenes

Proto-oncogenes are normal genes that promote progression through the cell cycle. They are often at the end of a *stimulatory pathway* extending from the plasma membrane to the nucleus. A stimulus, such as an injury, results in the release of a growth factor that binds to a receptor protein in the plasma membrane. This sets in motion a whole series of enzymatic reactions leading to the activation of genes that promote the cell cycle, both directly and indirectly. Proto-oncogenes include the receptors and signal molecules that make up these pathways.

When mutations occur in proto-oncogenes, they become **oncogenes,** or cancer-causing genes. Oncogenes are under constant stimulation and keep on promoting the cell cycle regardless of circumstances. For example, an oncogene may code for a faulty receptor in the stimulatory pathway that stimulates the cell cycle even when no growth factor is present! Or, an oncogene may specify either an abnormal protein product or produce abnormally high levels of a normal product that stimulates the cell cycle to begin or to go to completion. As a result, uncontrolled cell division may occur.

Researchers have identified perhaps 100 oncogenes that can cause increased growth and lead to tumors. The oncogenes most frequently involved in human cancers belong to the *ras* gene family. Mutant forms of the *BRCA1* oncogene (breast cancer predisposition gene 1) are associated with certain hereditary forms of breast and ovarian cancer.

Tumor Suppressor Genes Become Inactive

Tumor suppressor genes, on the other hand, directly or indirectly inhibit the cell cycle and prevent cells from dividing uncontrollably. Some tumor suppressor genes prevent progression of the cell cycle when DNA is damaged. Other tumor suppressor genes may promote apoptosis as a last resort.

A mutation in a tumor suppressor gene is much like brake failure in a car; when the mechanism that slows down and stops cell division does not function, the cell cycle accelerates and does not halt. Researchers have identified about a half-dozen tumor suppressor genes. Among these are *RB* and *p53* genes that code for RB and p53. The Science Focus on page 154 discussed the function of these proteins in controlling the cell cycle. The *RB* tumor suppressor gene was discovered when the inherited condition retinoblastoma was being studied, but malfunctions of this gene have now been identified in many other cancers as well, including breast, prostate, and bladder cancers. Another major tumor suppressor gene is *p53,* a gene that turns on the expression of other genes that inhibit the cell cycle. The p53 protein can also stimulate apoptosis, programmed cell death. It is estimated that over half of human cancers involve an abnormal or deleted *p53* gene.

Other Causes of Cancer

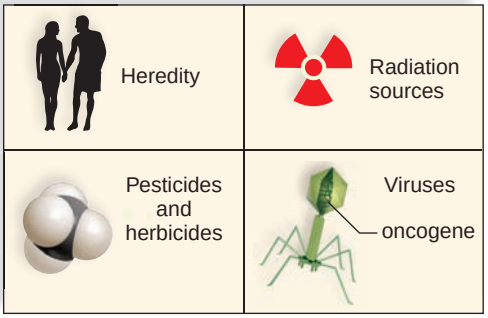
As mentioned previously, cancer develops when the delicate balance between promotion and inhibition of cell division is tilted towards uncontrolled cell division. Thus, other mutations may occur within a cell that affect this balance. For example, while a mutation affecting the cell's DNA repair system will not immediately cause cancer, it leads to a much greater chance of a mutation occurring within a proto-oncogene or tumor suppressor gene. And in some cancer cells, mutation of an enzyme that regulates the length of **telomeres,** or the ends of chromosomes, causes telomeres to remain at a constant length. Since cells with shortened telomeres normally stop dividing, keeping the telomeres at a constant length allows the cancer cells to continue dividing over and over again.

Check Your Progress 9.3

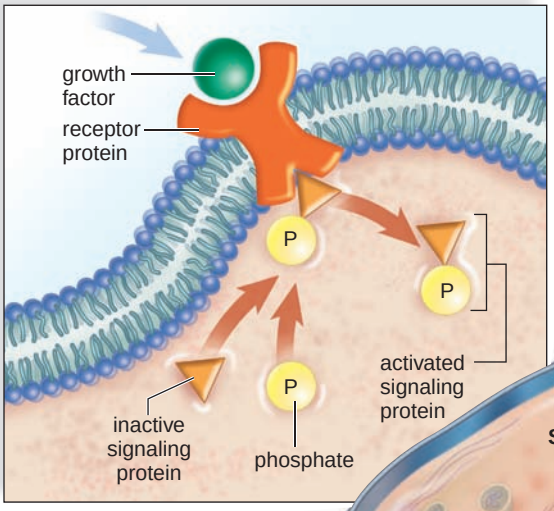
1. What are the major characteristics of cancer cells that distinguish them from normal cells?
2. What are the usual steps in development of a malignant tumor from a benign tumor?
3. Compare and contrast the effect on the cell cycle of **(a)** a mutation in a proto-oncogene to **(b)** a mutation in a tumor suppressor gene.

FIGURE 9.8 Causes of cancer.

a. Mutated genes that cause cancer can be due to the influences noted. **b.** A growth factor that binds to a receptor protein initiates a reaction that triggers a stimulatory pathway. **c.** A stimulatory pathway that begins at the plasma membrane turns on proto-oncogenes. The products of these genes promote the cell cycle and double back to become part of the stimulatory pathway. When proto-oncogenes become oncogenes, they are turned on all the time. An inhibitory pathway begins with tumor suppressor genes whose products inhibit the cell cycle. When tumor suppressor genes mutate, the cell cycle is no longer inhibited. **d.** Cancerous skin cell.

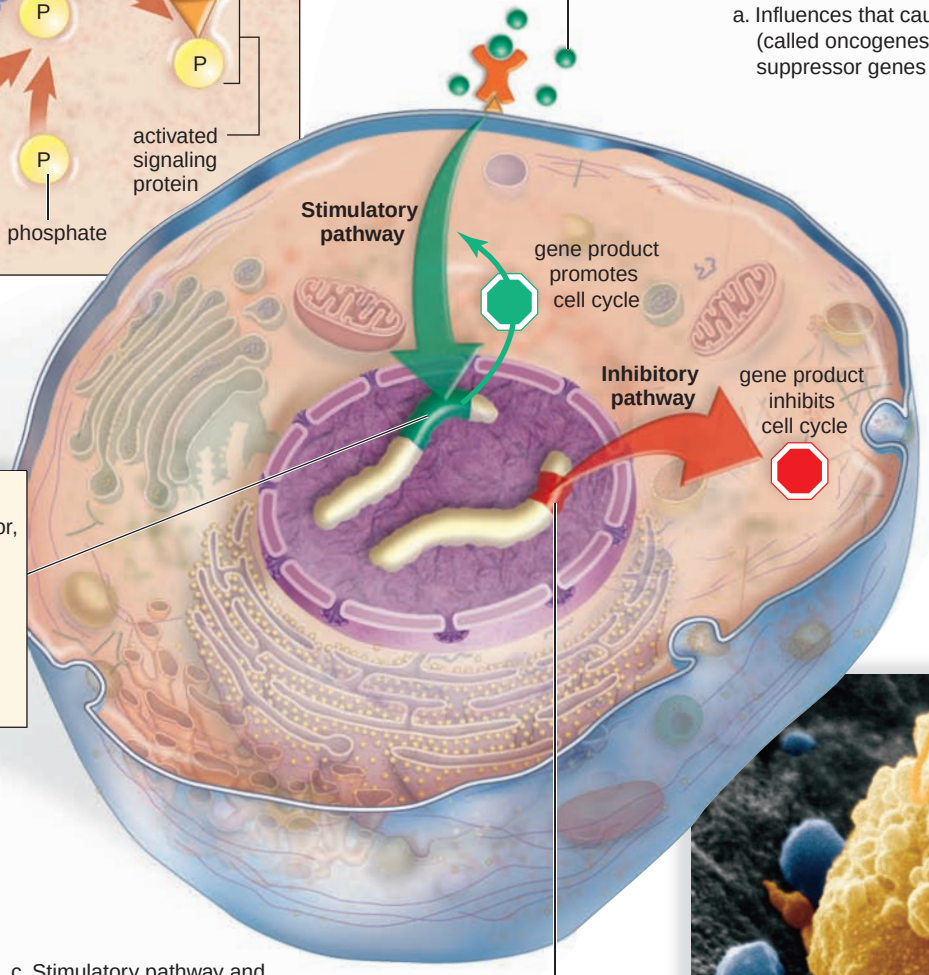


a. Influences that cause mutated proto-oncogenes (called oncogenes) and mutated tumor suppressor genes



b. Effect of growth factor

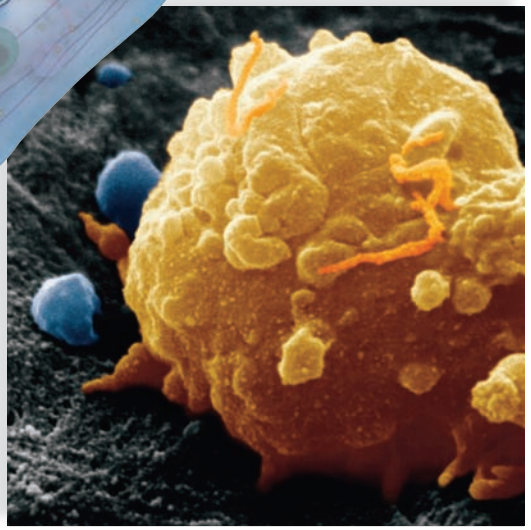
growth factor
Activates signaling proteins in a stimulatory pathway that extends to the nucleus.



c. Stimulatory pathway and inhibitory pathway

proto-oncogene
Codes for a growth factor, a receptor protein, or a signaling protein in a stimulatory pathway. If a proto-oncogene becomes an oncogene, the end result can be active cell division.

tumor suppressor gene
Codes for a signaling protein in an inhibitory pathway. If a tumor suppressor gene mutates, the end result can be active cell division.



d. Cancerous skin cell 1,100×

9.4 Prokaryotic Cell Division

Cell division in unicellular organisms, such as prokaryotes, produces two new individuals. This is **asexual reproduction** in which the offspring are genetically identical to the parent. In prokaryotes, reproduction consists of duplicating the single chromosome and distributing a copy to each of the daughter cells. Unless a mutation has occurred, the daughter cells will be genetically identical to the parent cell.

The Prokaryotic Chromosome

Prokaryotes (bacteria and archaea) lack a nucleus and other membranous organelles found in eukaryotic cells. Still, they do have a chromosome, which is composed of DNA and a limited number of associated proteins. The single chromosome of prokaryotes contains just a few proteins and is organized differently from eukaryotic chromosomes. A eukaryotic chromosome has many more proteins than a prokaryotic chromosome.

In electron micrographs, the bacterial chromosome appears as an electron-dense, irregularly shaped region called the **nucleoid** [L. *nucleus,* nucleus, kernel; Gk. *-eides,* like], which is not enclosed by membrane. When stretched out, the chromosome is seen to be a circular loop with a length that is up to about a thousand times the length of the cell. No wonder it is folded when inside the cell.

Binary Fission

Prokaryotes reproduce asexually by binary fission. The process is termed **binary fission** because division (fission) produces two (binary) daughter cells that are identical to the original parent cell. Before division takes place, the cell enlarges, and after DNA replication occurs, there are two chromosomes. These chromosomes attach to a special plasma membrane site and separate by an elongation of the cell that pulls them apart. During this period, new plasma membrane and cell wall develop and grow inward to divide the cell. When the cell is approximately twice its original length, the new cell wall and plasma membrane for each cell are complete (Fig. 9.9).

Escherichia coli, which lives in our intestines, has a generation time (the time it takes the cell to divide) of about 20 minutes under favorable conditions. In about seven hours, a single cell can increase to over 1 million cells! The division rate of other bacteria varies depending on the species and conditions.

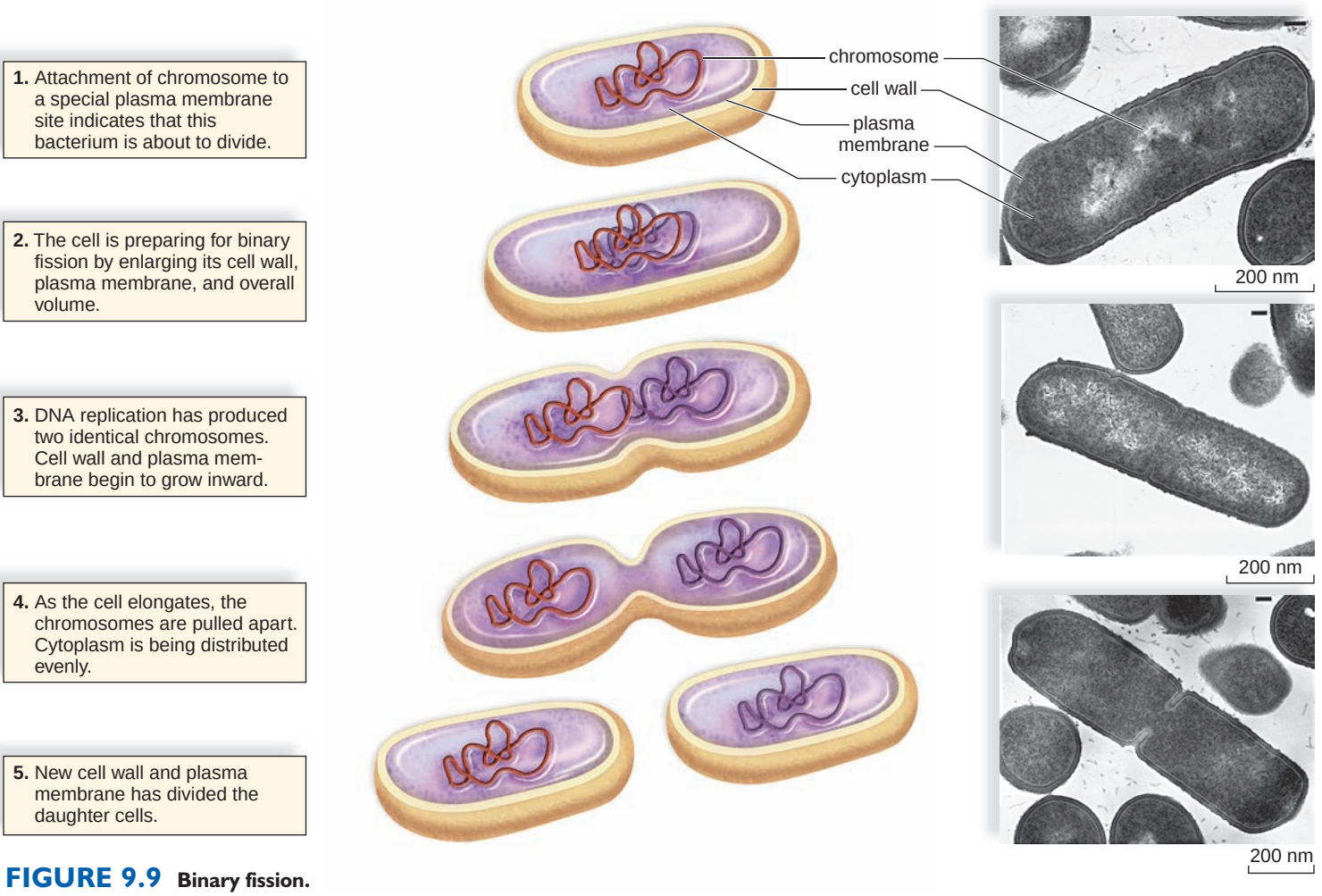


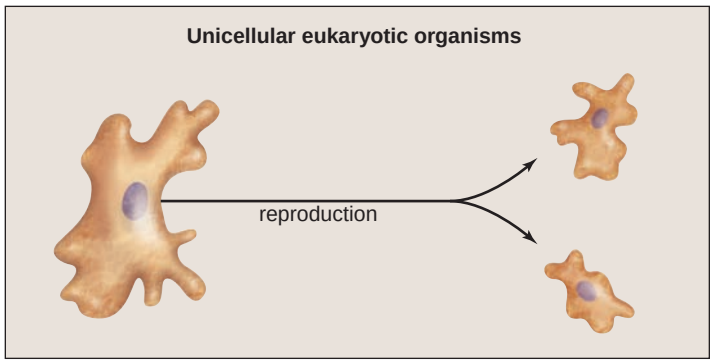
FIGURE 9.9 Binary fission.

First, DNA replicates, and as the cell lengthens, the two chromosomes separate, and the cells become divided. The two resulting bacteria are identical.

Comparing Prokaryotes and Eukaryotes

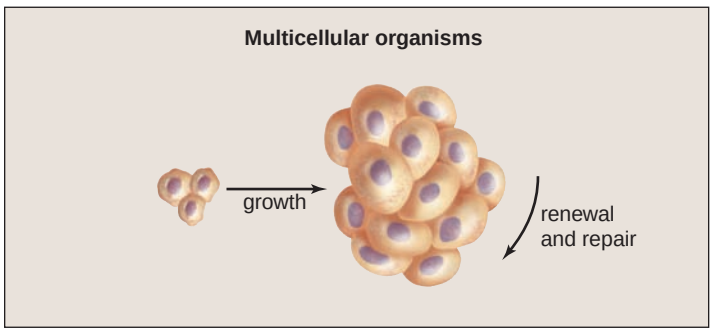
Both binary fission and mitosis ensure that each daughter cell is genetically identical to the parent cell. The genes are portions of DNA found in the chromosomes.

Prokaryotes (bacteria and archaea), protists (many algae and protozoans), and some fungi (yeasts) are unicellular. Cell division in unicellular organisms produces two new individuals:



This is a form of asexual reproduction because one parent has produced identical offspring (Table 9.3).

In multicellular fungi (molds and mushrooms), plants, and animals, cell division is part of the growth process. It produces the multicellular form we recognize as the mature organism. Cell division is also important in multicellular forms for renewal and repair:



The chromosomes of eukaryotic cells are composed of DNA and many associated proteins. The histone proteins organize a chromosome, allowing it to extend as chromatin during interphase and to coil and condense just prior to mitosis. Each species of multicellular eukaryotes has a characteristic number of chromosomes in the nuclei. As a result of mitosis, each daughter cell receives the same number and kinds of chromosomes as the parent cell. The spindle, which appears during mitosis, is involved in distributing the daughter chromosomes to the daughter nuclei. Cytokinesis, either by the formation of a cell plate (plant cells) or by furrowing (animal cells), is division of the cytoplasm.

In prokaryotes, the single chromosome consists largely of DNA with some associated proteins. During binary fission, this chromosome duplicates, and each daughter cell receives one copy as the parent cell elongates, and a new cell wall and plasma membrane form between the daughter cells. No spindle is involved in binary fission.

TABLE 9.3

Functions of Cell Division

Type of Organism	*Cell Division*	*Function*
Prokaryotes Bacteria and archaea	Binary fission	Asexual reproduction
Eukaryotes		
Protists, and some fungi (yeast)	Mitosis and cytokinesis	Asexual reproduction
Other fungi, plants, and animals	Mitosis and cytokinesis	Development, growth, and repair

Check Your Progress 9.4

1. How does binary fission in prokaryotes differ from mitosis and cytokinesis in eukaryotes?
2. How are prokaryotic and eukaryotic chromosomes different?

