Modern Genetics

26

Like a twisted ladder spiraling from end to end, each DNA molecule has the same basic shape. They are so small that scientists use computers to picture and study them. Yet, these molecules command the very look, makeup, and traits of an organism and what it will pass on to its offspring. The rungs of the ladder form a kind of genetic code. It is this code that translates into traits. In this chapter, you will learn about DNA and the ways in which it determines the traits of all living things. You will also learn about the mechanisms for passing on traits to new generations.

Guide for Reading

Key words: sex-linked trait, linkage group, nucleotide, transcription, translation, operon

Questions to think about:

- What evidence helped confirm that genes are found on chromosomes?
- How was the composition, structure, and function of DNA determined?
- What roles do DNA and RNA play in protein synthesis?

26-1 Chromosomal Inheritance

Section Objectives:

- *Explain* why *Drosophila* is a good experimental animal for genetics experiments.
- *State* the role of the X and Y chromosomes in determining sex.
- *Define* the terms *linkage group* and *crossing-over*.
- *Describe* multiple-gene inheritance.

Laboratory Investigation: *Explore* how gene linkage affects the inheritance of traits (p. 540).

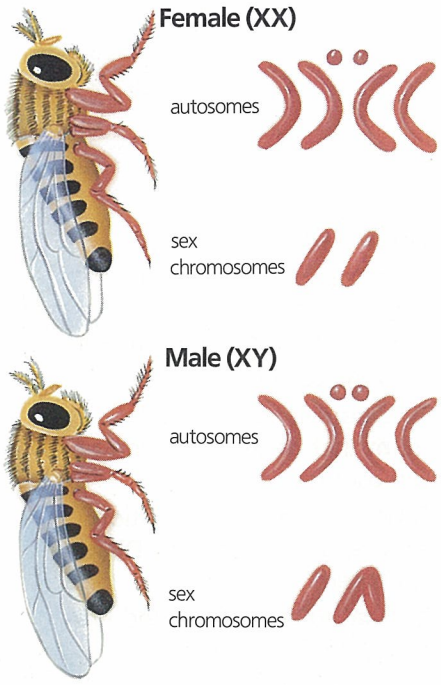
T. H. Morgan and *Drosophila*

In the early 1900s, Thomas Hunt Morgan, an American geneticist, offered the first evidence that genes are parts of chromosomes. For his work, Morgan won a Nobel Prize in 1933. One reason for Morgan's successful research was his choice of the fruit fly, *Drosophila* (droh SAHF uh luh), as his experimental animal.

The fruit fly, which is often found around ripening fruits, is a useful organism for genetic experiments. It is so tiny that large numbers can be kept in a small space. It is easy to raise, and it produces hundreds of offspring. It also has a reproductive cycle of about 14 days. This allows a geneticist to study many generations of flies in a short time. Another advantage to studying *Drosophila* is that it has only four pairs of chromosomes.

▲ **Figure 26–1**

Drosophila. Morgan used the fruit fly, *Drosophila*, as his subject for genetic experiments.



▲ **Figure 26–2**
***Drosophila* Sex Chromosomes.** A normal female *Drosophila* has two X chromosomes. A normal male has one X chromosome and one Y chromosome.

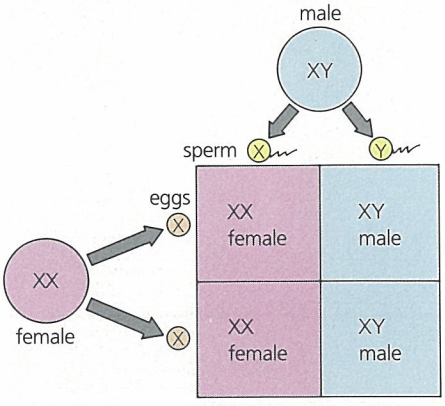
Sex Determination and Chromosomes

Around 1890, scientists observed that chromosomes in cells from males and females were identical except for one pair. Scientists suspected that these different chromosomes determined the sex of the organism. This hypothesis now has been well confirmed. The two unmatched chromosomes are known as the **sex chromosomes;** the other homologous chromosomes are called **autosomes** (AW tuh sohmz). The discovery of sex chromosomes was important in the study of genetics because it linked an inherited trait (male or female) to a particular pair of chromosomes.

In the female *Drosophila,* the two sex chromosomes look the same. See Figure 26–2. Both are rod-shaped chromosomes, known as the **X chromosomes.** Male *Drosophila*, on the other hand, have one X chromosome and one hook-shaped chromosome, called the **Y chromosome.**

The sex of *Drosophila* is determined at fertilization. All the female gametes, or eggs, contain one X chromosome. They do because each egg cell receives one X chromosome during meiosis. The male gametes, or sperm, contain either one X chromosome or one Y chromosome. When a sperm containing a Y chromosome joins with a female gamete, the zygote will have one X and one Y chromosome. This zygote will develop into a male (XY). When a sperm containing an X chromosome joins with a female gamete, the zygote will be female (XX). Thus, the sex of the fruit fly is determined by the kind of sperm that fertilizes an egg cell. See Figure 26–3.