Connecting the Concepts

Cell division is a remarkable, complex process that is only a small part of the cell cycle, the life cycle of a cell. The cell cycle is heavily regulated to ensure that conditions are favorable and that it is permissible for the cell to divide, because there may be serious consequences if control of cell division breaks down. For example, in humans, overproduction of skin cells due to an overstimulated cell cycle produces a chronic inflammatory condition known as psoriasis. On the other hand, aggressive inhibition of the cell cycle that destroys the reproductive capacity of all the body's cells leads to a condition called progeria, which causes young people to grow old and die at an early age. Many different types of cancer can result when the signals that keep the cell cycle in check are not transmitted or received properly. Learning how the cell cycle is regulated and how to control it may lead to many important scientific advances, such as the possibility of therapeutic cloning and tissue engineering which forms organs in the laboratory.

Mitosis involves division of the nucleus and the distribution of its contents, the chromosomes, into the daughter cells. Before this occurs, the chromosomes must be duplicated so that each daughter cell can receive one of each kind of chromosome. However, as we will soon see, a special type of cell division, meiosis, reduces the chromosome number in order to produce gametes.

summary

9.1 The Cell Cycle

Eukaryotic cells go through a cell cycle that includes (1) interphase and (2) a mitotic stage that consists of mitosis and cytokinesis. Interphase, in turn, is composed of three stages: G_1 (growth as certain organelles double), S (the synthesis stage, where the chromosomes are duplicated), and G_2 (growth as the cell prepares to divide). Most cells of the body are no longer dividing and are said to be arrested in a G_0 state, from which cells must receive signals to return to G_1 stage and complete the cell cycle. During the mitotic stage (M), the chromosomes are sorted into two daughter cells so that each receives a full complement of chromosomes.

The cell cycle is regulated by three well-known checkpoints—the restriction point, or G_1 checkpoint, the G_2 checkpoint prior to the M stage, and the M stage checkpoint, or spindle assembly checkpoint, immediately before anaphase. The G_1 checkpoint ensures that conditions are favorable and that the proper signals are present, and also checks the DNA for damage. If the DNA is damaged beyond repair, the p53 protein may initiate apoptosis. During apoptosis, enzymes called caspases bring about destruction of the nucleus and the rest of the cell. Cell division and apoptosis are two opposing processes that keep the number of healthy cells in balance.

9.2 Mitosis and Cytokinesis

Interphase represents the portion of the cell cycle between nuclear divisions, and during this time, preparations are made for cell division. These preparations include duplication of most cellular contents, including the centrosome, which organizes the mitotic spindle. The DNA is duplicated during S stage, at which time the chromosomes, which consisted of a single chromatid each, are duplicated. The G_2 checkpoint ensures that DNA has replicated properly. This results in a nucleus containing the same number of chromosomes, with each now consisting of two chromatids attached at the centromere. During interphase, the chromosomes are not distinct and are collectively called chromatin. Each eukaryotic species has a characteristic number of chromosomes. The total number is called the diploid number, and half this number is the haploid number.

Among eukaryotes, cell division involves both mitosis (nuclear division) and division of the cytoplasm (cytokinesis). As a result of mitosis, the chromosome number stays constant because each chromosome is duplicated and gives rise to two daughter chromosomes that consist of a single chromatid each.

Mitosis consists of five phases:

Prophase—The nucleolus disappears, the nuclear envelope fragments, and the spindle forms between centrosomes. The chromosomes condense and become visible under a light microscope. In animal cells, asters radiate from the centrioles within the centrosomes. Plant cells lack centrioles and, therefore, asters. Even so, the mitotic spindle forms.

Prometaphase (late prophase)—The kinetochores of sister chromatids attach to kinetochore spindle fibers extending from opposite poles. The chromosomes move back and forth until they are aligned at the metaphase plate.

Metaphase—The spindle is fully formed, and the duplicated chromosomes are aligned at the metaphase plate. The spindle consists of polar spindle fibers that overlap at the metaphase plate and kinetochore spindle fibers that are attached to chromosomes. The M stage checkpoint, or spindle assembly checkpoint, must be satisfied before progressing to the next phase.

Anaphase—Sister chromatids separate, becoming daughter chromosomes that move toward the poles. The polar spindle fibers slide past one another, and the kinetochore spindle fibers disassemble. Cytokinesis by furrowing begins.

Telophase—Nuclear envelopes re-form, chromosomes begin changing back to chromatin, the nucleoli reappear, and the spindle disappears. Cytokinesis continues, and is complete by the end of telophase.

Cytokinesis in animal cells is a furrowing process that divides the cytoplasm. Cytokinesis in plant cells involves the formation of a cell plate from which the plasma membrane and cell wall are completed.

9.3 The Cell Cycle and Cancer

The development of cancer is primarily due to the mutation of genes involved in control of the cell cycle. Cancer cells lack differentiation, have abnormal nuclei, do not undergo apoptosis, form tumors, and undergo metastasis and angiogenesis. Cancer often follows a progression in which mutations accumulate, gradually causing uncontrolled growth and the development of a tumor.

Proto-oncogenes stimulate the cell cycle after they are turned on by environmental signals such as growth factors. Oncogenes are mutated proto-oncogenes that stimulate the cell cycle without need of environmental signals. Tumor suppressor genes inhibit the cell cycle. Mutated tumor suppressor genes no longer inhibit the cell cycle, allowing unchecked cell division.

9.4 Prokaryotic Cell Division

Binary fission (in prokaryotes) and mitosis (in unicellular eukaryotic protists and fungi) allow organisms to reproduce asexually. Mitosis in multicellular eukaryotes is primarily for the purpose of development, growth, and repair of tissues.

The prokaryotic chromosome has a few proteins and a single, long loop of DNA. When binary fission occurs, the chromosome attaches to the inside of the plasma membrane and replicates. As the cell elongates, the chromosomes are pulled apart. Inward growth of the plasma membrane and formation of new cell wall material divide the cell in two.

understanding the terms

anaphase 158
angiogenesis 162
apoptosis 153
asexual reproduction 164
aster 156
benign 161
binary fission 164
cancer 161
caspase 153
cell cycle 152
cell plate 159
centriole 155
centromere 155
centrosome 155
chromatid 152
chromatin 155
cyclin 153
cytokinesis 152
diploid (2n) number 155
growth factor 153
haploid (n) number 155
histone 155
interphase 152
kinetochore 155
malignant 161
metaphase 157
metaphase plate 157
metastasis 162
mitosis 152
mitotic spindle 155
nucleoid 164
oncogene 162
p53 153
prometaphase 157
prophase 156
proto-oncogene 162
RB 153
reproductive cloning 159
signal 153
sister chromatid 155
somatic cell 153
telomere 162
telophase 158
therapeutic cloning 159
tumor 161
tumor suppressor gene 162

Match the terms to these definitions:

a _____ Central microtubule organizing center of cells, consisting of granular material. In animal cells, it contains two centrioles.
b. _____ Constriction where sister chromatids of a chromosome are held together.
c. _____ Microtubule structure that brings about chromosome movement during nuclear division.
d. _____ One of two genetically identical chromosome units that are the result of DNA replication.
e. _____ Programmed cell death that is carried out by enzymes routinely present in the cell

reviewing this chapter

1. Describe the cell cycle, including its different stages. 152
2. Describe three checkpoints of the cell cycle. 153
3. What is apoptosis, and what are its functions? 153
4. Distinguish between chromosome, chromatin, chromatid, centriole, cytokinesis, centromere, and kinetochore. 152–55
5. Describe the preparations for mitosis. 155
6. Describe the events that occur during the phases of mitosis. 156–58
7. How does plant cell mitosis differ from animal cell mitosis? 156–59
8. Contrast cytokinesis in animal cells and plant cells. 158–59
9. List and discuss characteristics of cancer cells that distinguish them from normal cells. 161–62
10. Compare and contrast the functions of proto-oncogenes and tumor suppressor genes in controlling the cell cycle. 162–63
11. Describe the prokaryotic chromosome and the process of binary fission. 164
12. Contrast the function of cell division in prokaryotic and eukaryotic cells. 165

testing yourself

Choose the best answer for each question.

1. In contrast to a eukaryotic chromosome, a prokaryotic chromosome
   a. is shorter and fatter.
   b. has a single loop of DNA.
   c. never replicates.
   d. contains many histones.
   e. All of these are correct.
2. The diploid number of chromosomes
   a. is the 2n number.
   b. is in a parent cell and therefore in the two daughter cells following mitosis.
   c. varies according to the particular organism.
   d. is in every somatic cell.
   e. All of these are correct.

For questions 3–5, match the descriptions that follow to the terms in the key.

KEY:

a. centrosome
b. chromosome
c. centromere
d. cyclin

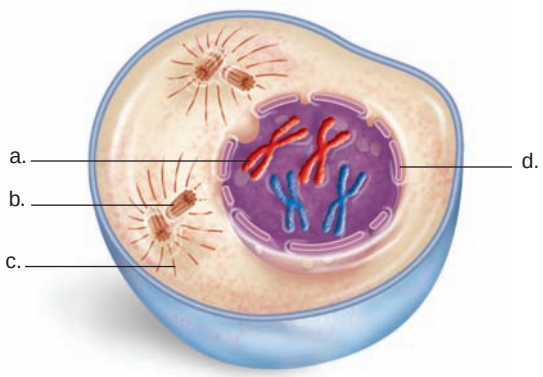
3. Point of attachment for sister chromatids
4. Found at a spindle pole in the center of an aster
5. Coiled and condensed chromatin
6. If a parent cell has 14 chromosomes prior to mitosis, how many chromosomes will each daughter cell have?
   a. 28 because each chromatid is a chromosome
   b. 14 because the chromatids separate
   c. only 7 after mitosis is finished
   d. any number between 7 and 28
   e. 7 in the nucleus and 7 in the cytoplasm, for a total of 14
7. In which phase of mitosis are the kinetochores of the chromosomes being attached to spindle fibers?
   a. prophase
   b prometaphase
   c. metaphase
   d. anaphase
   e. telophase
8. Interphase
   a. is the same as prophase, metaphase, anaphase, and telophase.
   b. is composed of G_1, S, and G_2 stages.
   c. requires the use of polar spindle fibers and kinetochore spindle fibers.
   d. is the majority of the cell cycle.
   e. Both b and d are correct.
9. At the metaphase plate during metaphase of mitosis, there are
   a. single chromosomes.
   b. duplicated chromosomes.
   c. G_1 stage chromosomes.
   d. always 23 chromosomes.
10. During which mitotic phases are duplicated chromosomes present?
    a. all but telophase
    b. prophase and anaphase
    c. all but anaphase and telophase
    d. only during metaphase at the metaphase plate
    e. Both a and b are correct.
11. Which of these is paired incorrectly?
    a. prometaphase—the kinetochores become attached to spindle fibers
    b. anaphase—daughter chromosomes are located at the spindle poles
    c. prophase—the nucleolus disappears and the nuclear envelope disintegrates
    d. metaphase—the chromosomes are aligned in the metaphase plate
    e. telophase—a resting phase between cell division cycles
12. When cancer occurs,
    a. cells cannot pass the G_1 checkpoint.
    b. control of the cell cycle is impaired.
    c. apoptosis has occurred.
    d. the cells can no longer enter the cell cycle.
    e. All of these are correct.
13. Which of the following is not characteristic of cancer cells?
    a. Cancer cells often undergo angiogenesis.
    b. Cancer cells tend to be nonspecialized.
    c. Cancer cells undergo apoptosis.
    d. Cancer cells often have abnormal nuclei.
    e. Cancer cells can metastasize.
14. Which of the following statements is true?
    a. Proto-oncogenes cause a loss of control of the cell cycle.
    b. The products of oncogenes may inhibit the cell cycle.
    c. Tumor-suppressor-gene products inhibit the cell cycle.
    d. A mutation in a tumor suppressor gene may inhibit the cell cycle.
    e. A mutation in a proto-oncogene may convert it into a tumor suppressor gene.

For questions 15–18, match the descriptions to a stage in the key.

KEY:

a. G_1 stage
b. S stage
c. G_2 stage
d. M (mitotic) stage

15. At the end of this stage, each chromosome consists of two attached chromatids.
16. During this stage, daughter chromosomes are distributed to two daughter nuclei.
17. The cell doubles its organelles and accumulates the materials needed for DNA synthesis.
18. The cell synthesizes the proteins needed for cell division.
19. Which is not true of the cell cycle?
    a. The cell cycle is controlled by internal/external signals.
    b. Cyclin is a signaling molcule that increases and decreases as the cycle continues.
    c. DNA damage can stop the cell cycle at the G_1 checkpoint.
    d. Apoptosis occurs frequently during the cell cycle.
20. In human beings, mitosis is necessary for
    a. growth and repair of tissues.
    b. formation of the gametes.
    c. maintaining the chromosome number in all body cells.
    d. the death of unnecessary cells
    e. Both a and c are correct.
21. Label this diagram. What phase of mitosis does it represent?



thinking scientifically

1. After DNA is duplicated in eukaryotes, it must be bound to histones. This requires the synthesis of hundreds of millions of new protein molecules. With reference to Figure 9.1, when in the cell cycle would histones be made?
2. The survivors of the atomic bombs that were dropped on Hiroshima and Nagasaki have been the subjects of long-term studies of the effects of ionizing radiation on cancer incidence. The frequencies of different types of cancer in these individuals varied across the decades. In the 1950s, high levels of leukemia and cancers of the lung and thyroid gland were observed. The 1960s and 1970s brought high levels of breast and salivary gland cancers. In the 1980s, rates of colon cancer were especially high. Why do you suppose the rates of different types of cancer varied across time?

bioethical issue

Paying for Cancer Treatment

The risk factors for developing cancer are generally well known. Many lifestyle factors, such as smoking, poor dietary habits, obesity, physical inactivity, risky sexual behavior, and alcohol abuse, among others, have all been linked to higher risks of developing cancer. The greatly increasing rates of cancer over the past few decades have been decried as a public health epidemic. But aside from the cost in human life, the rising tide of cancer is causing a major crisis in today's society—how to pay for it all.

Despite increasing cure rates, effective new drugs, and novel treatments for various types of cancer, the costs of treatment continue to skyrocket. Nowhere is this more apparent than in the pharmaceutical industry. For example, new cancer drugs, while effective, are extremely expensive. Drug companies claim that it costs them between $500 million and $1 billion to bring a single new medicine to market. This cost may seem overblown, especially when you consider that the National Cancer Institute funds basic research into cancer biology and that drug companies often benefit indirectly from the findings. But the drug companies tell us that they need one successful drug to pay for the many drugs they try to develop that do not pay off. Still, it does seem as if successful drug companies try to keep lower-cost competitors out of the market. The question of how much drug companies can charge for drugs and who should pay for them is a thorny one. If drug companies don't show a profit, they may go out of business and there will be no new drugs. The same is true for insurance companies if they can't raise the cost of insurance to pay for expensive drugs. If the government buys drugs for Medicare patients, taxes may go up dramatically.

But how should the cost of treatment be met? Cancer is an illness that can be the direct result of poor lifestyle choices, but it can also occur in otherwise healthy individuals who make proper choices. And with increasing life spans, the incidence of cancer can only be expected to increase in future years. Should people who develop cancer due to poor lifestyle choices be held fully or partly responsible for paying for treatment? And if so, how? And how should the cost of developing new drugs and treatments be borne? There are no easy answers for any of these questions, but as cancer continues to extract a high toll in both human life and financial resources, future generations may face some difficult choices.

Biology website

The companion website for *Biology* provides a wealth of information organized and integrated by chapter. You will find practice tests, animations, videos, and much more that will complement your learning and understanding of general biology.

http://www.mhhe.com/maderbiology10

10

Meiosis and Sexual Reproduction

Nanu Ram Jogi, at 90 years old, recently became the world's oldest new father. As he hoisted his newborn daughter into the air amid a throng of cameras, microphones, and reporters, he boasted that he plans to continue fathering children with his wife, Saburi, now 50, until he is 100. He cannot even recall how many children he has fathered over the many years of his life, but it is estimated that he has at least twelve sons, nine daughters, and twenty grandchildren. Extreme cases such as this remind us of the huge reproductive potential of most species.

This chapter discusses meiosis, the process that occurs during sexual reproduction and ensures that offspring will have a different combination of genes compared to their parents. Occasionally, offspring inherit a detrimental number of genes and chromosomes. Such events do not detract from the principle that genetic variations are essential to the survival of species, because they allow them to evolve and become adapted to an ever-changing environment.

Nanu Ram Jogi, the world's oldest father.

concepts

10.1 Halving the Chromosome Number

In sexually reproducing organisms, **meiosis** [Gk. *mio,* less, and *-sis,* act or process of] is the type of nuclear division that reduces the chromosome number from the diploid (2n) number [Gk. *diplos,* twofold, and *-eides,* like] to the haploid (n) number [Gk. *haplos,* single, and *-eides,* like]. The **diploid (2n) number** refers to the total number of chromosomes. The **haploid (n) number** of chromosomes is half the diploid number. In humans, the diploid number of 46 is reduced to the haploid number of 23. **Gametes** (reproductive cells, often the sperm and egg) usually have the haploid number of chromosomes. Gamete formation and then fusion of gametes to form a cell called a zygote are integral parts of **sexual reproduction.** A **zygote** always has the full or diploid (2n) number of chromosomes. In plants and animals, the zygote undergoes development to become an adult organism.

Obviously, if the gametes contained the same number of chromosomes as the body cells, the number of chromosomes would double with each new generation. Within a few generations, the cells of an animal would be nothing but chromosomes! For example, in humans with a diploid number of 46 chromosomes, in five generations the chromosome number would increase to 1,472 chromosomes (46×2^5). In 10 generations this number would increase to a staggering 47,104 chromosomes (46×2^{10}). The early cytologists (biologists who study cells) realized this, and Pierre-Joseph van Beneden, a Belgian, was gratified to find in 1883 that the sperm and the egg of the roundworm *Ascaris* each contain only two chromosomes, while the zygote and subsequent embryonic cells always have four chromosomes.

Homologous Pairs of Chromosomes

In diploid body cells, the chromosomes occur in pairs. Figure 10.1*a,* a pictorial display of human chromosomes, shows the chromosomes arranged according to pairs. The members of each pair are called homologous chromosomes. **Homologous chromosomes** or **homologues** [Gk. *homologos,* agreeing, corresponding] look alike; they have the same length and centromere position. When stained, homologues have a similar banding pattern because they contain genes for the same traits in the same order. But while homologous chromosomes have genes for the same traits, such as finger length, the gene on one homologue may code for short fingers and the gene at the same location on the other homologue may code for long fingers. Alternate forms of a gene (as for long fingers and short fingers) are called **alleles.**

The chromosomes in Figure 10.1*a* are duplicated as they would be just before nuclear division. Recall that during the S stage of the cell cycle, DNA replicates and the chromosomes become duplicated. The results of the duplication process are depicted in Figure 10.1*b.* When duplicated, a chromosome is composed of two identical parts called sister chromatids, each containing one DNA double helix molecule. The sister chromatids are held together at a region called the centromere.

Why does the zygote have two chromosomes of each kind? One member of a homologous pair was inherited from the male parent, and the other was inherited from the female parent by way of the gametes. In Figure 10.1*b* and throughout the chapter, the paternal chromosome is colored blue, and the maternal chromosome is colored red. *Therefore, you should use length and centromere location, not color, to recognize homologues.* We will see how meiosis reduces the chromosome number. Whereas the zygote and body cells have homologous pairs of chromosomes, the gametes have only one chromosome of each kind—derived from either the paternal or maternal homologue.

Overview of Meiosis

Meiosis requires two nuclear divisions and produces four haploid daughter cells, each having one of each kind of chromosome. Replication occurs only once and the daughter cells have half the total number of chromosomes as were in the diploid parent nucleus. The daughter cells receive one of each kind of parental chromosome, but in different combinations. Therefore, the daughter cells are not genetically identical to the parent cell or to each other.

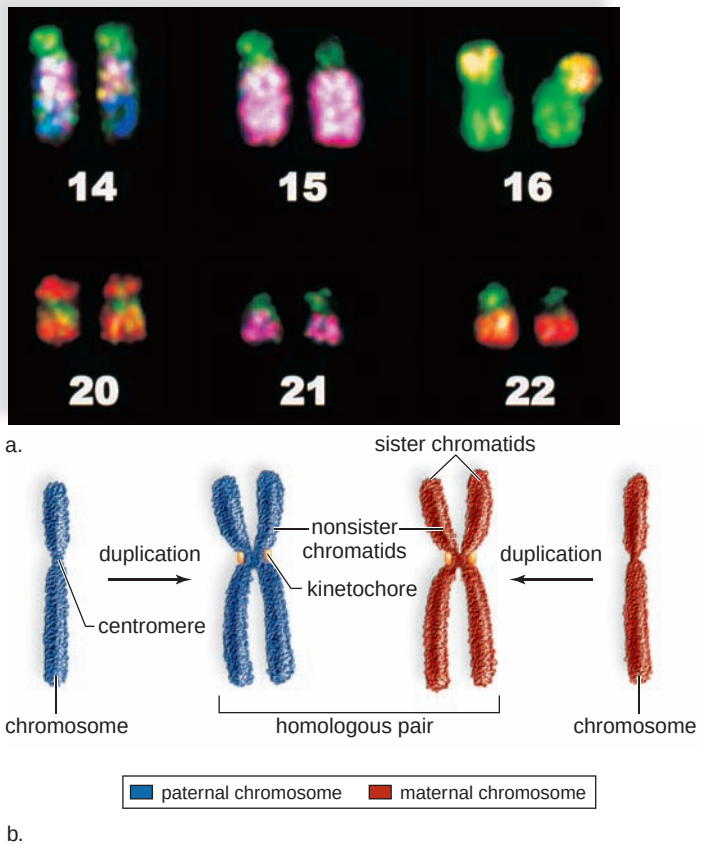


FIGURE 10.1 Homologous chromosomes.

In diploid body cells, the chromosomes occur in pairs called homologous chromosomes. **a.** In this micrograph of stained chromosomes from a human cell, the pairs have been numbered. **b.** These chromosomes are duplicated, and each one is composed of two chromatids. The sister chromatids contain the exact same genes; the nonsister chromatids contain genes for the same traits (e.g., type of hair, color of eyes), but they may differ in that one could "call for" dark hair and eyes and the other for light hair and eyes.

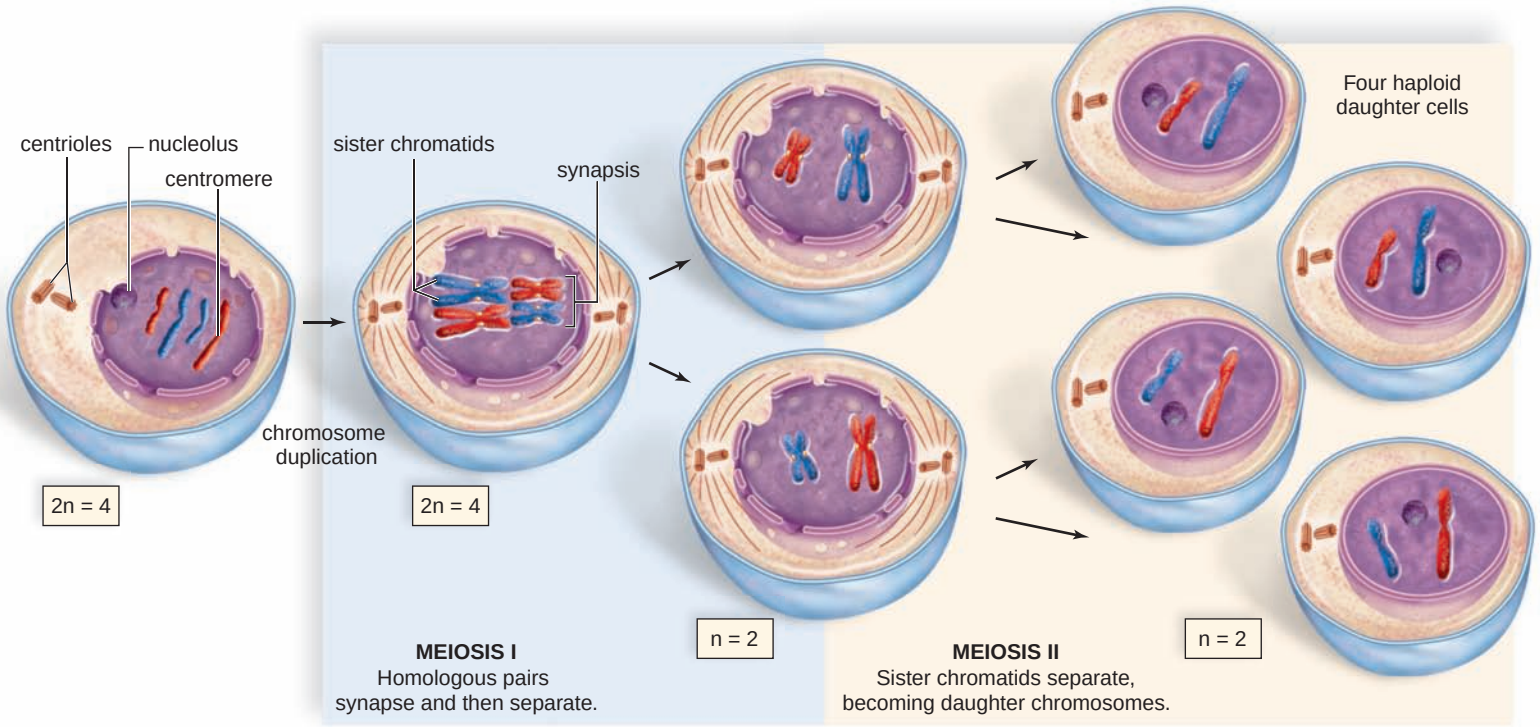


FIGURE 10.2 Overview of meiosis.

Following DNA replication, each chromosome is duplicated and consists of two chromatids. During meiosis I, homologous chromosomes pair and separate. During meiosis II, the sister chromatids of each duplicated chromosome separate. At the completion of meiosis, there are four haploid daughter cells. Each daughter cell has one of each kind of chromosome.

Figure 10.2 presents an overview of meiosis, indicating the two cell divisions, meiosis I and meiosis II. Prior to meiosis I, DNA (deoxyribonucleic acid) replication has occurred; therefore, each chromosome has two sister chromatids. During meiosis I, something new happens that does not occur in mitosis. The homologous chromosomes come together and line up side by side due to a means of attraction still unknown. This process is called **synapsis** [Gk. *synaptos*, united, joined together] and results in a **bivalent** [L. *bis*, two, and *valens*, strength]—that is, two homologous chromosomes that stay in close association during the first two phases of meiosis I. Sometimes the term tetrad [Gk. *tetra*, four] is used instead of bivalent because, as you can see, a bivalent contains four chromatids.

Following synapsis, homologous pairs align at the metaphase plate, and then the members of each pair separate. This separation means that only one duplicated chromosome from each homologous pair reaches a daughter nucleus. It is important for each daughter nucleus to have a member from each pair of homologous chromosomes because only in that way can there be a copy of each kind of chromosome in the daughter nuclei. Notice in Figure 10.2 that two possible combinations of chromosomes in the daughter cells are shown: short red with long blue and short blue with long red. Knowing that all daughter cells have to have one short chromosome and one long chromosome, what are the other two possible combinations of chromosomes for these particular cells?

Notice that replication occurs only once during meiosis; no replication of DNA is needed between meiosis I and meiosis II because the chromosomes are still duplicated; they already have two sister chromatids. During meiosis II, the sister chromatids separate, becoming daughter chromosomes that move to opposite poles. The chromosomes in the four daughter cells contain only one DNA double helix molecule because they are not duplicated.

The number of centromeres can be counted to verify that the parent cell has the diploid number of chromosomes. At the end of meiosis I, the chromosome number has been reduced because there are half as many centromeres present, even though each chromosome still consists of two chromatids each. Each daughter cell that forms has the haploid number of chromosomes. At the end of meiosis II, sister chromatids separate, and each daughter cell that forms still contains the haploid number of chromosomes, each consisting of a single chromatid.

Fate of Daughter Cells

In the plant life cycle, the daughter cells become haploid spores that germinate to become a haploid generation. This generation produces the gametes by mitosis. The plant life cycle is studied in Chapter 24. In the animal life cycle, the daughter cells become the gametes, either sperm or eggs. The body cells of an animal normally contain the diploid number of chromosomes due to the fusion of sperm and egg during fertilization. If meiotic events go wrong, the gametes can contain the wrong number of chromosomes or altered chromosomes. This possibility and its consequences are discussed on pages 180–85.

Check Your Progress 10.1

1. Define what is meant by a homologous pair of chromosomes.
2. How does chromosome sorting in meiosis I differ from mitosis?

10.2 Genetic Variation

We have seen that meiosis provides a way to keep the chromosome number constant generation after generation. Without meiosis, the chromosome number of the next generation would continually increase. The events of meiosis also help ensure that genetic variation occurs with each generation. Asexually reproducing organisms, such as the prokaryotes, depend primarily on mutations to generate variation among offspring. This is sufficient because they produce great numbers of offspring very quickly. Although mutations also occur among sexually reproducing organisms, the reshuffling of genetic material during sexual reproduction ensures that offspring will have a different combination of genes from their parents. Meiosis brings about genetic variation in two key ways: crossing-over and independent assortment of homologous chromosomes.

Genetic Recombination

Crossing-over is an exchange of genetic material between nonsister chromatids of a bivalent during meiosis I. It is estimated that an average of two or three crossovers occur per human chromosome. At synapsis, homologues line up side by side, and a nucleoprotein lattice appears between them (Fig. 10.3). This lattice holds the bivalent together in such a way that the DNA of the duplicated chromosomes of each homologue pair is aligned. This ensures that the genes contained on the nonsister chromatids are directly aligned. Now crossing-over may occur. As the lattice breaks down, homologues are temporarily held together by *chiasmata* (sing., chiasma), regions where the nonsister chromatids are attached due to crossing-over. Then homologues separate and are distributed to different daughter cells. Crossing-over has been shown to be essential for the normal segregation of chromosomes during meiosis. For example, reduced levels of crossing-over have been linked to Down syndrome, which is caused by an extra copy of chromosome 21.

To appreciate the significance of crossing-over, it is necessary to remember that the members of a homologous pair can carry slightly different instructions for the same genetic traits. In the end, due to a swapping of genetic material during crossing-over, the chromatids held together by a centromere are no longer identical. Therefore, when the chromatids separate during meiosis II, some of the daughter cells receive daughter chromosomes with recombined alleles. Due to **genetic recombination,** the offspring have a different set of alleles, and therefore genes, than their parents.

Independent Assortment of Homologous Chromosomes

During **independent assortment,** the homologous chromosome pairs separate independently, or in a random manner. When homologues align at the metaphase plate, the maternal or paternal homologue may be oriented toward either pole. Figure 10.4 shows the possible orientations for a cell that contains only three pairs of homologous chromosomes. Once all possible alignments are considered, the result will be 2^3, or eight, combinations of maternal and paternal chromosomes in the resulting gametes from this cell, simply due to independent assortment of homologues.

Significance of Genetic Variation

In humans, who have 23 pairs of chromosomes, the possible chromosomal combinations in the gametes is a staggering 2^{23}, or 8,388,608. The variation that results from meiosis is enhanced by **fertilization,** the union of the male and female gametes. The chromosomes donated by the parents are combined, and in humans, this means that there are $(2^{23})^2$, or 70,368,744,000,000, chromosomally different zygotes possible, even assuming no crossing-over. If crossing-over occurs once, then $(4^{23})^2$, or 4,951,760,200,000,000,000,000,000,000, genetically different zygotes are possible for every couple. Keep in mind that crossing-over can occur several times in each chromosome!

The staggering amount of genetic variation achieved through meiosis is particularly important to the long-term survival of a species because it increases genetic variation within a population. (While asexual reproduction passes on exactly the same combination of chromosomes and genes.) The process of sexual reproduction brings about genetic re-

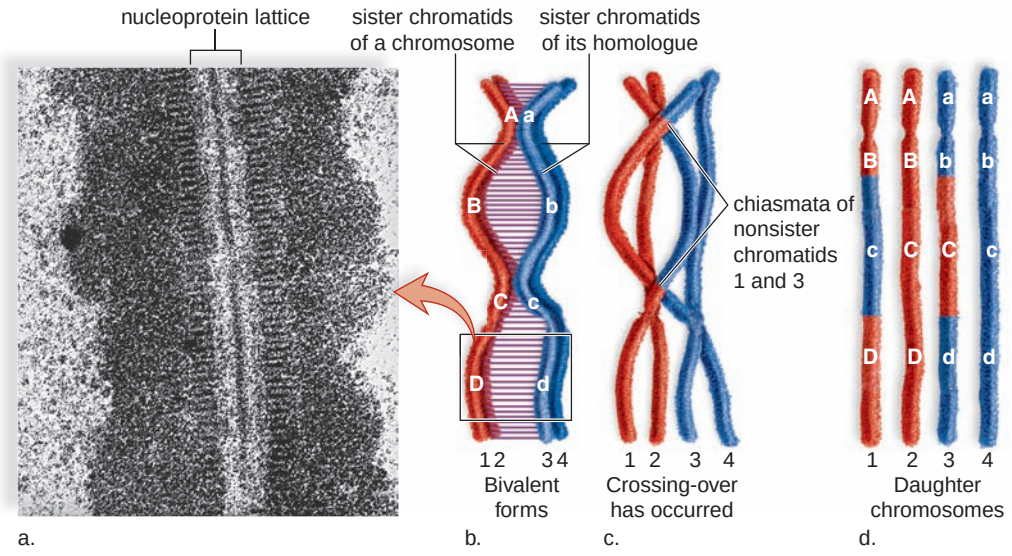


FIGURE 10.3 Crossing-over occurs during meiosis I.

a. The homologous chromosomes pair up, and a nucleoprotein lattice develops between them. This is an electron micrograph of the lattice. It zippers the members of the bivalent together so that corresponding genes are in alignment. **b.** This diagrammatic representation shows only two places where nonsister chromatids 1 and 3 have come into contact. Actually, the other two nonsister chromatids most likely are also crossing-over. **c.** Chiasmata indicate where crossing-over has occurred. The exchange of color represents the exchange of genetic material. **d.** Following meiosis II, daughter chromosomes have a new combination of genetic material due to crossing-over, which occurred between nonsister chromatids during meiosis I.

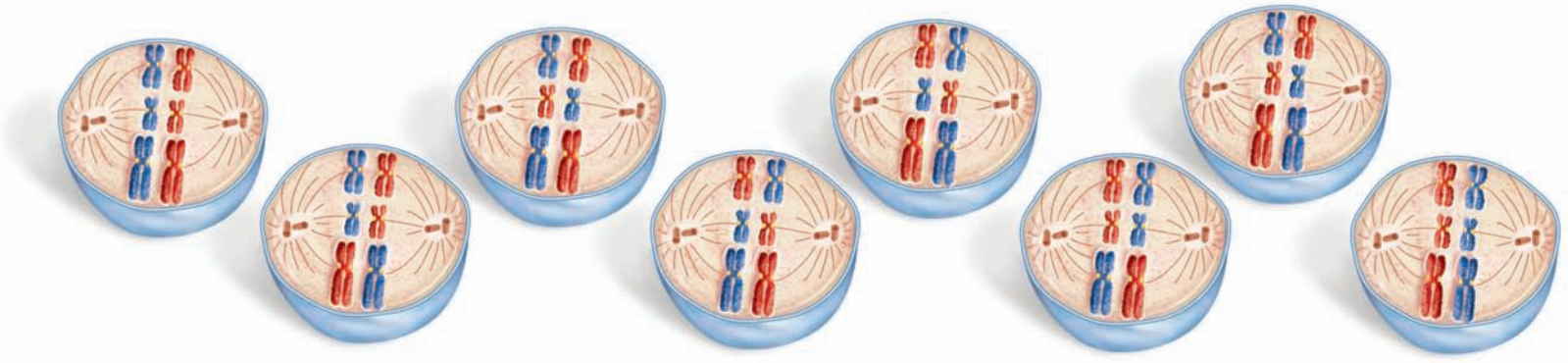


FIGURE 10.4 **Independent assortment.**

When a parent cell has three pairs of homologous chromosomes, there are 2^3, or 8, possible chromosome alignments at the metaphase plate due to independent assortment. Among the 16 daughter nuclei resulting from these alignments, there are 8 different combinations of chromosomes.

combinations among members of a population (Fig. 10.5). If a parent is already successful in a particular environment, is asexual reproduction advantageous? It would seem so as long as the environment remains unchanged. However, if the environment changes, genetic variability among offspring introduced by sexual reproduction may be advantageous. Under the new conditions, some offspring may have a better chance of survival and reproductive success than others in a population. For example, suppose the ambient temperature were to rise due to global warming. Perhaps a dog with genes for the least amount of fur may have an advantage over other dogs of its generation.

In a changing environment, sexual reproduction, with its reshuffling of genes due to meiosis and fertilization, might give a few offspring a better chance of survival.

Check Your Progress 10.2

1. Briefly describe the two main ways in which meiosis contributes to genetic variation.
2. In a cell with four pairs of homologous chromosomes, how many combinations of chromosomes are possible in the gametes?
3. Why are meiosis and sexual reproduction important in responding to the changing environment?

FIGURE 10.5 **Genetic variation.**

Why do the puppies in this litter have a different appearance even though they have the same two parents? Because crossing-over and independent assortment occurred during meiosis, and fertilization brought different gametes together.

10.3 The Phases of Meiosis

Meiosis consists of two unique cell divisions, meiosis I and meiosis II. The phases of both meiosis I and meiosis II—prophase, metaphase, anaphase, and telophase—are described.

Prophase I

It is apparent during prophase I that nuclear division is about to occur because a spindle forms as the centrosomes migrate away from one another. The nuclear envelope fragments, and the nucleolus disappears.

The homologous chromosomes, each having two sister chromatids, undergo synapsis to form bivalents. As depicted in Figure 10.3 by the exchange of color, crossing-over between the nonsister chromatids may occur at this time. After crossing-over, the sister chromatids of a duplicated chromosome are no longer identical.

Throughout prophase I, the chromosomes have been condensing so that by now they have the appearance of metaphase chromosomes.

Metaphase I

During metaphase I, the bivalents held together by chiasmata (see Fig. 10.3) have moved toward the metaphase plate (equator of the spindle). Metaphase I is characterized by a fully formed spindle and alignment of the bivalents at the metaphase plate. As in mitosis, kinetochores are seen, but the two kinetochores of a duplicated chromosome are attached to the same kinetochore spindle fiber.

Bivalents independently align themselves at the metaphase plate of the spindle. The maternal homologue of each bivalent may be oriented toward either pole, and the paternal homologue of each bivalent may be oriented toward either pole. The orientation of one bivalent is not dependent on the orientation of the other bivalents. This contributes to the genetic variability of the daughter cells because all possible combinations of chromosomes can occur in the daughter cells.

Anaphase I

During anaphase I, the homologues of each bivalent separate and move to opposite poles, but sister chromatids do not separate. Therefore, each chromosome still has two chromatids (see Fig. 10.6, page 174).