The sex of an organism is determined in a similar way in humans and other mammals. Not all animals, however, have the same system of sex chromosomes. In birds, butterflies, and some fish, the male has the two identical sex chromosomes, and the female has two different sex chromosomes. In these animals, the female produces two different types of gametes. The egg of the female determines the sex of the offspring for these animals.

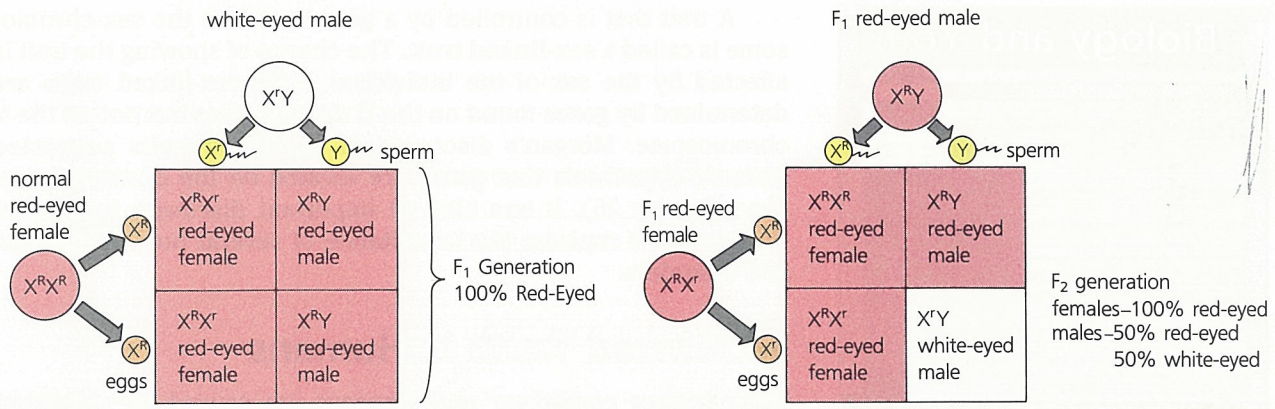


▲ **Figure 26–3**
Sex Determination in *Drosophila*. In *Drosophila,* as in humans, the male gamete can carry an X or a Y chromosome. For this reason, the male gamete determines the sex of the offspring.

Sex-Linked Traits

Morgan looked at thousands of fruit flies to find interesting traits to study. As you saw in Figure 26–1, the normal eye color of *Drosophila* is bright red. One day, Morgan discovered a white-eyed male fly. Since he had never seen this trait before, he decided to study it. His first step was to mate the white-eyed male with a normal red-eyed female. All offspring of this mating showed red eyes. Morgan concluded that the allele for white eyes is recessive.

If his cross obeyed the rules of Mendelian genetics, all the red-eyed flies of the F_1 generation would be heterozygous for eye color. If R represents the dominant allele for red eyes, and r the recessive allele for white eyes, the genotype of the F_1 generation should be Rr. To test this, Morgan mated males and females of the F_1 generation. The F_2 generation had the expected ratio of red eyes to white. About three-fourths of the flies had red eyes, and about one-fourth had white eyes. However, there was one peculiarity in



▲ **Figure 26–4**

Inheritance of the White-Eye Trait in *Drosophila*. The allele for white eyes is recessive and is carried only on the X chromosome. A white-eyed male (left) is crossed with a homozygous red-eyed female. Since all the offspring inherit the dominant red-eye allele from the female parent, all have red eyes. However, the females are heterozygous for eye color. A red-eyed male (right) is crossed with a heterozygous red-eyed female. Since all the female offspring receive the dominant allele from the male parent, they are all red eyed. However, the male offspring do not receive a gene for eye color from the male parent, only from the female parent. Half the males receive the recessive allele and are white eyed. While all the females are red eyed, half are carriers of the recessive allele. What are the genotypes of a male and female *Drosophila* that could result in a white-eyed female?

the results—all the white-eyed flies were male. All the females were red-eyed. For this reason, the inheritance of eye color seemed to be related to the sex of the offspring.

To learn more, Morgan performed a test cross. He mated the original white-eyed male with a red-eyed female from the F_1 generation. This time one-half the females had white eyes, and one-half had red. The males were also divided half white and half red.