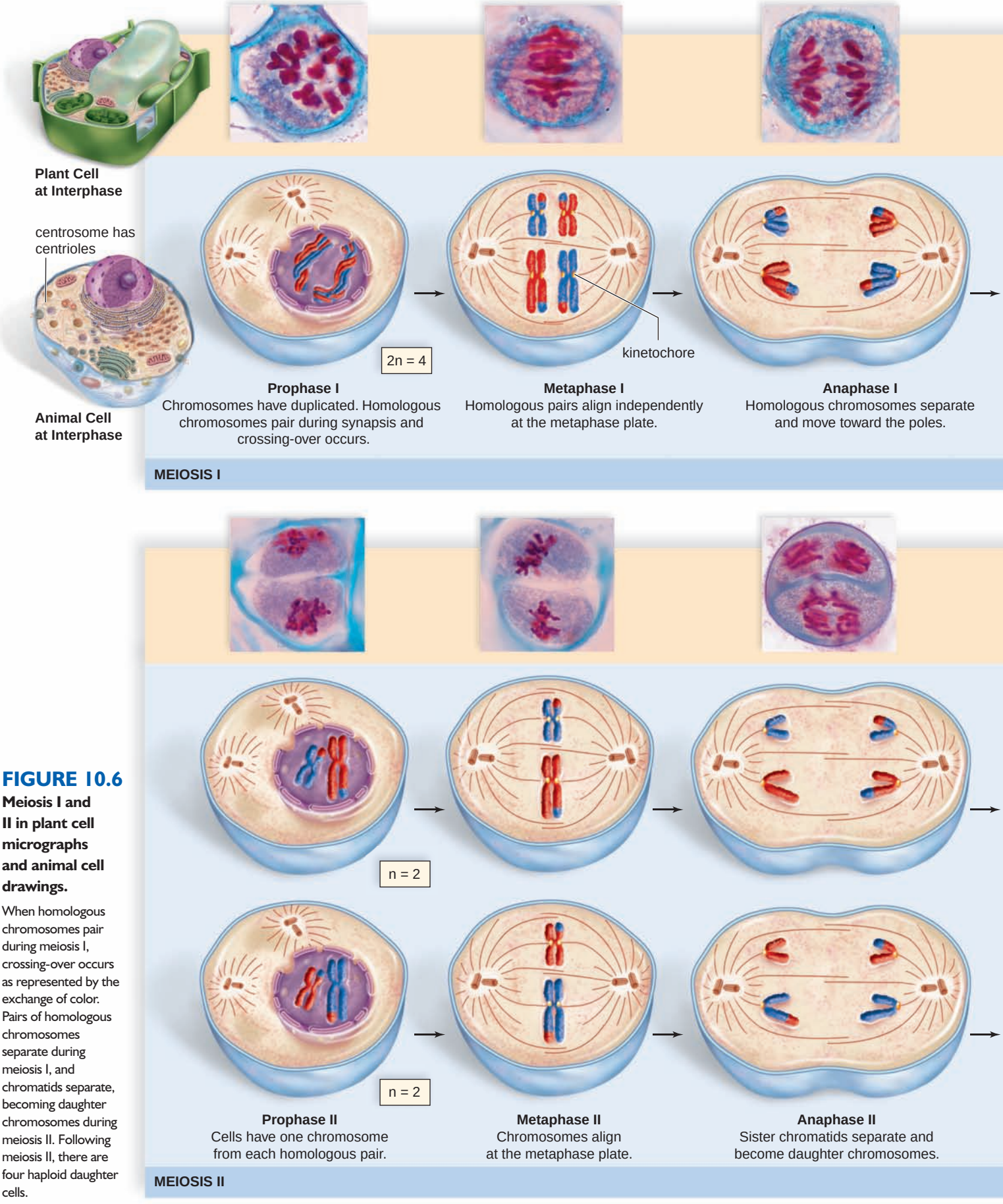
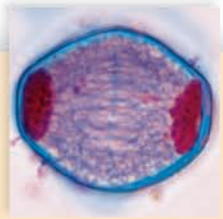
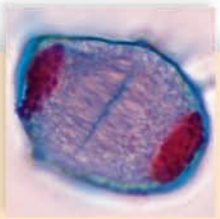
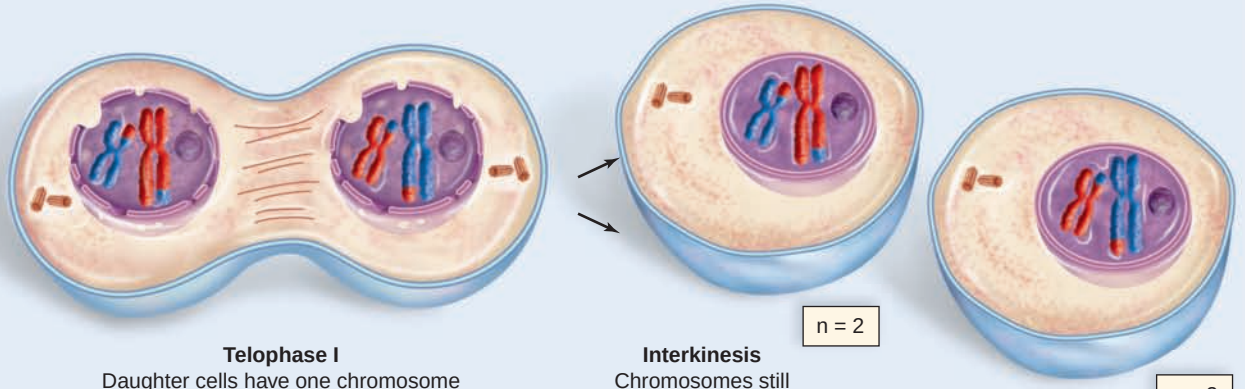


FIGURE 10.6
Meiosis I and II in plant cell micrographs and animal cell drawings.

When homologous chromosomes pair during meiosis I, crossing-over occurs as represented by the exchange of color. Pairs of homologous chromosomes separate during meiosis I, and chromatids separate, becoming daughter chromosomes during meiosis II. Following meiosis II, there are four haploid daughter cells.



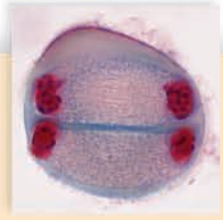


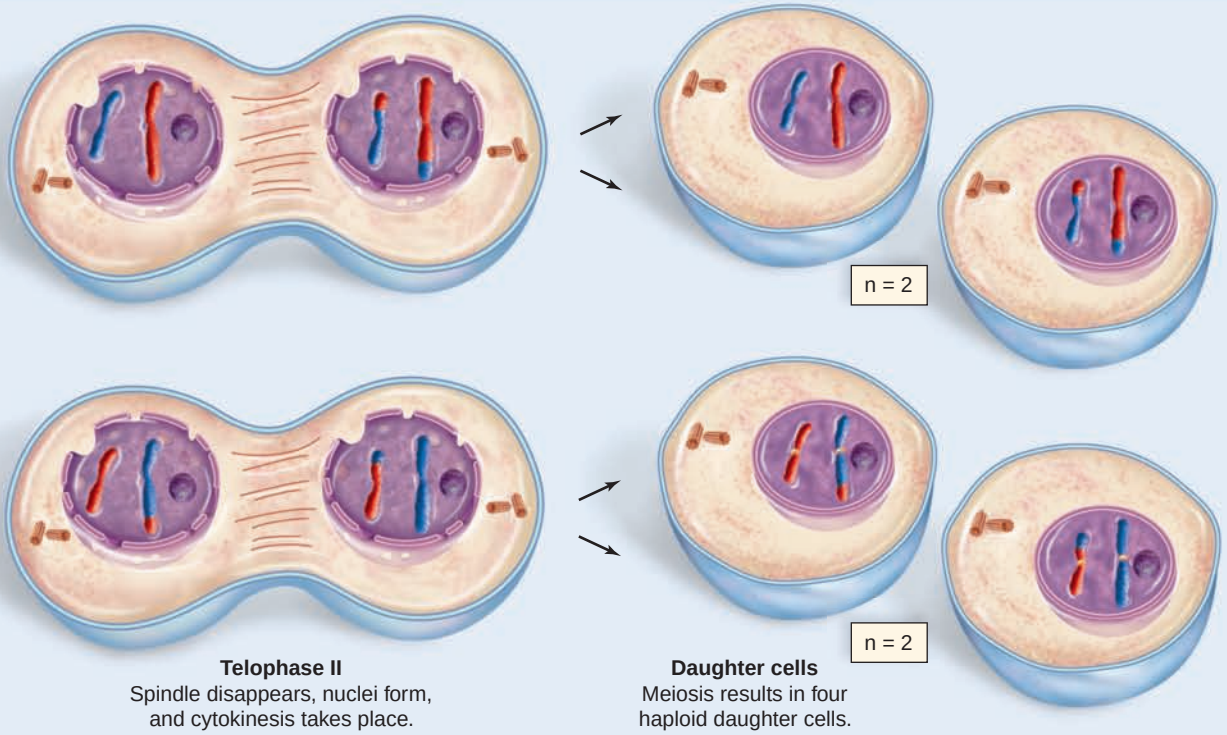


Telophase I
Daughter cells have one chromosome from each homologous pair.

Interkinesis
Chromosomes still consist of two chromatids.

MEIOSIS I cont'd

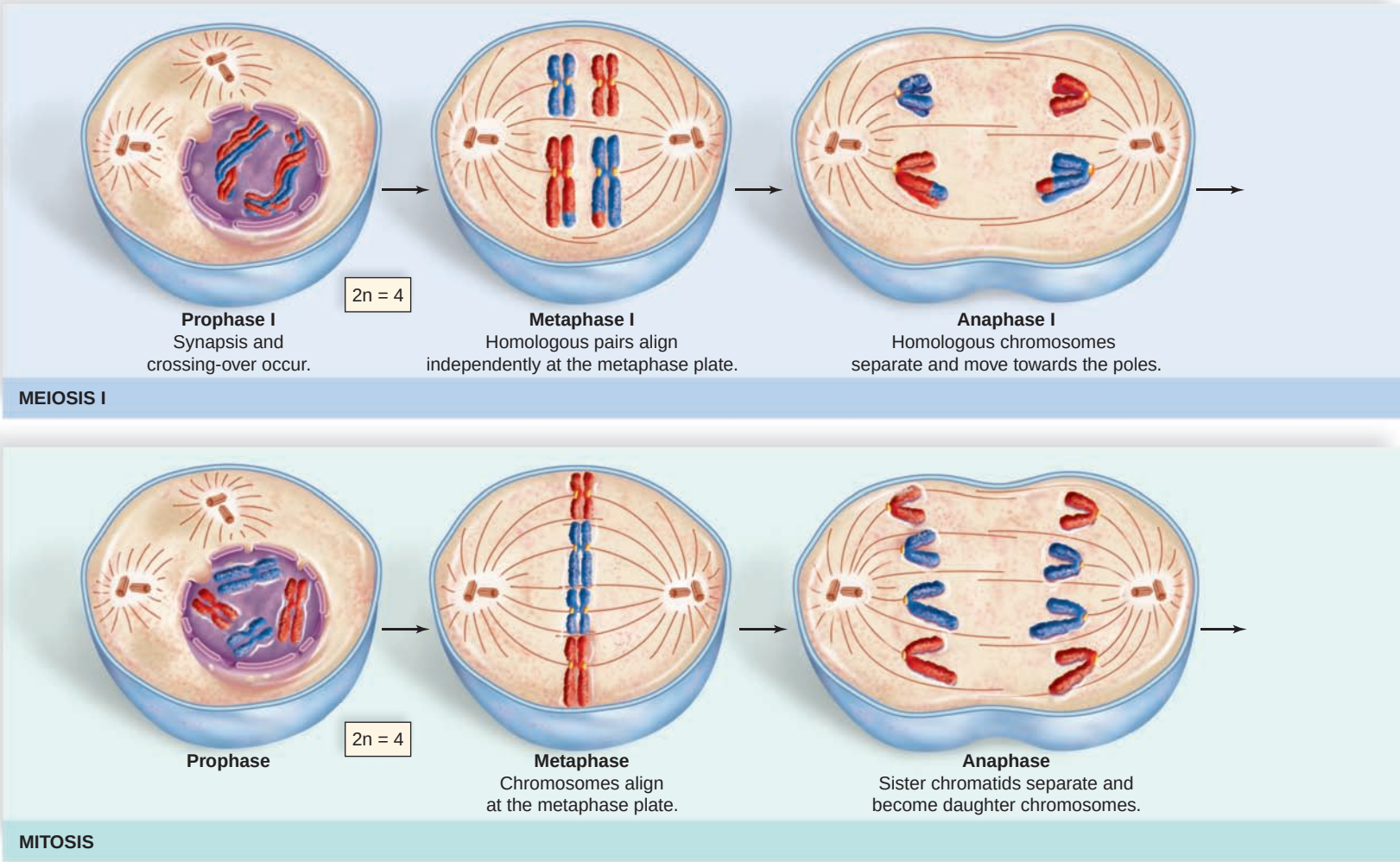




Telophase II
Spindle disappears, nuclei form, and cytokinesis takes place.

Daughter cells
Meiosis results in four haploid daughter cells.

MEIOSIS II cont'd



Telophase I

Completion of telophase I is not necessary during meiosis. That is, the spindle disappears, but new nuclear envelopes need not form before the daughter cells proceed to meiosis II. Also, this phase may or may not be accompanied by cytokinesis, which is separation of the cytoplasm. Figure 10.6, page 174, shows only two of the four possible combinations of haploid chromosomes when the parent cell has two homologous pairs of chromosomes. Can you determine what the other two possible combinations of chromosomes are?

Interkinesis

Following telophase, the cells enter interkinesis. The process of **interkinesis** is similar to interphase between mitotic divisions except that DNA replication does not occur because the chromosomes are already duplicated.

Meiosis II and Gamete Formation

At the beginning of meiosis II, the two daughter cells contain the haploid number of chromosomes, or one chromosome from each homologous pair. Note that these chromosomes still consist of duplicated sister chromatids at this point. During metaphase II, the chromosomes align at the metaphase plate, but do not align in homologous pairs as in meiosis I because only one chromosome of each homologous pair is present (see Fig. 10.6, page 174). Thus, the alignment of the chromosomes at the metaphase plate is similar to what is observed during mitosis. During anaphase II, the sister chromatids separate, becoming daughter chromosomes that are not duplicated. These daughter chromosomes move toward the poles. At the end of telophase II and cytokinesis, there are four haploid cells. Due to crossing-over of chromatids during meiosis I, each gamete will most likely contain chromosomes with varied genes.

As mentioned, following meiosis II, the haploid cells become gametes in animals (see Section 10.5). In plants, they become **spores,** reproductive cells that develop into new multicellular structures without the need to fuse with another reproductive cell. The multicellular structure is the haploid generation, which produces gametes. The resulting zygote develops into a diploid generation. Therefore, plants have both haploid and diploid phases in their life cycle, and plants are said to exhibit an **alternation of generations.** In most fungi and algae, the zygote undergoes meiosis, and the daughter cells develop into new individuals. Therefore, the organism is always haploid.

Check Your Progress 10.3

1. What would cause certain daughter cells following meiosis II to be identical? What would cause them to not be identical?
2. How does interkinesis differ from interphase?

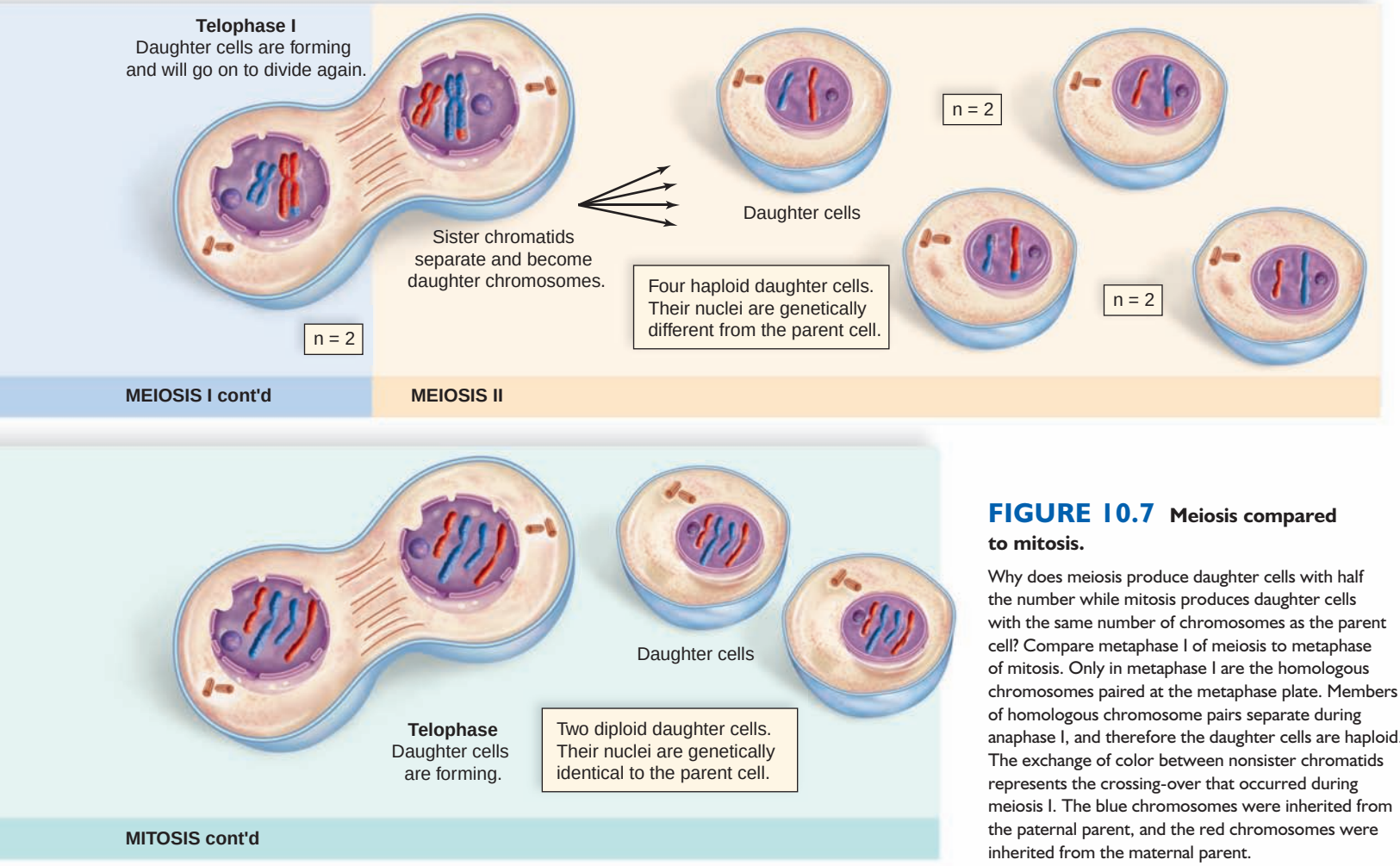


FIGURE 10.7 Meiosis compared to mitosis.

Why does meiosis produce daughter cells with half the number while mitosis produces daughter cells with the same number of chromosomes as the parent cell? Compare metaphase I of meiosis to metaphase of mitosis. Only in metaphase I are the homologous chromosomes paired at the metaphase plate. Members of homologous chromosome pairs separate during anaphase I, and therefore the daughter cells are haploid. The exchange of color between nonsister chromatids represents the crossing-over that occurred during meiosis I. The blue chromosomes were inherited from the paternal parent, and the red chromosomes were inherited from the maternal parent.

10.4 Meiosis Compared to Mitosis

Figure 10.7 graphically compares meiosis and mitosis. Several of the fundamental differences between the two processes include:

- Meiosis requires two nuclear divisions, but mitosis requires only one nuclear division.
- Meiosis produces four daughter nuclei. Following cytokinesis there are four daughter cells. Mitosis followed by cytokinesis results in two daughter cells.
- Following meiosis, the four daughter cells are haploid and have half the chromosome number as the diploid parent cell. Following mitosis, the daughter cells have the same chromosome number as the parent cell.
- Following meiosis, the daughter cells are neither genetically identical to each other or to the parent cell. Following mitosis, the daughter cells are genetically identical to each other and to the parent cell.

In addition to the fundamental differences between meiosis and mitosis, two specific differences between the two types of nuclear divisions can be categorized. These differences involve occurrence and process.

Occurrence

Meiosis occurs only at certain times in the life cycle of sexually reproducing organisms. In humans, meiosis occurs only in the reproductive organs and produces the gametes. Mitosis is more common because it occurs in all tissues during growth and repair.

Process

We will compare both meiosis I and meiosis II to mitosis.

Meiosis I Compared to Mitosis

Notice that these events distinguish meiosis I from mitosis:

- During prophase I, bivalents form and crossing-over occurs. These events do not occur during mitosis.
- During metaphase I of meiosis, bivalents independently align at the metaphase plate. The paired chromosomes have a total of four chromatids each. During metaphase in mitosis, individual chromosomes align at the metaphase plate. They each have two chromatids.
- During anaphase I of meiosis, homologues of each bivalent separate and duplicated chromosomes (with centromeres intact) move to opposite poles. During anaphase of mitosis, sister chromatids separate, becoming daughter chromosomes that move to opposite poles.

TABLE 10.1

Meiosis I Compared to Mitosis

Meiosis I	*Mitosis*
Prophase I	*Prophase*
Pairing of homologous chromosomes	No pairing of chromosomes
Metaphase I	*Metaphase*
Bivalents at metaphase plate	Duplicated chromosomes at metaphase plate
Anaphase I	*Anaphase*
Homologues of each bivalent separate and duplicated chromosomes move to poles	Sister chromatids separate, becoming daughter chromosomes that move to the poles
Telophase I	*Telophase*
Two haploid daughter cells, not identical to the parent cell	Two diploid daughter cells, identical to the parent cell

TABLE 10.2

Meiosis II Compared to Mitosis

Meiosis II	*Mitosis*
Prophase II	*Prophase*
No pairing of chromosomes	No pairing of chromosomes
Metaphase II	*Metaphase*
Haploid number of duplicated chromosomes at metaphase plate	Diploid number of duplicated chromosomes at metaphase plate
Anaphase II	*Anaphase*
Sister chromatids separate, becoming daughter chromosomes that move to the poles	Sister chromatids separate, becoming daughter chromosomes that move to the poles
Telophase II	*Telophase*
Four haploid daughter cells, not genetically identical	Two diploid daughter cells, identical to the parent cell

Meiosis II Compared to Mitosis

The events of meiosis II are similar to those of mitosis except in meiosis II, the nuclei contain the haploid number of chromosomes. In mitosis, the original number of chromosomes is maintained. Meiosis II produces two daughter cells from each parent cell that completes meiosis I, for a total of four daughter cells. These daughter cells contain the same number of chromosomes as they did at the end of meiosis I. Tables 10.1 and 10.2 compare meiosis I and II to mitosis.

Check Your Progress 10.4

1. How does the alignment of chromosomes in metaphase I differ from the alignment of chromosomes in metaphase of mitosis?
2. How is meiosis II more similar to mitosis than to meiosis I? How does it differ?

10.5 The Human Life Cycle

The term **life cycle** refers to all the reproductive events that occur from one generation to the next similar generation. In animals, including humans, the individual is always diploid, and meiosis produces the gametes, the only haploid phase of the life cycle (Fig. 10.8). In contrast, plants have a haploid phase that alternates with a diploid phase. The haploid generation, known as the **gametophyte,** may be larger or smaller than the diploid generation, called the **sporophyte.** Mosses growing on bare rocks and forest floors are the haploid generation, and the diploid generation is short-lived. In most fungi and algae, the zygote is the only diploid portion of the life cycle, and it undergoes meiosis. Therefore, the black mold that grows on bread and the green scum that floats on a pond are haploid. The majority of plant species, including pine, corn, and sycamore, are usually diploid, and the haploid generation is short-lived. In plants, algae, and fungi, the haploid phase of the life cycle produces gamete nuclei without the need for meiosis because it occurred earlier.

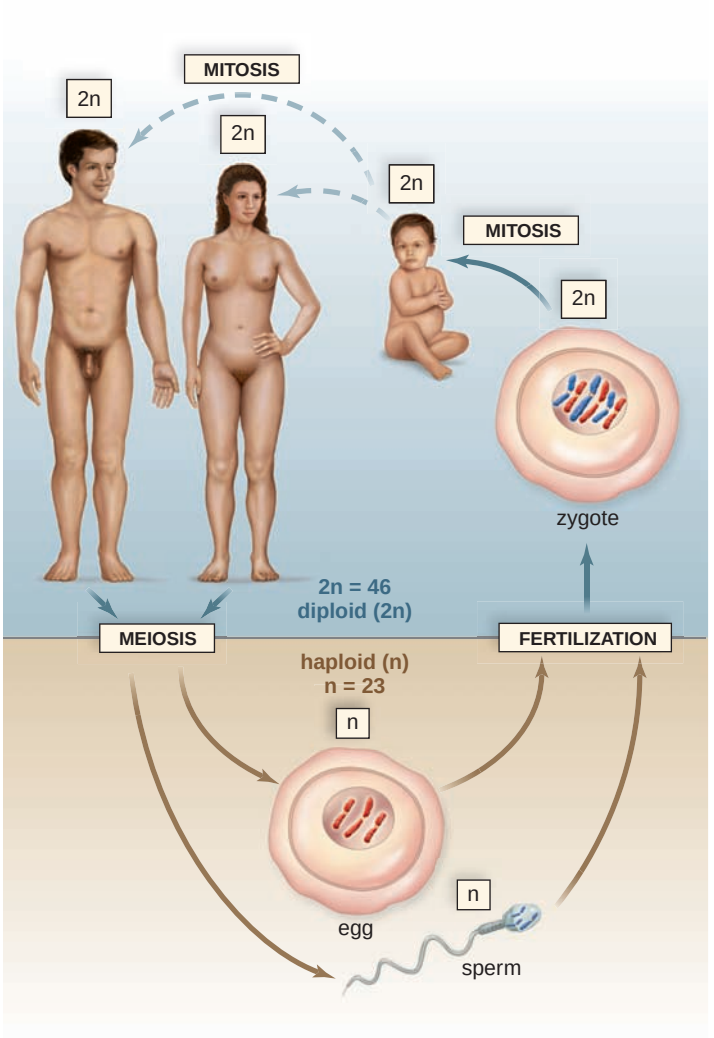


FIGURE 10.8 Life cycle of humans.

Meiosis in males is a part of sperm production, and meiosis in females is a part of egg production. When a haploid sperm fertilizes a haploid egg, the zygote is diploid. The zygote undergoes mitosis as it develops into a newborn child. Mitosis continues throughout life during growth and repair.

Animals are diploid and meiosis occurs during the production of gametes **(gametogenesis).** In males, meiosis is a part of **spermatogenesis** [Gk. *sperma,* seed; L. *genitus,* producing], which occurs in the testes and produces sperm. In females, meiosis is a part of **oogenesis** [Gk. *oon,* egg; L. *genitus,* producing], which occurs in the ovaries and produces eggs. A sperm and egg join at fertilization, restoring the diploid chromosome number. The resulting zygote undergoes mitosis during development of the fetus. After birth, mitosis is involved in the continued growth of the child and repair of tissues at any time.

Spermatogenesis and Oogenesis in Humans

In human males, spermatogenesis occurs within the testes, and in females, oogenesis occurs within the ovaries. The testes contain stem cells called spermatogonia, and these cells keep the testes supplied with primary spermatocytes that undergo spermatogenesis as described in Figure 10.9, *top.* Primary spermatocytes with 46 chromosomes undergo meiosis I to form two secondary spermatocytes, each with 23 duplicated chromosomes. Secondary spermatocytes undergo meiosis II to produce four spermatids with 23 daughter chromosomes. Spermatids then differentiate into viable sperm (spermatozoa). Upon sexual arousal, the sperm enter ducts and exit the penis upon ejaculation.

The ovaries contain stem cells called oogonia that produce many primary oocytes with 46 chromosomes during fetal development. They even begin oogenesis, but only a few continue when a female is sexually mature. The result of meiosis I is two haploid cells with 23 chromosomes each (Fig. 10.9, *bottom*). One of these cells, termed the **secondary oocyte** [Gk, *oon,* egg, and *kytos,* cell], receives almost all the cytoplasm. The other is a **polar body** that may either disintegrate or divide again. The secondary oocyte begins meiosis II but stops at metaphase II. Then the secondary oocyte leaves the ovary and enters an oviduct, where sperm may be present. If no sperm are in the oviduct or one does not enter the secondary oocyte, it eventually disintegrates without completing meiosis. If a sperm does enter the oocyte, some of its contents trigger the completion of meiosis II in the secondary oocyte, and another polar body forms. At the completion of oogenesis, following entrance of a sperm, there is one egg and two to three polar bodies. The polar bodies are a way to dispose of chromosomes while retaining much of the cytoplasm in the egg. Cytoplasmic molecules are needed by a developing embryo following fertilization. Some zygote components, such as the centrosome, are contributed by the sperm.

The mature egg has 23 chromosomes, but the zygote formed when the sperm and egg nuclei fuse has 46 chromosomes. Therefore, fertilization restores the diploid number of chromosomes.

Check Your Progress 10.5

1. Which cells in humans are capable of meiosis?
2. What is the benefit for one egg per oogenesis?

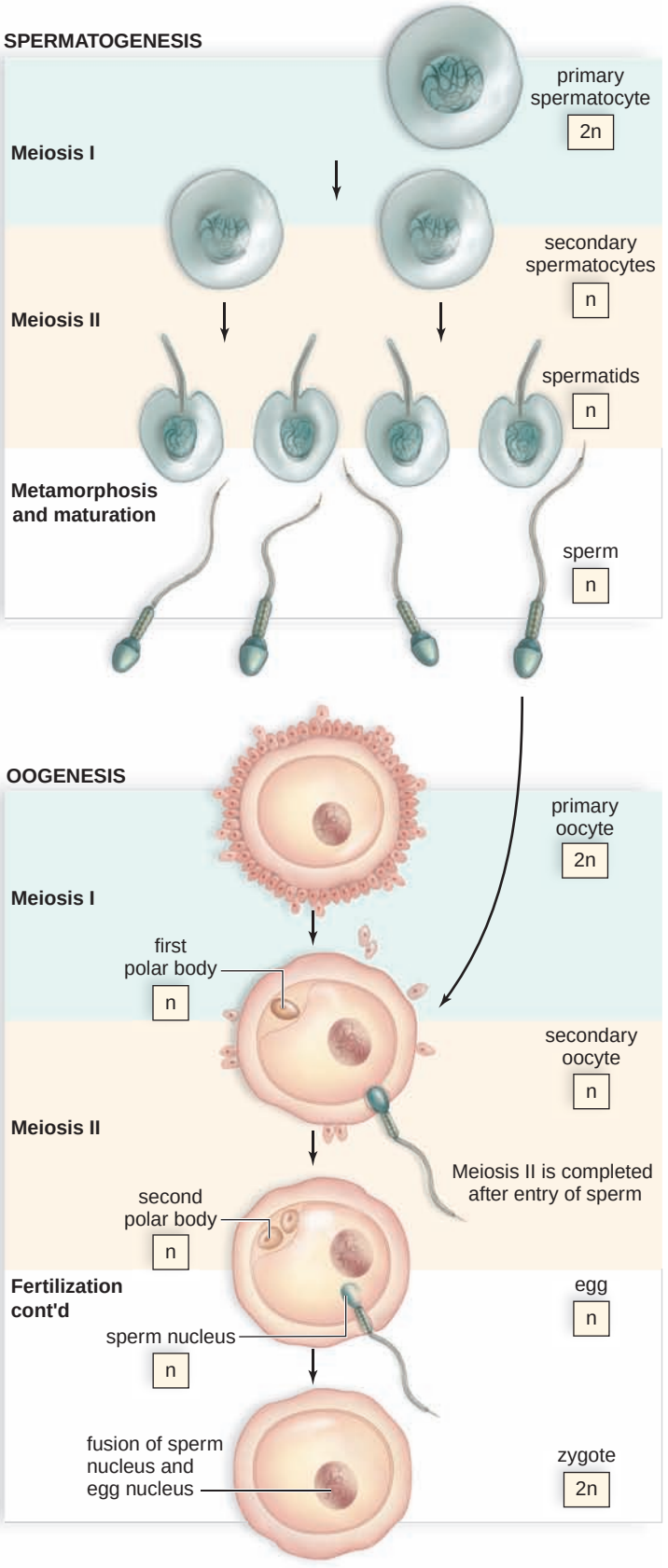


FIGURE 10.9 Spermatogenesis and oogenesis in mammals.

Spermatogenesis produces four viable sperm, whereas oogenesis produces one egg and at least two polar bodies. In humans, both sperm and egg have 23 chromosomes each; therefore, following fertilization, the zygote has 46 chromosomes.

10.6 Changes in Chromosome Number and Structure

We have seen that crossing-over creates variation within a population and is essential for the normal separation of chromosomes during meiosis. Furthermore, the proper separation of homologous chromosomes during meiosis I and the separation of sister chromatids during meiosis II are essential for the maintenance of normal chromosome numbers in living organisms. Although meiosis almost always proceeds normally, nondisjunction may occur, resulting in the gain or loss of chromosomes. Errors in crossing-over may result in extra or missing parts of chromosomes.

Aneuploidy

The correct number of chromosomes in a species is known as **euploidy.** A change in the chromosome number resulting from nondisjunction during meiosis is called **aneuploidy.** Aneuploidy is seen in both plants and animals. Monosomy and trisomy are two aneuploid states.

Monosomy (2n − 1) occurs when an individual has only one of a particular type of chromosome, and **trisomy** (2n + 1) occurs when an individual has three of a particular type of chromosome. Both monosomy and trisomy are the result of nondisjunction, or the failure of chromosomes to separate normally during mitosis or meiosis. *Primary nondisjunction* occurs during meiosis I when both members of a homologous pair go into the same daughter cell (Fig. 10.10*a*). *Secondary nondisjunction* occurs during meiosis II when the sister chromatids fail to separate and both daughter chromosomes go into the same gamete (Fig. 10.10*b*). Notice that when secondary nondisjunction occurs, there are two normal gametes and two aneuploid gametes. However, when primary nondisjunction occurs, there are no normal gametes produced.

In animals, autosomal monosomies and trisomies are generally lethal, but a trisomic individual is more likely to survive than a monosomic one. In humans, only three autosomal trisomic conditions are known to be viable beyond birth: trisomy 13, 18, and 21. Only trisomy 21 is viable beyond early childhood, and is characterized by a distinctive set of physical and mental abnormalities. On the other hand, sex chromosome aneuploids are better tolerated in animals and have a better chance of producing survivors.

Trisomy 21

The most common autosomal trisomy seen among humans is trisomy 21, also called Down syndrome. This syndrome is easily recognized by these characteristics: short stature; an eyelid fold; a flat face; stubby fingers; a wide gap between

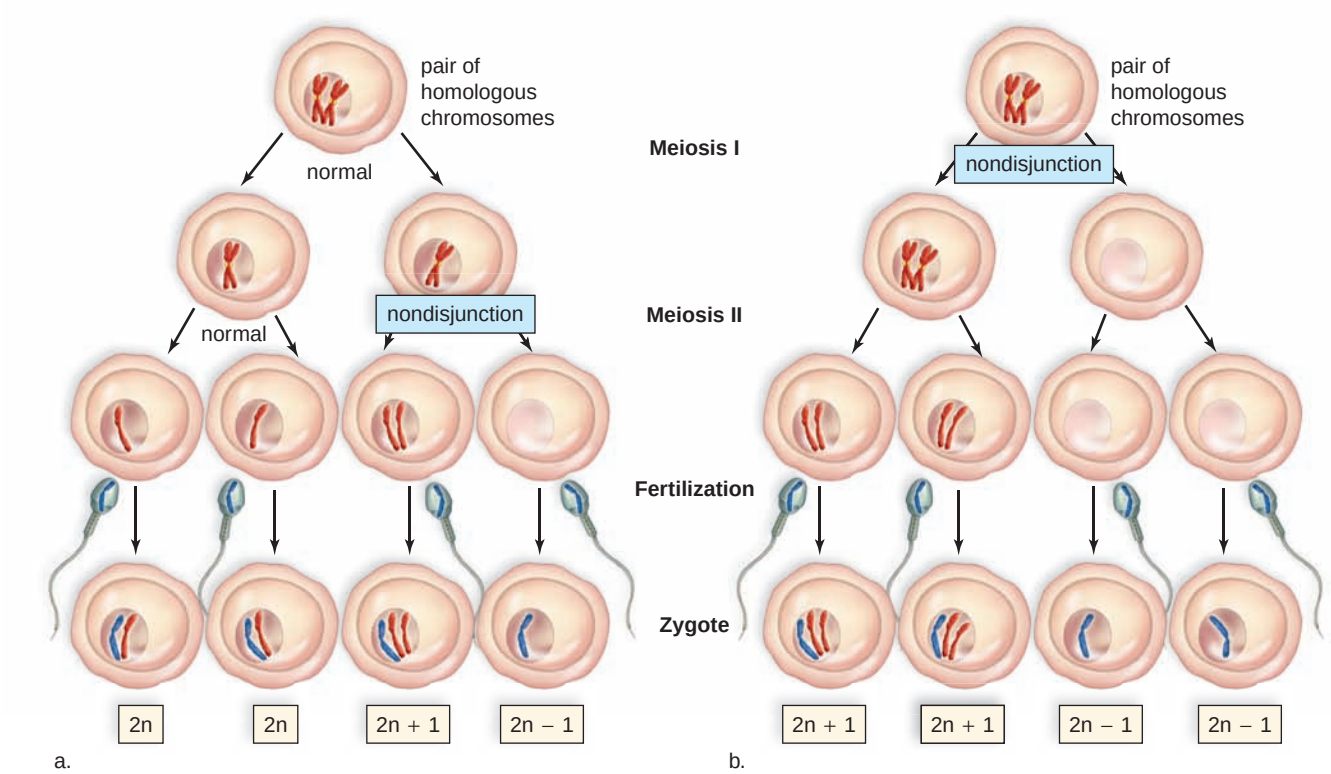


FIGURE 10.10 Nondisjunction of chromosomes during oogenesis, followed by fertilization with normal sperm.

a. Nondisjunction can occur during meiosis II if the sister chromatids separate but the resulting chromosomes go into the same daughter cell. Then the egg will have one more or one less than the usual number of chromosomes. Fertilization of these abnormal eggs with normal sperm produces an abnormal zygote with abnormal chromosome numbers. **b.** Nondisjunction can also occur during meiosis I and result in abnormal eggs that also have one more or one less than the normal number of chromosomes. Fertilization of these abnormal eggs with normal sperm results in a zygote with abnormal chromosome numbers. 2n = diploid number of chromosomes.