Morgan knew that the Y chromosome is shorter than the X chromosome. He reasoned that some of the genes found on the X chromosome might be missing from the Y chromosome. It was possible, he reasoned, that the allele for eye color was carried on the X chromosome of the fruit fly, but the Y chromosome did not have a corresponding allele. If this were true, a male fly would show the recessive allele. To have white eyes, a female fly would have to have the recessive allele on both of her X chromosomes.

By means of Punnett squares, you can see that Morgan's hypothesis explains the results of the crosses he made. See Figure 26–4. In these diagrams, X^R represents an X chromosome carrying the dominant allele for red eyes. X^r indicates an X chromosome with the recessive allele for white eyes. Y stands for a Y chromosome with no gene for eye color.

Once a white-eyed female had been obtained, it was possible to make another test cross. Morgan crossed a white-eyed female with a red-eyed male. All the female offspring were red-eyed; all the males were white-eyed. You may want to draw a Punnett square that will explain this result.

Biology and You

Q: Are there any mental illnesses that are inherited?

A: Although research is incomplete, many scientists believe that some mental illnesses are passed genetically from one generation to the next. The current theory is that some mental illnesses are inherited but activated by environmental factors such as stress.

Experts generally agree that genes play a role in manic depression, a condition marked by extreme mood swings. Scientists have found a connection between manic depression and two distinct defects at the tip of the X chromosome. Another study, however, links this illness to a defect at the tip of chromosome 11. It may be that manic depression is controlled by more than one gene.

Scientists agree that genetics may also play a role in schizophrenia, a disorder in which the sufferer is out of touch with reality. Limited studies connect this illness to a gene defect in chromosome 5. Identifying the genes that cause mental illnesses may help us develop more effective treatments.

■ ***List some reasons why the inheritance pattern of mental illnesses is more difficult to trace than that of hemophilia or other physical illnesses.***

A trait that is controlled by a gene found on the sex chromosome is called a **sex-linked trait.** The chance of showing the trait is affected by the sex of the individual. Most sex-linked traits are determined by genes found on the X chromosome but not on the Y chromosome. Morgan's discovery of sex-linked traits supported Sutton's hypothesis that genes are located on the chromosomes. (See Chapter 25). It was also an important discovery in its own right, since it explains the inheritance of several human diseases and disorders.

Sex-Linked Traits in Humans

Many human conditions and diseases are caused by abnormal recessive alleles of certain genes. The normal allele lets the body perform some function that the abnormal allele does not. The term *defective allele* is often used to refer to the abnormal alleles that cause genetic diseases. Several defective alleles in human genetics are sex-linked. Among the human diseases caused by defective sex-linked alleles are hemophilia, a disorder of the blood-clotting system, and muscular dystrophy, which results in the gradual destruction of muscle cells. A form of night blindness and color blindness are less serious sex-linked hereditary disorders.

Color blindness is a condition in which the individual cannot perceive certain colors, usually red and green. This condition is more common in males than in females. Few females suffer from red-green color blindness, although they may be *carriers* for it. Carriers have the allele for color blindness on one X chromosome. Females are not affected by the defective recessive allele because they have a normal dominant allele on the other X chromosome.

Every male receives an X chromosome from his mother and a Y chromosome from his father. If the mother is a carrier for color blindness, there is a 50 percent chance that any son she has will receive the defective allele. See Figure 26–5. Since the Y chromosome has no gene for color vision, when a son inherits the defective allele from his mother, the allele is expressed, and the son will be color blind. A female, on the other hand, receives an X from her mother and an X from her father. A daughter is a carrier only if she has a defective allele from her mother and a normal allele from her father or a normal allele from her mother and a defective allele from her father.

Since a father contributes only a Y chromosome to his sons, a color-blind father cannot transmit the allele to his sons. He will, however, transmit this defective allele to all his daughters. If the mother is a carrier of the defective allele, there is a 50 percent chance that a daughter will inherit the defective allele from her mother as well as from her father. Thus, on the average, half the daughters will be color blind. The other half will be carriers. Half the sons will be color blind also, but this result has nothing to do with the father's genotype. If both parents are color blind, all their offspring will be color blind because neither parent is carrying a normal dominant allele.

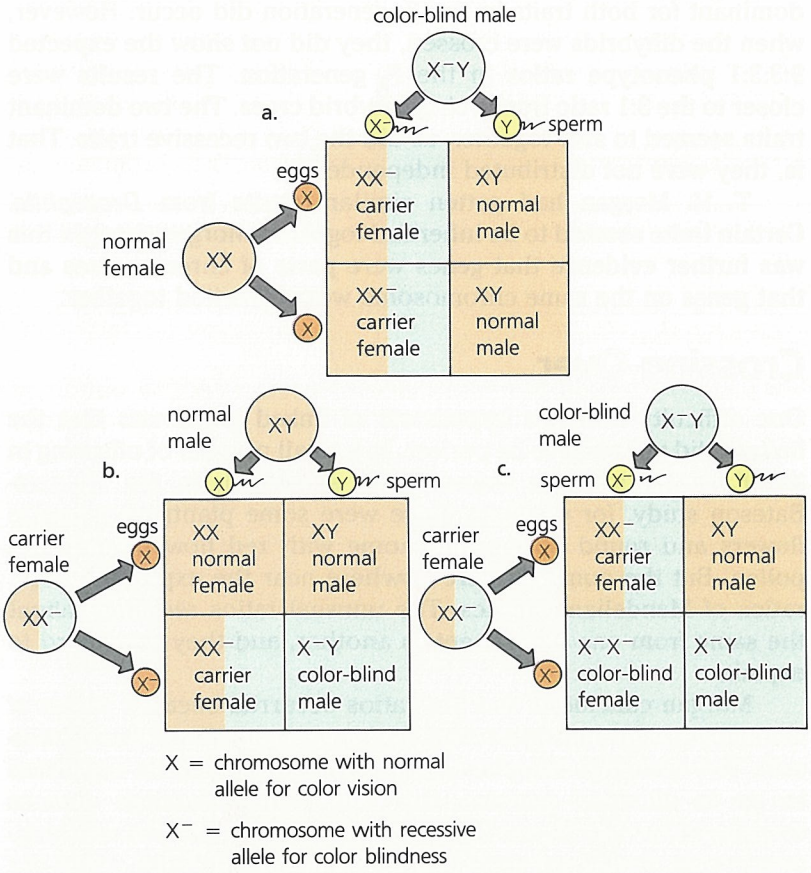


Figure 26–5

Inheritance of Color Blindness in Humans. (A and B) The allele for color blindness cannot be transmitted from father to son. It can be transmitted only through the female to later generations. (C) For a female to be color blind, she must inherit defective alleles from both parents, a relatively rare event.

Gene Linkage

Every organism has thousands of genes. Every organism also has a certain small number of chromosomes in each body cell. Therefore, many genes must be present on each chromosome. Genes on the same chromosome are said to be *linked.* All of the genes that are on the same chromosome make up a **linkage group.** *Drosophila,* with four pairs of chromosomes, has four linkage groups. Humans, with 23 pairs of chromosomes, have 23 linkage groups.

If genes are linked on the same chromosome, they cannot be distributed independently during meiosis. Therefore, linked genes do not obey Mendel's law of independent assortment, which was discussed in Chapter 25. Mendel arrived at the law of independent assortment only because the dihybrid traits he studied happened to be controlled by genes on different pairs of chromosomes.

One of the first examples of *gene linkage* was found by R. C. Punnett and William Bateson at Cambridge University in England. They were studying the inheritance of flower color in pea plants. Purple flowers were dominant; red flowers were recessive. Long pollen grains were dominant. Round pollen grains were recessive. Plants pure for both dominant traits were crossed with plants pure for both recessive traits. The expected phenotype of 100 percent

dominant for both traits in the F_1 generation did occur. However, when the dihybrids were crossed, they did not show the expected 9:3:3:1 phenotype ratios in the F_2 generation. The results were closer to the 3:1 ratio from a single hybrid cross. The two dominant traits seemed to stay together, as did the two recessive traits. That is, they were not distributed independently.

T. H. Morgan had gotten similar results from *Drosophila.* Certain traits seemed to be inherited together. Morgan thought this was further evidence that genes were parts of chromosomes and that genes on the same chromosome were inherited together.

Crossing-Over

One difficulty with the hypothesis of linked genes was that the linkage did not seem to be perfect. In a small number of offspring in the F_2 generation, the linked genes separated. In the Punnett-Bateson study, for example, there were some plants with purple flowers and round pollen, and some with red flowers and long pollen. But the numbers were nowhere near the expected 9:3:3:1 ratios of Mendelian genetics. The unusual ratios remained about the same from one experiment to another, and they were hard to explain.

Morgan concluded that the ratios occurred because pieces of homologous chromosomes were exchanged sometimes during meiosis. The exchange happened before the chromosomes separated to go to different gametes. He called this exchange process **crossing-over.** See Figure 26–6. Scientists now know that crossing-over occurs during synapsis of the first meiotic division, when the four chromatids of each homologous chromosome pair are in close contact.

Because of crossing-over, the chromosomes that go into the gametes have new gene linkages. They are not identical to the chromosomes in the parent cells. Thus, crossing-over is an important source of variations, or genetic differences, in offspring.