FIGURE 10.11 Trisomy 21.

Persons with Down syndrome, or trisomy 21, have an extra chromosome 21. **a.** Common characteristics of the syndrome include a wide, rounded face and a fold on the upper eyelids. Mental disabilities, along with an enlarged tongue, make it difficult for a person with Down syndrome to speak distinctly. **b.** The karyotype of an individual with Down syndrome shows three copies of chromosome 21. Therefore, the individual has three copies instead of two copies of each gene on chromosome 21. Researchers are using new techniques to discover which genes on chromosome 21 are causing the syndrome's disabilities.

the first and second toes; a large, fissured tongue; a round head; a distinctive palm crease; heart problems; and, unfortunately, mental retardation, which can sometimes be severe. Individuals with Down syndrome also have a greatly increased risk of developing leukemia and tend to age rapidly, resulting in a shortened life expectancy. In addition, these individuals have an increased chance of developing Alzheimer disease later in life.

Many scientists agree that the symptoms of Down syndrome are caused by gene dosage effects resulting from the presence of the extra chromosome. However, recent studies indicate that not all of the genes on the chromosome are expressed at a level of 150%, challenging this theory. However, scientists have identified several genes that have been linked to increased risk of leukemia, cataracts, aging, and mental retardation.

The chances of a woman having a child with Down syndrome increase rapidly with age. In women age 20 to 30, 1 in 1,400 births have Down syndrome, and in women 30 to 35, about 1 in 750 births have Down syndrome. It is thought that the longer the oocytes are stored in the female, the greater the chances of nondisjunction occurring. However, even though an older woman is more likely to have a Down syndrome child, most babies with Down syndrome are born to women younger than age 40 because this is the age group having the most babies. Furthermore, some recent research also indicate that in 23% of the cases studied, the sperm contributed an extra chromosome. A **karyotype,** a visual display of the chromosomes arranged by size, shape, and banding pattern, may be performed to identify babies with Down syndrome and other aneuploid conditions (Fig. 10.11).

Changes in Sex Chromosome Number

An abnormal sex chromosome number is the result of inheriting too many or too few X or Y chromosomes. Nondisjunction during oogenesis or spermatogenesis can result in gametes with an abnormal number of sex chromosomes. However, extra copies of the sex chromosomes are much more easily tolerated in humans than are extra copies of autosomes.

A person with Turner syndrome (XO) is a female, and a person with Klinefelter syndrome (XXY) is a male. However, deletion of the *SRY* gene on the short arm of the Y chromosome results in Swyer syndrome, or an "XY female." Individuals with Swyer syndrome lack a hormone called testis-determining factor, which plays a critical role in the development of male genitals. Furthermore, movement of this same gene onto the X chromosome may result in de la Chapelle syndrome, or an "XX male." Men with de la Chapelle syndrome exhibit undersized testes, sterility, and rudimentary breast development. Together, these observations suggest that in humans, the presence of the *SRY* gene, not the number of X chromosomes, determines maleness. In its absence, a person develops as a female.

Why are newborns with an abnormal sex chromosome number more likely to survive than those with an abnormal autosome number? Since females have two X chromosomes and males have only one, one would expect females

to produce twice the amount of each gene from this chromosome, but both males and females produce roughly the same amount. In reality, both males and females only have one functioning X chromosome. In females, and in males with extra X chromosomes, the others become an inactive mass called a **Barr body,** named after Murray Barr, the person who discovered it. This provides a natural method for gene dosage compensation of the sex chromosomes and explains why extra sex chromosomes are more easily tolerated than extra autosomes.

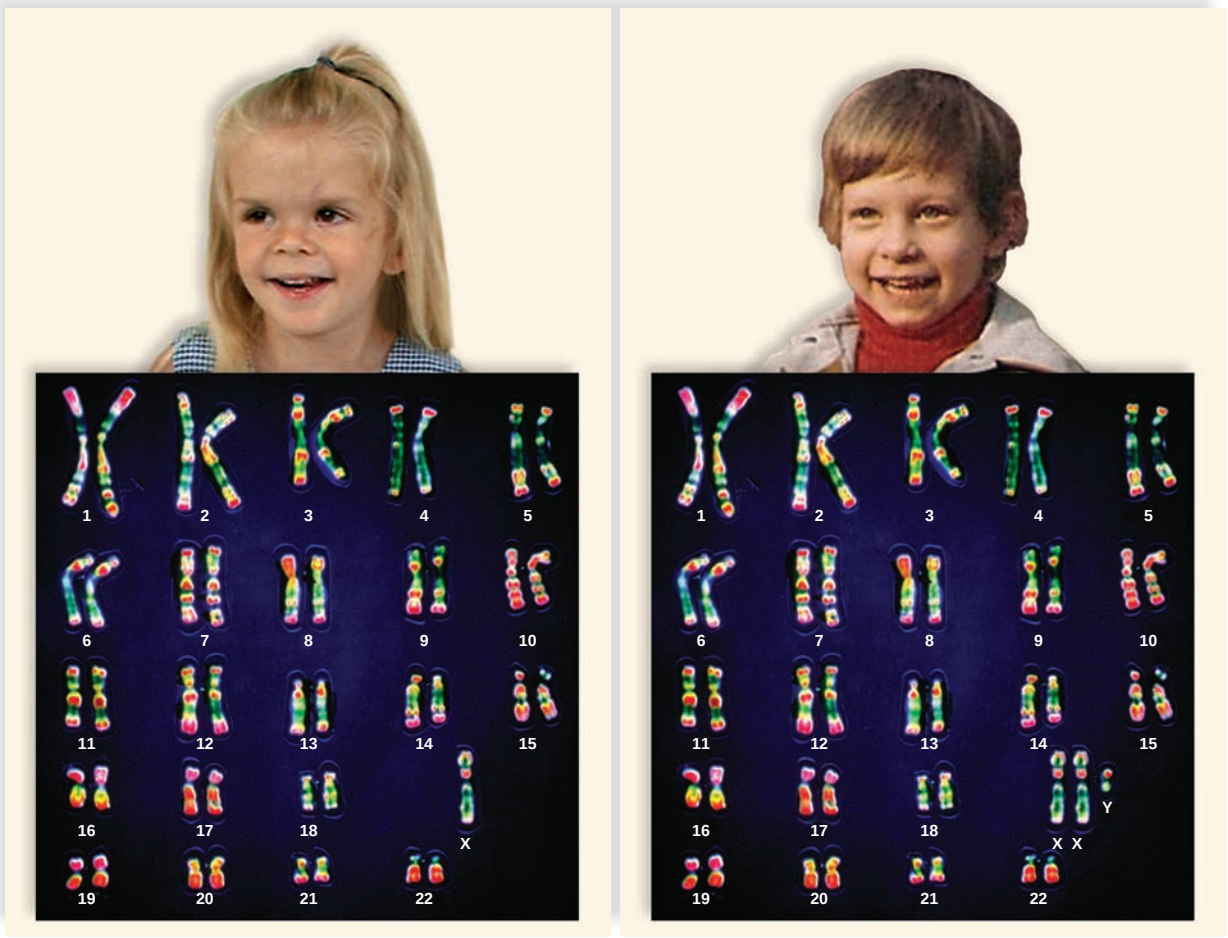
Turner Syndrome. From birth, an XO individual with Turner syndrome has only one sex chromosome, an X; the O signifies the absence of a second sex chromosome (Fig. 10.12*a*). Therefore, the nucleus does not contain a Barr body. The approximate incidence is 1 in 10,000 females.

Turner females are short, with a broad chest and widely spaced nipples. These individuals also have a low posterior hairline and neck webbing. The ovaries, oviducts, and uterus are very small and underdeveloped. Turner females do not undergo puberty or menstruate, and their breasts do not develop. However, some have given birth following in vitro fertilization using donor eggs. They usually are of normal intelligence and can lead fairly normal lives if they receive hormone supplements.

Klinefelter Syndrome. A male with Klinefelter syndrome has two or more X chromosomes in addition to a Y chromosome (Fig. 10.12*b*). The extra X chromosomes become Barr bodies. The approximate incidence for Klinefelter syndrome is 1 in 500 to 1,000 males.

In Klinefelter males, the testes and prostate gland are underdeveloped and there is no facial hair. But there may be some breast development. Affected individuals have large hands and feet and very long arms and legs. They are usually slow to learn but not mentally retarded unless they inherit more than two X chromosomes. No matter how many X chromosomes there are, an individual with a Y chromosome is a male.

While males with Klinefelter syndrome exhibit no other major health abnormalities, there is an increased risk of some disorders, including breast cancer, osteoporosis, and lupus,



a. Turner syndrome b. Klinefelter syndrome

FIGURE 10.12 Abnormal sex chromosome number.

People with (**a**) Turner syndrome, who have only one sex chromosome, an X, as shown, and (**b**) Klinefelter syndrome, who have more than one X chromosome plus a Y chromosome, as shown, can look relatively normal (especially as children) and can lead relatively normal lives.

health focus

Living with Klinefelter Syndrome

In 1996, at the age of 25, I was diagnosed with Klinefelter syndrome (KS). Being diagnosed has changed my life for the better.

I was a happy baby, but when I was still very young, my parents began to believe that there was something wrong with me. I knew something was different about me, too, as early on as five years old. I was very shy and had trouble making friends. One minute I'd be well behaved, and the next I'd be picking fights and flying into a rage. Many psychologists, therapists, and doctors tested me because of school and social problems and severe mood changes. Their only diagnosis was "learning disabilities" in such areas as reading comprehension, abstract thinking, word retrieval, and auditory processing. No one could figure out what the real problem was, and I hated the tutoring sessions I had. In the seventh grade, a psychologist told me that I was stupid and lazy, I would probably live at home for the rest of my life, and I would never amount to anything. For the next five years, he was basically right, and I barely graduated from high school.

I believe, though, that I have succeeded because I was told that I would fail. I quit the tutoring sessions when I enrolled at a community college; I decided I could figure things out on my own. I received an associate degree there, then transferred to a small liberal arts college. I never told anyone about my learning disabilities and never sought special help. However, I never had a semester below a 3.0, and I graduated with two B.S. degrees. I was accepted into a graduate program but decided instead to accept a job as a software engineer even though I did not have an educational background in this field. As I later learned, many KS'ers excel in computer skills. I had been using a computer for many years and had learned everything I needed to know on my own, through trial and error.

Around the time I started the computer job, I went to my physician for a physical. He sent me for blood tests because he noticed that my testes were smaller than usual. The results were conclusive: Klinefelter syndrome with sex chromosomes XXY. I initially felt denial, depression, and anger, even though I now had an explanation for many of the problems I had experienced all my life. But then I decided to learn as much as I could about the condition and treatments available. I now give myself a testosterone injection once every two weeks, and it has made me a different person, with improved learning abilities and stronger thought processes in addition to a more outgoing personality.

I found, though, that the best possible path I could take was to help others live with the condition. I attended my first support group meeting four months after I was diagnosed. By spring 1997, I had developed an interest in KS that was more than just a part-time hobby. I wanted to be able to work with this condition and help people forever. I have been very involved in KS conferences and have helped to start support groups in the United States, Spain, and Australia.

Since my diagnosis, it has been my dream to have a son with KS, although when I was diagnosed, I found out it was unlikely that I could have biological children. Through my work with KS, I had the opportunity to meet my fiancée Chris. She has two wonderful children: a daughter, and a son who has the same condition that I do. There are a lot of similarities between my stepson and me, and I am happy I will be able to help him get the head start in coping with KS that I never had. I also look forward to many more years of helping other people seek diagnosis and live a good life with Klinefelter syndrome.

Stefan Schwarz

which disproportionately affect females. Although men with Klinefelter syndrome typically do not need medical treatment, some have found that testosterone therapy may help increase muscle strength, sex drive, and concentration ability. Testosterone treatment, however, will not reverse the sterility associated with Klinefelter syndrome due to the incomplete testicle development associated with it.

The Health Focus on this page tells of the experiences of a person with Klinefelter syndrome. He suggests that it is best for parents to know right away that they have a child with this abnormality because much can be done to help the child lead a normal life.

Poly-X Females. A poly-X female, sometimes called a superfemale, has more than two X chromosomes and, therefore, extra Barr bodies in the nucleus. Females with three X chromosomes have no distinctive phenotype aside from a tendency to be tall and thin. Although some have delayed motor and language development, as well as learning problems, most poly-X females are not mentally retarded. Some may have menstrual difficulties, but many menstruate regularly and are fertile. Children usually have a normal karyotype. The incidence for poly-X females is about 1 in 1,500 females.

Females with more than three X chromosomes occur rarely. Unlike XXX females, XXXX females are usually tall and severely retarded. Various physical abnormalities are seen, but they may menstruate normally.

Jacobs Syndrome. XYY males with Jacobs syndrome can only result from nondisjunction during spermatogenesis. These individuals are sometimes called supermales. Among all live male births, the frequency of the XYY karyotype is about 1 in 1,000. Affected males are usually taller than average, suffer from persistent acne, and tend to have speech and reading problems, but are fertile and may have children. Based upon the number of XYY individuals in prisons and mental facilities, at one time it was suggested that these men were likely to be criminally aggressive, but it has since been shown that the incidence of such behavior among them may be no greater than among XY males.

Changes in Chromosome Structure

Changes in chromosome structure are another type of chromosomal mutation. Some, but not all, changes in chromosome structure can be detected microscopically. Various agents in the environment, such as radiation, certain organic chemicals, or even viruses, can cause chromosomes to break. Ordinarily, when breaks occur in chromosomes, the two broken ends reunite to give the same sequence of genes. Sometimes, however, the broken ends of one or more chromosomes do not rejoin in the same pattern as before, and the result is various types of chromosomal mutations.

Changes in chromosome structure include deletions, duplications, translocations, and inversions of chromosome segments. A **deletion** occurs when an end of a chromosome breaks off or when two simultaneous breaks lead to the loss of an internal segment (Fig. 10.13*a*). Even when only one member of a pair of chromosomes is affected, a deletion often causes abnormalities.

A **duplication** is the presence of a chromosomal segment more than once in the same chromosome (Fig. 10.13*b*). Duplications may or may not cause visible abnormalities, depending on the size of the duplicated region. An **inversion** has occurred when a segment of a chromosome is turned around 180° (Fig. 10.13*c*). Most individuals with inversions exhibit no abnormalities, but this reversed sequence of genes can result in duplications or deletions being passed on to their children, as described in Figure 10.14.

A **translocation** is the movement of a chromosome segment from one chromosome to another, nonhomologous chromosome. The translocation shown in Figure 10.13*d* is *balanced*, meaning that there is a reciprocal swap of one piece of the chromosome for the other. Often, there are no visible effects of the swap, but if the individual has children, they will receive one normal copy of the chromosome from the normal parent and one of the abnormal chromosomes. The translocation is now *unbalanced*, and there is extra material from one chromosome and missing material from another chromosome. Unbalanced translocations usually miscarry, but those that do not often have severe symptoms.

Some Down syndrome cases are caused by an unbalanced translocation between chromosomes 21 and 14. In other words, because a portion of chromosome 21 is now attached to a portion of chromosome 14, the individual has three copies of the genes that bring about Down syndrome when they are present in triplet copy. In these cases, Down syndrome is not caused by nondisjunction during meiosis, but is passed on normally like any other genetic trait as described in Chapter 11.

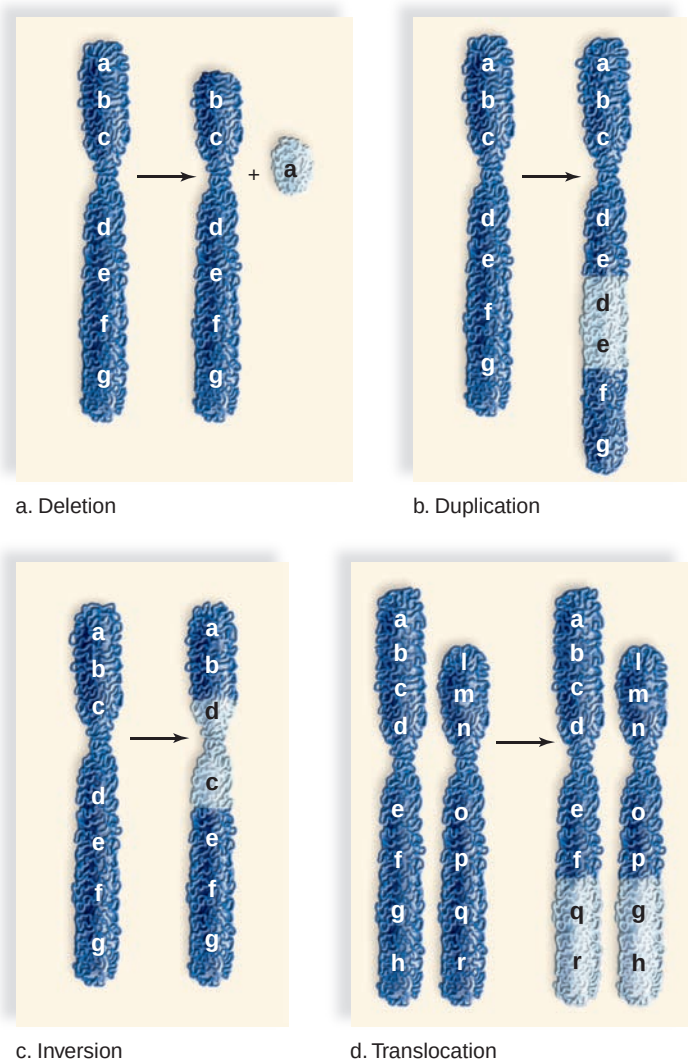


FIGURE 10.13 **Types of chromosomal mutations.**

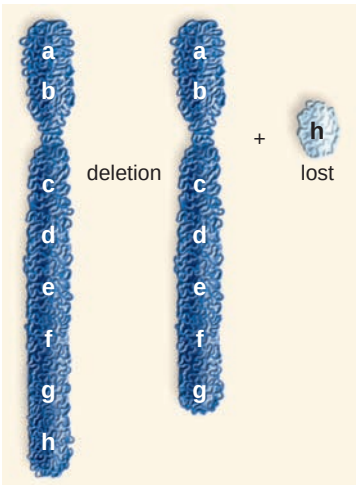
a. Deletion is the loss of a chromosome piece. **b.** Duplication occurs when the same piece is repeated within the chromosome. **c.** Inversion occurs when a piece of chromosome breaks loose and then rejoins in the reversed direction. **d.** Translocation is the exchange of chromosome pieces between nonhomologous pairs.

Human Syndromes

Changes in chromosome structure occur in humans and lead to various syndromes, many of which are just now being discovered. Sometimes changes in chromosome structure can be detected in humans by doing a karyotype. They may also be discovered by studying the inheritance pattern of a disorder in a particular family.

Deletion Syndromes. Williams syndrome occurs when chromosome 7 loses a tiny end piece (Fig. 10.14). Children who have this syndrome look like pixies, with turned-up noses, wide mouths, a small chin, and large ears. Although their academic skills are poor, they exhibit excellent verbal and musical abilities. The gene that governs the production of the protein elastin is missing, and this affects the health of the cardiovascular system and causes their skin to age prematurely. Such individuals are very friendly but need an ordered life, perhaps because of the loss of a gene for a protein that is normally active in the brain.

Cri du chat (cat's cry) syndrome is seen when chromosome 5 is missing an end piece. The affected individual has a small head, is mentally retarded, and has facial abnormalities. Abnormal development of the glottis and larynx results in the most characteristic symptom—the infant's cry resembles that of a cat.