Morgan reasoned that genes that are far apart on the same chromosome would become separated by crossing-over more often than genes that are close together. By studying the offspring ratios of dihybrid crosses for many different pairs of linked genes, Morgan was able to figure out how close or how far apart each particular pair was. In this way, Morgan was able to make gene maps of the chromosomes in *Drosophila.* Each gene map showed the order of genes on the chromosome. The order was based on how often the genes became separated by crossing-over.

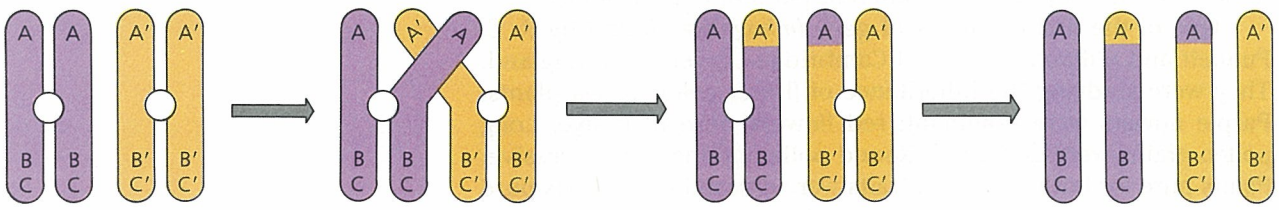
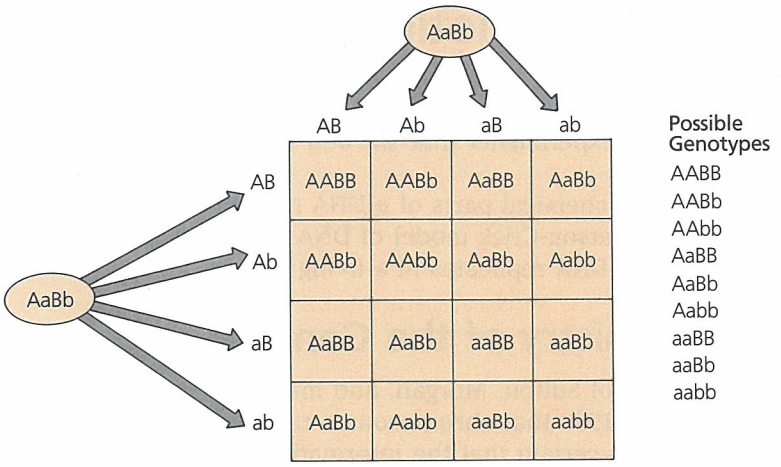


Figure 26–6

Crossing-Over. During synapsis in meiosis, segments of homologous chromatids may be interchanged. If the exchanged segments carry different alleles for certain traits, new gene combinations result. ▼



◀ **Figure 26–7**

Multiple-Gene Inheritance. In multiple-gene inheritance, when there are two genes controlling a trait, there are nine different possible genotypes. There is a range of phenotypes between the pure dominant and the pure recessive extremes.

Multiple-Gene Inheritance

Many traits in both plants and animals do not appear in two contrasting forms. For example, humans are not just either tall or short. Instead, human height varies from very short to very tall. Traits that vary between two extremes are not controlled by the alleles of a single gene, but by the alleles of two or more different genes. When two or more independent genes affect one characteristic, it is called **multiple-gene,** or *polygenic,* **inheritance.**

The simplest example of multiple-gene inheritance would involve two genes, each with its own pair of alleles. For example, the length of the ears in corn is controlled by two genes. Suppose the genes for length are Aa and Bb. With these two genes, there can be four possible gametes and nine different genotypes. See Figure 26–7. Suppose that the greater the number of capital letters in the genotype, the longer the corn ear. Then, the longest corn ears would have the genotype AABB. The shortest corn ears would have the genotype aabb. All other genotypes would show ear sizes between these two extremes.

26-1 Section Review

1. Which sex chromosomes characterize female and male *Drosophila?*
2. Name a sex-linked trait in humans.
3. In what process are pieces of homologous chromosomes exchanged during meiosis?
4. Give an example of a human trait controlled by multiple genes.

Critical Thinking

5. Why might a geneticist use fruit flies to study how genes function? Why might a scientist choose *not* to use fruit flies? (*Identifying Reasons*)

26-2 The Genetic Material

Section Objectives:

- *Describe* the experiments that showed that DNA is the genetic material.
- *List* the three chemical parts of a DNA nucleotide.
- *Explain* the Watson-Crick model of DNA.
- *Describe* how DNA replicates in a living cell.

The Chemistry of the Gene

From the work of Sutton, Morgan, and many other researchers, it was known by 1950 that chromosomes carry hereditary information. It was also certain that the information is present in distinct units, called genes, arranged along the chromosomes like beads on a string. Still, no one knew what a gene was or how it worked. Without that knowledge, heredity and genetics could not be truly understood. This understanding came in the 1950s, when the chemical nature of the gene was discovered. The first clues to the chemical nature of the hereditary material were uncovered much earlier, however.

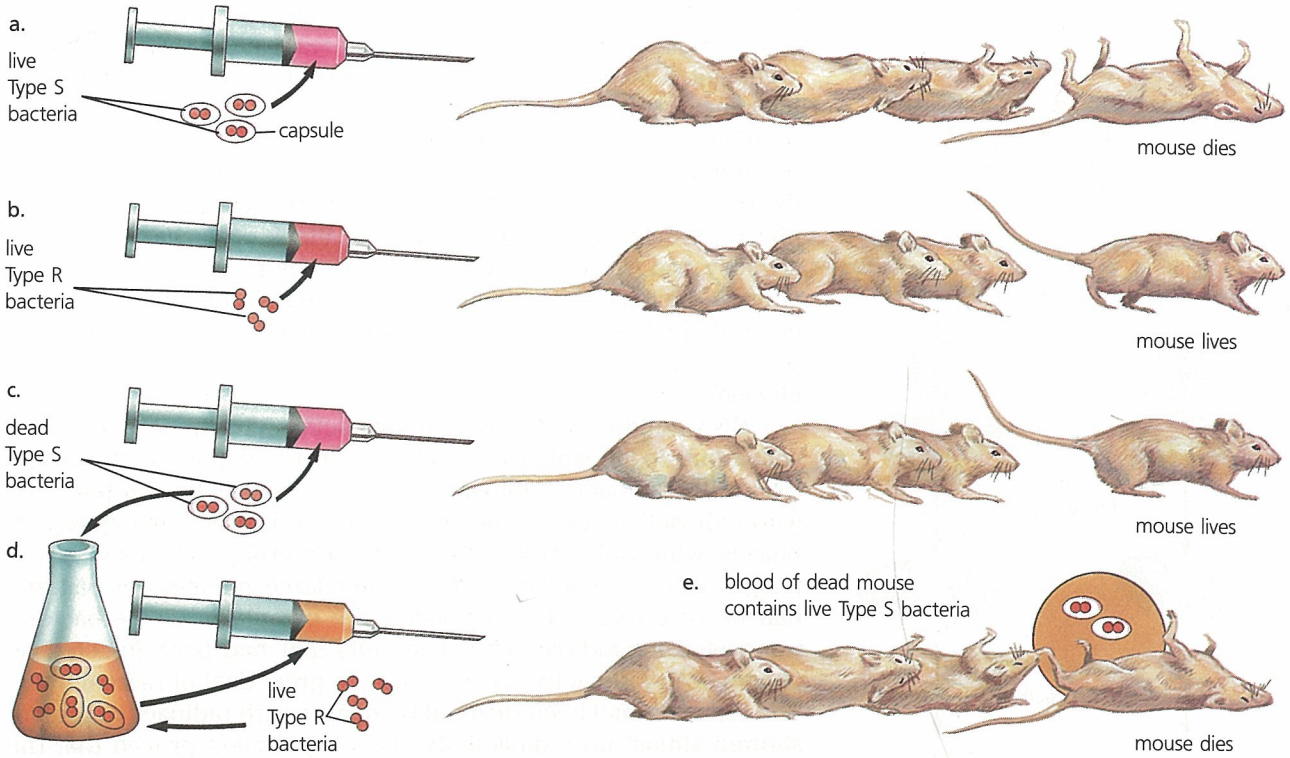
In 1869, Friedrich Miescher, a Swiss biochemist, isolated a material from the nuclei of fish sperm. He called the material *nuclein* (NOO klee un). Other scientists showed that nuclein was made of carbon, hydrogen, oxygen, and nitrogen. It was also rich in phosphorus. When nuclein was shown to be acidic, its name was changed to *nucleic acid.* Later research found two kinds of nucleic acid—deoxyribonucleic acid, or DNA, and ribonucleic acid, or RNA. DNA occurs mainly in the nuclei of cells. RNA is found mainly in the cytoplasm.

In the 1920s, scientists found that chromosomes contained DNA. It was already known that chromosomes contained proteins. While the chemical structure of proteins was well understood, the structure of DNA was completely unknown. Although a few scientists suggested that DNA was the hereditary material, most scientists believed that only proteins were complex enough to carry genetic information.

Protein vs. Nucleic Acids

It did not become clear until the 1950s that the hereditary material of the chromosomes was DNA. To understand how this came about, you need to understand the experiments performed by Frederick Griffith and several other researchers.