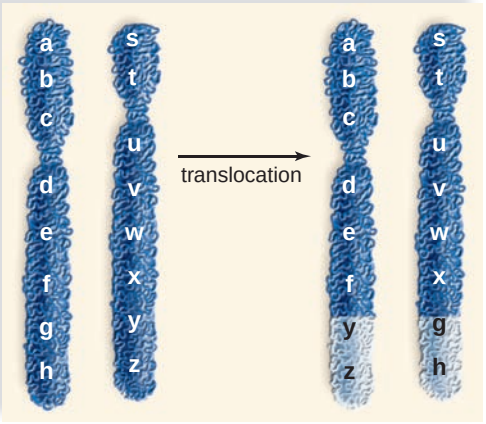


a.

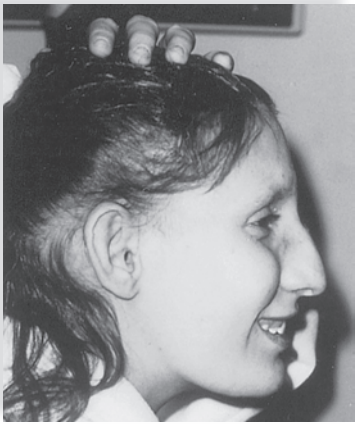
b.

FIGURE 10.14
Deletion.

a. When chromosome 7 loses an end piece, the result is Williams syndrome. **b.** These children, although unrelated, have the same appearance, health, and behavioral problems.



a.



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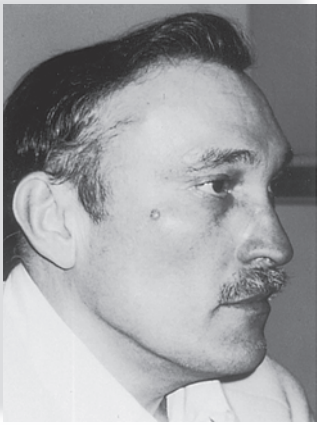


FIGURE 10.15
Translocation.

a. When chromosomes 2 and 20 exchange segments, (**b**) Alagille syndrome, with distinctive facial features, sometimes results because the translocation disrupts an allele on chromosome 20.

Translocation Syndromes. A person who has both of the chromosomes involved in a translocation has the normal amount of genetic material and is healthy, unless the chromosome exchange breaks an allele into two pieces. The person who inherits only one of the translocated chromosomes will no doubt have only one copy of certain alleles and three copies of certain other alleles. A genetic counselor begins to suspect a translocation has occurred when spontaneous abortions are commonplace and family members suffer from various syndromes. A special microscopic technique allows a technician to determine that a translocation has occurred.

Figure 10.15 shows a daughter and her father who have a translocation between chromosomes 2 and 20. Although they have the normal amount of genetic material, they have the distinctive face, abnormalities of the eyes and internal organs, and severe itching characteristic of Alagille syndrome. People with this syndrome ordinarily have a deletion on chromosome 20; therefore, it can be deduced that the translocation disrupted an allele on chromosome 20 in the father. The symptoms of Alagille syndrome range from mild to severe, so some people may not be aware they have the syndrome. This father did not realize it until he had a child with the syndrome.

Translocations can also be responsible for a variety of other disorders including certain types of cancer. In the 1970s, new staining techniques identified that a translocation from a portion of chromosome 22 to chromosome 9 was responsible for many cases of chronic myelogenous leukemia. This translocated chromosome was called Philadelphia chromosome. In Burkitt lymphoma, a cancer common in children in equatorial Africa, a large tumor develops from lymph glands in the region of the jaw. This disorder involves a translocation from a portion of chromosome 8 to chromosome 14.

Check Your Progress 10.6

1. What kind of changes in chromosome number may be caused by nondisjunction in meiosis?
2. Why is sex chromosome aneuploidy more common than autosome aneuploidy?
3. Describe the difference between an inversion and a translocation.

Connecting the Concepts

Meiosis is similar to mitosis except that meiosis is a more elaborate process. Like the cell cycle and mitosis, meiosis is tightly controlled. Regulatory mechanisms exist to ensure that homologous chromosomes first pair and then separate during the first division and that sister chromatids do not separate until the second division. In addition, meiosis only occurs in certain types of cells during a restricted period of an organism's life span.

Meiosis facilitates sexual reproduction, and there are both evolutionary costs and benefits involved. Although the increased number of genes controlling the process can lead to an increased chance of mutations and chromosomal abnormalities, and therefore the possibility of faulty gametes, there is the advantage in that sexually reproducing species have a greater likelihood of survival than asexually reproducing species because of the greater genetic diversity that sexual reproduction introduces.

Understanding the behavior of chromosomes during meiosis is critical to understanding the manner in which genes segregate during gamete formation and how this contributes to patterns of inheritance. Chapter 11 reviews the fundamental laws of genetics established by Gregor Mendel. Although Mendel had no knowledge of chromosome behavior, modern students have the advantage of applying their knowledge of meiosis to their understanding of Mendel's laws.

summary

10.1 Halving the Chromosome Number

Meiosis ensures that the chromosome number in offspring stays constant generation after generation. The nucleus contains pairs of chromosomes, called homologous chromosomes (homologues).

Meiosis requires two cell divisions and results in four daughter cells. Replication of DNA takes place before meiosis begins. During meiosis I, the homologues undergo synapsis (resulting in a bivalent) and align independently at the metaphase plate. The daughter cells receive one member of each pair of homologous chromosomes. There is no replication of DNA during interkinesis. During meiosis II, the sister chromatids separate, becoming daughter chromosomes that move to opposite poles as they do in mitosis. The four daughter cells contain the haploid number of chromosomes and only one of each kind.

10.2 Genetic Variation

Sexual reproduction ensures that the offspring have a different genetic makeup than the parents. Meiosis contributes to genetic variability in two ways: crossing-over and independent assortment of the homologous chromosomes. When homologous chromosomes lie side by side during synapsis, nonsister chromatids may exchange genetic material. Due to crossing-over, the chromatids that separate during meiosis II have a different combination of genes.

When the homologous chromosomes align at the metaphase plate during metaphase I, either the maternal or the paternal chromosome can be facing either pole. Therefore, there will be all possible combinations of chromosomes in the gametes.

10.3 The Phases of Meiosis

Meiosis I is divided into four phases:

Prophase I—Bivalents form, and crossing-over occurs as chromosomes condense; the nuclear envelope fragments.

Metaphase I—Bivalents independently align at the metaphase plate.

Anaphase I—Homologous chromosomes separate, and duplicated chromosomes move to poles.

Telophase I—Nuclei become haploid, having received one duplicated chromosome from each homologous pair.

Meiosis II is divided into four phases:

Prophase II—Chromosomes condense, and the nuclear envelope fragments.

Metaphase II—The haploid number of still duplicated chromosomes align at the metaphase plate.

Anaphase II—Sister chromatids separate, becoming daughter chromosomes that move to the poles.

Telophase II—Four haploid daughter cells are genetically different from the parent cell.

10.4 Meiosis Compared to Mitosis

Mitosis and meiosis can be compared in this manner:

Meiosis I	Mitosis
Prophase	
Pairing of homologous chromosomes	No pairing of chromosomes
Metaphase	
Bivalents at metaphase plate	Duplicated chromosomes at metaphase plate
Anaphase	
Homologous chromosomes separate and move to poles	Sister chromatids separate, becoming daughter chromosomes that move to the poles
Telophase	
Daughter nuclei have the haploid number of chromosomes	Daughter nuclei have the parent cell chromosome number

Meiosis II is like mitosis except the nuclei are haploid.

10.5 The Human Life Cycle

Meiosis occurs in any life cycle that involves sexual reproduction. In the animal life cycle, only the gametes are haploid; in plants, meiosis produces spores that develop into a multicellular haploid adult that produces the gametes. In unicellular protists and fungi, the zygote undergoes meiosis, and spores become a haploid adult that gives rise to gametes.

During the life cycle of humans and other animals, meiosis is involved in spermatogenesis and oogenesis. Whereas spermatogenesis produces four sperm per meiosis, oogenesis produces one egg and two to three nonfunctional polar bodies. Spermatogenesis occurs in males, and oogenesis occurs in females. When a sperm fertilizes an egg, the zygote has the diploid number of chromosomes. Mitosis, which is involved in growth and repair, also occurs during the life cycle of all animals.

10.6 Changes in Chromosome Number and Structure

Nondisjunction during meiosis I or meiosis II may result in aneuploidy (extra or missing copies of chromosomes). Monosomy occurs when an individual has only one of a particular type of chromosome ($2n - 1$); trisomy occurs when an individual has three of a particular type of chromosome ($2n + 1$). Down syndrome is a well-known trisomy in human beings resulting from an extra copy of chromosome 21.

Aneuploidy of the sex chromosomes is tolerated more easily than aneuploidy of the autosomes. Turner syndrome, Klinefelter syndrome, poly-X females, and Jacobs syndrome are examples of sex chromosome aneuploidy.

Abnormalities in crossing-over may result in deletions, duplications, inversions, and translocations within chromosomes. Many human syndromes, including Williams syndrome, cri du chat syndrome, and Alagille syndrome, result from changes in chromosome structure.

understanding the terms

allele 170
alternation of generations 176
aneuploidy 180
Barr body 182
bivalent 171
crossing-over 172
deletion 184
diploid (2n) number 170
duplication 184
euploidy 180
fertilization 172
gamete 170
gametogenesis 179
gametophyte 178
genetic recombination 172
haploid (n) number 170
homologous chromosome 170
homologue 170
independent assortment 172
interkinesis 176
inversion 184
karyotype 181
life cycle 178
meiosis 170
monosomy 180
oogenesis 179
polar body 179
secondary oocyte 179
sexual reproduction 170
spermatogenesis 179
spore 176
sporophyte 178
synapsis 171
translocation 184
trisomy 180
zygote 170

Match the terms to these definitions:

a. _____ Production of sperm in males by the process of meiosis and maturation.
b. _____ Pair of homologous chromosomes at the metaphase plate during meiosis I.
c. _____ A nonfunctional product of oogenesis.
d. _____ The functional product of meiosis I in oogenesis becomes the egg.
e. _____ Member of a pair of chromosomes in which both members carry genes for the same traits.

reviewing this chapter

1. Why did early investigators predict that there must be a reduction division in the sexual reproduction process? 170
2. What are homologous chromosomes? Contrast the genetic makeup of sister chromatids with that of nonsister chromatids. 170–71
3. Draw and explain a diagram that illustrates crossing-over and another that shows all possible results from independent assortment of homologous pairs. How do these events ensure genetic variation among the gametes? 172–73
4. Draw and explain a series of diagrams that illustrate the stages of meiosis I and meiosis II. 173–76
5. What accounts for **(a)** the genetic similarity between daughter cells and the parent cell following mitosis, and **(b)** the genetic dissimilarity between daughter cells and the parent cell following meiosis? 176–78
6. Explain the human (animal) life cycle and the roles of meiosis and mitosis. 178–79
7. Compare spermatogenesis in males to oogenesis in females. 179
8. How does aneuploidy occur? Why is sex chromosome aneuploidy more common than autosomal aneuploidy? What are some human syndromes associated with aneuploidy? 180–83
9. Name and explain four types of changes in chromosome structure. 184
10. Name some syndromes that occur in humans due to changes in chromosome structure. 184–85

testing yourself

Choose the best answer for each question.

1. A bivalent is
   a. a homologous chromosome.
   b. the paired homologous chromosomes.
   c. a duplicated chromosome composed of sister chromatids.
   d. the two daughter cells after meiosis I.
   e. the two centrioles in a centrosome.
2. If a parent cell has 16 chromosomes, then each of the daughter cells following meiosis will have
   a. 48 chromosomes.
   b. 32 chromosomes.
   c. 16 chromosomes.
   d. 8 chromosomes.
3. At the metaphase plate during metaphase I of meiosis, there are
   a. chromosomes consisting of one chromatid.
   b. unpaired duplicated chromosomes.
   c. bivalents.
   d. homologous pairs of chromosomes.
   e. Both c and d are correct.
4. At the metaphase plate during metaphase II of meiosis, there are
   a. chromosomes consisting of one chromatid.
   b. unpaired duplicated chromosomes.
   c. bivalents.
   d. homologous pairs of chromosomes.
   e. Both c and d are correct.
5. Gametes contain one of each kind of chromosome because
   a. the homologous chromosomes separate during meiosis.
   b. the chromatids separate during meiosis.
   c. only one replication of DNA occurs during meiosis.
   d. crossing-over occurs during prophase I.
   e. the parental cell contains only one of each kind of chromosome.
6. Crossing-over occurs between
   a. sister chromatids of the same chromosome.
   b. two different kinds of bivalents.
   c. two different kinds of chromosomes.
   d. nonsister chromatids of a bivalent.
   e. two daughter nuclei.
7. During which phase of meiosis do homologous chromosomes separate?
   a. prophase I
   b. telophase I
   c. anaphase I
   d. anaphase II

8. During which phase of meiosis does crossing-over occur?
   a. prophase I
   b. interkinesis
   c. metaphase II
   d. anaphase I
9. Which of the following statements is false?
   a. Oogenesis occurs in females, and spermatogenesis occurs in males.
   b. Spermatogenesis produces four viable gametes, while oogenesis only produces one.
   c. Daughter cells produced from oogenesis are diploid, while daughter cells produced by spermatogenesis are haploid.
   d. Spermatogenesis goes to completion, while oogenesis does not always go to completion.
10. Nondisjunction during meiosis I of oogenesis will result in eggs that have
    a. the normal number of chromosomes.
    b. one too many chromosomes.
    c. one less than the normal number of chromosomes.
    d. Both b and c are correct.
11. Which two of these chromosomal mutations are most likely to occur when an inverted chromosome is undergoing synapsis?
    a. deletion and translocation
    b. deletion and duplication
    c. duplication and translocation
    d. inversion and duplication
12. A male with underdeveloped testes and some breast development most likely has
    a. Down syndrome.
    b. Jacobs syndrome.
    c. Turner syndrome.
    d. Klinefelter syndrome.

For questions 13–17, fill in the blanks.

13. If the parent cell has 24 chromosomes, the daughter cells following mitosis will have _____ chromosomes and following meiosis will have _____ chromosomes.
14. Meiosis in males is a part of _____, and meiosis in females is a part of _____.
15. Oogenesis will not go to completion unless _____ occurs.
16. In humans, meiosis produces _____, and in plants, meiosis produces _____.
17. During oogenesis, the primary oocyte has the _____ and the secondary oocyte has the _____ number of chromosomes.

For questions 18–24, match the statements that follow to the items in the key. Answers may be used more than once, and more than one answer may be used.

KEY:

a. mitosis
b. meiosis I
c. meiosis II
d. Both meiosis I and meiosis II are correct.
e. All of these are correct.

18. Spindle fibers are attached to kinetochores.
19. A parent cell with ten duplicated chromosomes will produce daughter cells with five duplicated chromosomes each.
20. Involves pairing of duplicated homologous chromosomes.
21. A parent cell with five duplicated chromosomes will produce daughter cells with five chromosomes consisting of one chromatid each.
22. Nondisjunction may occur, causing abnormal gametes to form.
23. A parent cell with ten duplicated chromosomes will produce daughter cells with ten chromosomes consisting of one chromatid each.
24. Involved in growth and repair of tissues.

thinking scientifically

1. Why is the first meiotic division considered to be the reduction division for chromosome number?
2. Recall that during interphase, the G_2 checkpoint ensures that the DNA has been faithfully replicated before the cell is allowed to divide by mitosis. Would you expect this checkpoint to be active during interkinesis? How might you set up an experiment to test your hypothesis?
3. A man has a balanced translocation between chromosome 2 and 6. If he reproduces with a normal woman could the child have the same translocation? Why or why not?

bioethical issue

The Risks of Advanced Maternal Age

In today's society, it is commonplace for women to embark on careers and pursue higher education, delaying marriage and childbirth until later years. Between 1991 and 2001, the birthrate among women aged 35 to 39 increased over 30%, while the birthrate among women aged 40 to 44 leaped by almost 70%. These increases have occurred as society has changed, spurred by the elimination of the social stigmas, better prenatal care, and new medical technologies that can overcome the decline in fertility associated with age and treat at-risk children.

The decision to delay childbirth does carry risks. Although the reasons are not well understood, the risk of many disorders associated with meiotic nondisjunction, such as Down syndrome, increase greatly with age, rising from nearly 1 in 900 at age 30 to 1 in 109 by age 40. The risk of complications to the mother, such as gestational diabetes, are also much higher in women over 30. Thus, the medical community has embarked on a campaign to ensure that women who are pregnant and over age 35 are offered more intensive prenatal care. Many people are concerned about the ultimate cost to society, through increased insurance premiums and increased costs to governments to pay for it.

While there are definitely risks associated with advanced maternal age, others contend that having children later in life provides many advantages. Women over age 35 are usually at a later stage in their careers and have higher salaries, lessening the need for many social welfare programs. Furthermore, women over 35 are much less likely to divorce or give birth out of wedlock and are often able to devote more time to the child than younger women. Therefore, while older mothers require more medical attention, the overall costs to society are lower.

Considering both the benefits and the disadvantages, are we as a society obligated to fund intense screening and prenatal care for women of advanced maternal age, and to pay for treating the maladies associated with it? As birthrates among women over age 30 continue to soar, the debate over advanced maternal age is not likely to abate any time soon.

Biology website

The companion website for *Biology* provides a wealth of information organized and integrated by chapter. You will find practice tests, animations, videos, and much more that will complement your learning and understanding of general biology.

http://www.mhhe.com/maderbiology10

11

Mendelian Patterns of Inheritance

Camille was painfully aware of her foul body odor because the children teased her relentlessly, calling her "Miss Fishy" and other nasty names. Little did she know, however, that she suffers from trimethylaminuria, or "fish odor syndrome," an extremely rare genetic disorder she shares with possibly 1 in 10,000 people. People with this syndrome all have a defective gene whose product is unable to break down the smelly chemical trimethylamine, and it ends up in their urine, sweat, and at times even in their breath.

Rare genetic disorders like Camille's constantly pique our curiosity about how traits are inherited from one generation to the next. In the following chapter, you will learn that the process of meiosis can be used to predict the inheritance of a trait. You will also learn how Mendel discovered that certain traits, such as trimethylaminuria, are recessive and it takes two copies of a gene before you are affected. In this chapter, you will be introduced to other human genetic disorders that can be definitely linked to specific genes on the chromosomes.

The other kids teased Camille because she had a fishy smell.

concepts

11.1 Gregor Mendel

The science of genetics explains the stability of inheritance (why you are human as are your parents) and also variations between offspring from one generation to the next (why you have a different combination of traits than your parents). Virtually every culture in history has attempted to explain observed inheritance patterns. An understanding of these patterns has always been important to agriculture, animal husbandry (the science of breeding animals), and medicine.

The Blending Concept of Inheritance

Until the late nineteenth century, most plant and animal breeders believed that traits were inherited by the blending concept of inheritance, which stated that an offspring's genetic makeup was intermediate to that of its parents. While they acknowledged that both sexes contribute equally to a new individual, they believed that parents of contrasting appearance always produce offspring of intermediate appearance. Therefore, according to this concept, a cross between plants with red flowers and plants with white flowers would yield only plants with pink flowers. However, this theory did not always explain observed inheritance patterns. For example, red and white flowers reappeared in future generations even though the parents had pink flowers.