Griffith's Experiments In 1928, Frederick Griffith, an English bacteriologist, was trying to find a vaccine against pneumonia. Pneumonia is a disease caused by a kind of bacteria called *pneumococcus* (noo muh KAHK us). Griffith knew that there are two types of pneumococcus. See Figure 26–8. One type, called Type S, is surrounded by an outer covering called a *capsule.* Type S bacteria



cause a severe case of pneumonia. The other type, called Type R, is not surrounded by a capsule. Type R bacteria do not cause pneumonia. If mice are injected with Type S bacteria, they develop pneumonia and die. Mice injected with Type R bacteria show no ill effects.

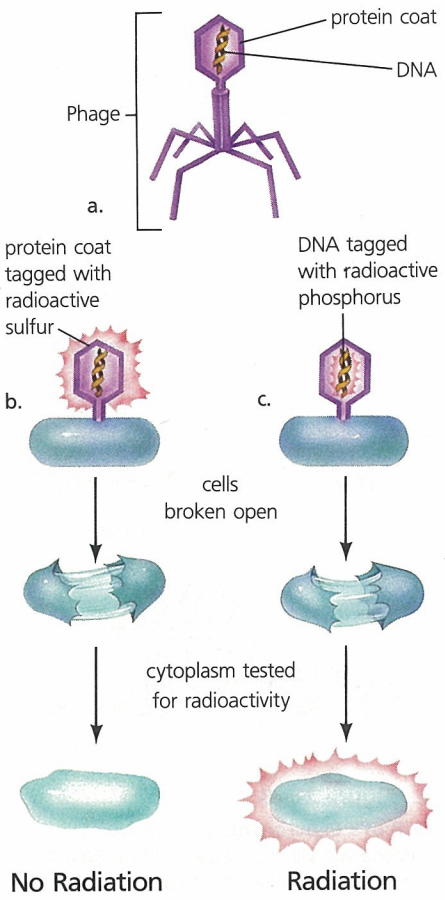
Dead Type S bacteria do not cause pneumonia when injected into mice. In Griffith's key experiment, he mixed dead Type S bacteria with live Type R. When he injected the mixture into mice, the mice developed pneumonia and died. Furthermore, the tissues of the dead mice showed living Type S bacteria.

Remember that neither dead Type S nor live Type R bacteria alone cause pneumonia. When brought together, however, they do cause pneumonia and living Type S bacteria appear. Griffith concluded that some factor from dead Type S bacteria could change, or transform, Type R bacteria into Type S. The changed bacteria were able to make capsules and to cause pneumonia in mice.

Avery, MacLeod, and McCarty In 1944, Oswald Avery, Colin MacLeod, and Maclyn McCarty of the Rockefeller Institute in New York identified the transforming material in Griffith's experiment as DNA. In other words, DNA produced the new inherited traits in Type R bacteria. Although this was strong evidence that DNA is the genetic substance, many scientists remained unconvinced. They still thought that protein must carry the hereditary information. The conclusive evidence supporting DNA was obtained by Alfred Hershey and Martha Chase in 1952.

▲ **Figure 26–8**

Griffith's Experiment. (A) Live Type S bacteria will kill the mouse. (B) Live Type R bacteria are harmless. (C) Dead Type S bacteria are harmless. (D) Dead Type S bacteria are mixed with live Type R bacteria. (E) The mixture kills the mouse, and live Type S are present in the mouse's tissues. Griffith concluded that the Type R bacteria had been transformed into Type S bacteria.



▲ **Figure 26–9**

The Hershey-Chase Experiment. (A) Structure of one type of bacteriophage. (B) Bacteria infected by phages with protein coats are tagged with radioactive sulfur. The cell contents do not become radioactive. (C) Bacteria infected by phages with DNA are tagged with radioactive phosphorus. The cell contents become radioactive. Hershey and Chase concluded that a phage infects a bacterial cell by injecting its DNA into the bacterium. The protein coat remains outside.

Hershey and Chase Alfred Hershey and Martha Chase made use of viruses called bacteriophages to resolve the DNA *vs.* protein argument. A *bacteriophage,* or *phage* (FAYJ) for short, is a virus that infects bacteria. This kind of virus is made of a DNA core surrounded by a protein coat. See Figure 26–9. A phage invades a bacterium and makes hundreds of new phage particles once inside the bacterial cell. The bacterial cell then breaks open, and the new phage particles are let go. These can attack other bacterial cells. Hershey and Chase wanted to discover whether the whole phage entered the bacterium or whether just the DNA or the protein coat entered. In hopes of answering this question, they tagged the protein and the DNA of the phage particle with different radioactive elements.