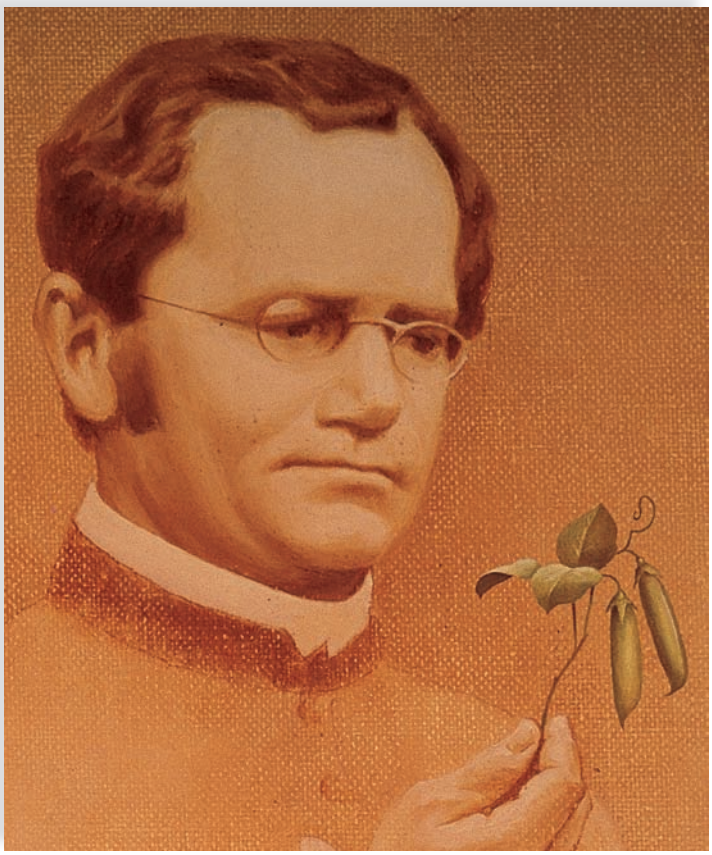


FIGURE 11.1 Gregor Mendel, 1822–84.

Mendel grew and tended the pea plants he used for his experiments. For each experiment, he observed as many offspring as possible. For a cross that required him to count the number of round seeds to wrinkled seeds, he observed and counted a total of 7,324 peas!

The breeders mistakenly attributed this to instability of the genetic material. The blending concept of inheritance offered little help to Charles Darwin, the father of evolution, whose treatise on natural selection lacked a strong genetic basis. If populations contained only intermediate individuals and normally lacked variations, how could diverse forms evolve?

Mendel's Particulate Theory of Inheritance

Gregor Mendel was an Austrian monk who developed a particulate theory of inheritance after performing a series of ingenious experiments in the 1860s (Fig. 11.1). Mendel studied science and mathematics at the University of Vienna, and at the time of his genetic research, he was a substitute natural science teacher at a local high school. Mendel was a successful scientist for several reasons. First, he was one of the first scientists to apply mathematics to biology. Most likely his background in mathematics prompted him to apply statistical methods and the laws of probability to his breeding experiments. He was also a careful, deliberate scientist who followed the scientific method very closely and kept very detailed, accurate records. He prepared for his experiments carefully and conducted many preliminary studies with various animals and plants.

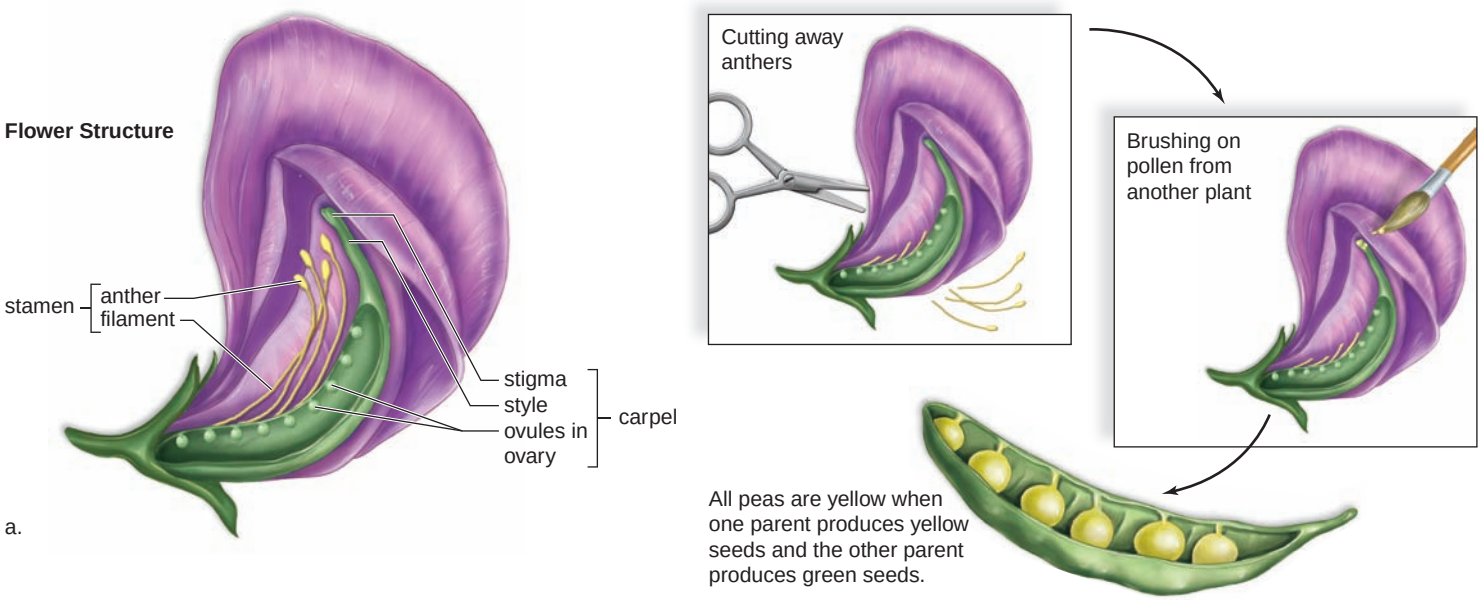
Mendel's theory of inheritance is called a particulate theory because it is based on the existence of minute particles or hereditary units we now call genes. Inheritance involves the reshuffling of the same genes from generation to generation. His laws of segregation and the law of independent assortment describe the behavior of these particulate units of heredity as they are passed from one generation to the next. Much of modern genetics is based upon Mendel's theories, which have withstood the test of time and have been supported by innumerable experiments.

Mendel Worked with the Garden Pea

Mendel's preliminary experiments prompted him to choose the garden pea, *Pisum sativum* (Fig. 11.2*a*), as his experimental material. The garden pea was a good choice for many reasons. The plants were easy to cultivate and had a short generation time. Although peas normally self-pollinate (pollen only goes to the same flower), they could be cross-pollinated by hand by transferring pollen from the anther to the stigma. Many varieties of peas were available, and Mendel chose 22 for his experiments. When these varieties self-pollinated, they were *true-breeding*—meaning that the offspring were like the parent plants and like each other. In contrast to his predecessors, Mendel studied the inheritance of relatively simple and discrete traits that were not subjective and were easy to observe, such as seed shape, seed color, and flower color. In his crosses, Mendel observed either dominant or recessive characteristics but no intermediate ones (Fig. 11.2*b*).

Check Your Progress 11.1

1. What made Gregor Mendel's experiments successful?
2. Why was the garden pea a good choice for Mendel's experiments?



Trait	Characteristics		F_2 Results*	
	*Dominant	*Recessive	Dominant	Recessive
Stem length	Tall	Short	787	277
Pod shape	Inflated	Constricted	882	299
Seed shape	Round	Wrinkled	5,474	1,850
Seed color	Yellow	Green	6,022	2,001
Flower position	Axial	Terminal	651	207
Flower color	Purple	White	705	224
Pod color	Green	Yellow	428	152

*All of these produce approximately a 3:1 ratio. For example, $\frac{787}{277} = \frac{3}{1}$.

b.

FIGURE 11.2 Garden pea anatomy and a few traits.

a. In the garden pea, *Pisum sativum,* pollen grains produced in the anther contain sperm, and ovules in the ovary contain eggs. When Mendel performed crosses, he brushed pollen from one plant onto the stigma of another plant. After sperm fertilized eggs, the ovules developed into seeds (peas). The open pod shows the results of a cross between plants with yellow seeds and plants with green seeds. **b.** Mendel selected traits like these for study. He made sure his parent (P generation) plants bred true, and then he cross-pollinated the plants. The offspring called F_1 (first filial) generation always resembled the parent with the dominant characteristic (*left*). Mendel then allowed the F_1 plants to self-pollinate. In the F_2 (second filial) generation, he always achieved a 3:1 (dominant to recessive) ratio. The text explains how Mendel went on to interpret these results.

11.2 Mendel's Laws

After ensuring that his pea plants were true-breeding—for example, that his tall plants always had tall offspring and his short plants always had short offspring—Mendel was ready to perform cross-pollination experiments (see Fig. 11.2*a*). These crosses allowed Mendel to formulate his law of segregation.

Law of Segregation

For these initial experiments, Mendel chose varieties that differed in only one trait. If the blending theory of inheritance were correct, the cross should yield offspring with an intermediate appearance compared to the parents. For example, the offspring of a cross between a tall plant and a short plant should be intermediate in height.

Mendel's Experimental Design and Results

Mendel called the original parents the *P generation* and the first generation the F_1, or filial [L. *filius*, sons and daughters], *generation* (Fig. 11.3). He performed *reciprocal crosses:* First he dusted the pollen of tall plants onto the stigmas of short plants, and then he dusted the pollen of short plants onto the stigmas of tall plants. In both cases, all F_1 offspring resembled the tall parent.

Certainly, these results were contrary to those predicted by the blending theory of inheritance. Rather than being intermediate, the F_1 plants were tall and resembled only one parent. Did these results mean that the other characteristic (i.e., shortness) had disappeared permanently? Apparently not, because when Mendel allowed the F_1 plants to self-pollinate, ¾ of the *F_2 generation* were tall and ¼ were short, a 3:1 ratio (Fig. 11.3). Therefore, the F_1 plants were able to pass on a factor for shortness—it didn't disappear, it just skipped a generation. Perhaps the F_1 plants were tall because tallness was dominant to shortness?

Mendel counted many plants. For this particular cross, called a **monohybrid cross** because the parents are hybrids in one way, he counted a total of 1,064 plants, of which 787 were tall and 277 were short. In all crosses that he performed, he found a 3:1 ratio in the F_2 generation (see Fig. 11.2*b*). The characteristic that had disappeared in the F_1 generation reappeared in ¼ of the F_2 offspring. *Today, we know that the expected phenotypic results of a monohybrid cross are always 3:1.*

Mendel's Conclusion

His mathematical approach led Mendel to interpret his results differently from previous breeders. He knew that the same ratio was obtained among the F_2 generation time and time again when he did a monohybrid cross involving the seven traits he was studying. Eventually Mendel arrived at this explanation: A 3:1 ratio among the F_2 offspring was possible if (1) the F_1 parents contained two separate copies of each hereditary factor, one of these being dominant and the other recessive; (2) the factors separated when the gametes were formed, and each gamete carried only one copy of each factor; and (3) random fusion of all possible gametes occurred upon fertilization. Only in this way could shortness reoccur in the F_2 generation. Thinking this, Mendel arrived at the first of his laws of inheritance—the law of segregation. The law of segregation is a cornerstone of his particulate theory of inheritance.

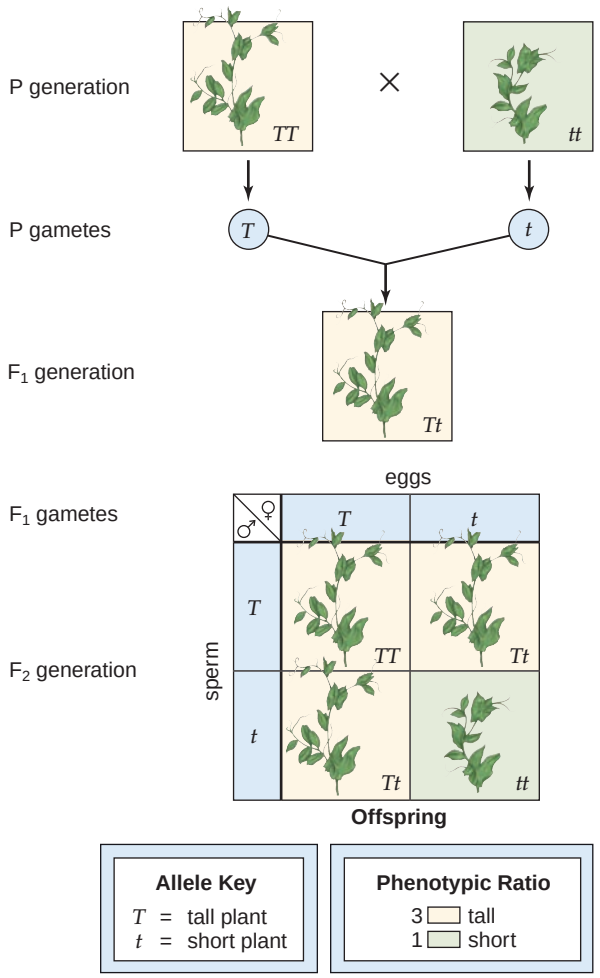


FIGURE 11.3 Monohybrid cross done by Mendel.

The P generation plants differ in one regard—length of the stem. The F_1 generation plants are all tall, but the factor for short has not disappeared because ¼ of the F_2 generation plants are short. The 3:1 ratio allowed Mendel to deduce that individuals have two discrete and separate genetic factors for each trait.

The law of segregation states the following:

- Each individual has two factors for each trait.
- The factors segregate (separate) during the formation of the gametes.
- Each gamete contains only one factor from each pair of factors.
- Fertilization gives each new individual two factors for each trait.

Mendel's Cross as Viewed by Classical Genetics

Figure 11.3 also shows how classical scientists interpreted the results of Mendel's experiments on inheritance of stem length in peas. Stem length in peas is controlled by a single gene. This gene occurs on a homologous pair of chromosomes at a particular location that is called the **gene locus** (Fig. 11.4). Alternative versions of a gene are called **alleles** [Gk. *allelon,* reciprocal, parallel]. The **dominant allele** is so named because of its ability to mask the expression of the other allele, called the **recessive allele.** The dominant allele is identified by a capital letter and the recessive allele by the same but lowercase letter. Usually, the first letter designating a trait is chosen to identify the allele. With reference to the cross being discussed, there is an allele for tallness (*T*) and an allele for shortness (*t*).

Meiosis is the type of cell division that reduces the chromosome number. During meiosis I, the members of bivalents (homologous chromosomes each having sister chromatids) separate. This means that the two alleles for each gene separate from each other during meiosis (see Fig. 11A). Therefore, the process of meiosis gives an explanation for Mendel's law of segregation, and why only one allele for each trait is in a gamete.

In Mendel's cross, the original parents (P generation) were true-breeding; therefore, the tall plants had two alleles for tallness (*TT*), and the short plants had two alleles for shortness (*tt*). When an organism has two identical alleles, as these had, we say it is **homozygous** [Gk. *homo,* same, and *zygos,* balance, yoke]. Because the parents were homozygous, all gametes produced by the tall plant contained the allele for tallness (*T*), and all gametes produced by the short plant contained an allele for shortness (*t*).

After cross-pollination, all the individuals of the resulting F_1 generation had one allele for tallness and one for shortness (*Tt*). When an organism has two different alleles at a gene locus, we say that it is **heterozygous** [Gk. *hetero,* different, and *zygos,* balance, yoke]. Although the plants of the F_1 generation had one of each type of allele, they were all tall. The allele that is expressed in a heterozygous individual is the dominant allele. The allele that is not expressed in a heterozygote is the recessive allele. This explains why shortness, the recessive trait, skipped a generation in Mendel's experiment.

Continuing with the discussion of Mendel's cross (see Fig. 11.3), the F_1 plants produce gametes in which 50% have the dominant allele *T* and 50% have the recessive allele *t.* During the process of fertilization, we assume that all types of sperm (i.e., *T* or *t*) have an equal chance to fertilize all types of eggs (i.e., *T* or *t*). When this occurs, such a monohybrid cross will always produce a 3:1 (dominant to recessive) ratio among the offspring. Figure 11.2*b* gives Mendel's results for several monohybrid crosses, and you can see that the results were always close to 3:1.

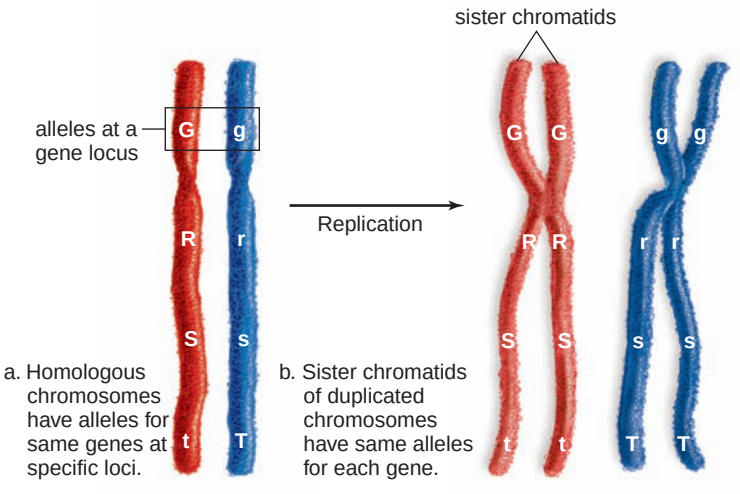


FIGURE 11.4 Classical view of homologous chromosomes.

a. The letters represent alleles; that is, alternate forms of a gene. Each allelic pair, such as *Gg* or *Tt,* is located on homologous chromosomes at a particular gene locus. **b.** Sister chromatids carry the same alleles in the same order.

TABLE 11.1

Genotype Versus Phenotype

Genotype	*Genotype*	*Phenotype*
TT	Homozygous dominant	Tall plant
Tt	Heterozygous	Tall plant
tt	Homozygous recessive	Short plant

Genotype Versus Phenotype

It is obvious from our discussion that two organisms with different allelic combinations for a trait can have the same outward appearance. (*TT* and *Tt* pea plants are both tall.) For this reason, it is necessary to distinguish between the alleles present in an organism and the appearance of that organism.

The word **genotype** [Gk. *genos,* birth, origin, race, and *typos,* image, shape] refers to the alleles an individual receives at fertilization. Genotype may be indicated by letters or by short, descriptive phrases. Genotype *TT* is called homozygous dominant, and genotype *tt* is called homozygous recessive. Genotype *Tt* is called heterozygous.

The word **phenotype** [Gk. *phaino,* appear, and *typos,* image, shape] refers to the physical appearance of the individual. The homozygous dominant (*TT*) individual and the heterozygous (*Tt*) individual both show the dominant phenotype and are tall, while the homozygous recessive individual shows the recessive phenotype and is short (Table 11.1). The phenotype is dependent upon the genotype of the individual.

Check Your Progress 11.2A

1. For each of the following genotypes, list all possible gametes, noting the proportion of each for the individual. **a.** *WW*; **b.** *Ww*; **c.** *Tt*; **d.** *TT*
2. In rabbits, if *B* = black and *b* = white, which of these genotypes (*Bb, BB, bb*) could a white rabbit have?
3. If a heterozygous rabbit reproduces with one of its own kind, what phenotypic ratio do you expect among the offspring? If there are 120 rabbits, how many are expected to be white?