DNA contains phosphorus but no sulfur. Virus protein contains sulfur but no phosphorus. Hershey and Chase tagged the phage DNA with radioactive phosphorus. They tagged the protein coat with radioactive sulfur. One group of bacteria was then exposed to phages with radioactive DNA. Another group was exposed to phages with radioactive protein. After large numbers of bacteria had become infected with phages, the cytoplasm of the bacteria was tested for radioactivity. The cells that had been infected by phages with radioactive DNA showed a great deal of radioactivity. The cells that had been infected by phages with radioactive protein showed almost no radioactivity. This experiment proved that the phage DNA enters the cells, while the phage protein stays outside when phages infect bacteria.

If phage DNA alone can cause bacteria to make more phages, it must be the DNA that carries the genetic instructions for making phages. This experiment established DNA as the genetic material. The problem then became that of finding what DNA is made of and how it works.

Composition of DNA

The first step in analyzing an unknown organic compound is to find out the chemical groups that form it. In the 1920s, P. A. Levene, a biochemist, carried out a chemical analysis of DNA. Levene found that the DNA molecule is made up of the following chemical groups: the 5-carbon sugar **deoxyribose** (dee ahk see RY bohs); a phosphate group; and four kinds of nitrogen-containing (nitrogenous) bases. Two of the four bases, known as **adenine** and **guanine,** are a kind of compound called a *purine* (PYOOR een). The other two, **cytosine** and **thymine,** are compounds called *pyrimidines* (pih RIM uh deenz).

Levene found that there was one phosphate group and one nitrogen-containing base for each sugar unit. He therefore concluded that the basic unit of DNA is a sugar, a phosphate, and one of the four nitrogen-containing bases. He called this unit a **nucleotide** (NOO klee uh tyd). Since there are four different bases, there are four different kinds of nucleotides. Many, many nucleotides make up a single DNA molecule.

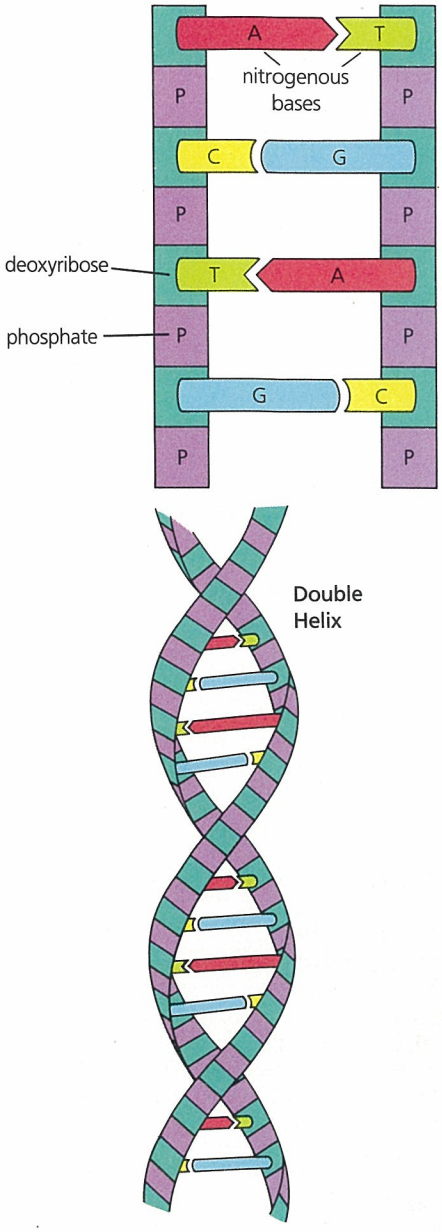
Structure of DNA

After the chemical makeup of DNA was known, the second step was to work out the structure of the DNA molecule. This was done in 1953 by James Watson, an American biochemist, and Francis Crick, an English physicist, working together in Cambridge, England. To develop their model of DNA, Watson and Crick used everything that was known about DNA. An important piece of information transmitted by Maurice Wilkins came from Rosalind Franklin of Oxford University in England. She had made X-ray studies of DNA crystals. These X-ray photographs showed that the repeating units in the crystal are arranged in the form of a **helix** (HEE liks). A helix is the shape of a coiled spring.

After trying many different arrangements, Watson and Crick arrived at a model DNA molecule in which there are two chains of sugar-phosphate groups running parallel to each other. Pairs of bases link the chains together like the rungs of a ladder. See Figure 26–10. Twisting or coiling the ladder forms the helix of the molecule. Thus, the DNA molecule is a *double helix.*

Watson and Crick found that their model could work only if the pairs of bases that made each rung of the ladder were an adenine unit connected to a thymine or a guanine connected to a cytosine. This model agreed with all the data for the DNA molecule. For example, it explained why the amount of adenine in DNA is always the same as the amount of thymine. It explained why the amount of guanine is always the same as the amount of cytosine. It also explained how, since the order of bases along the chain could vary, the order could be a code for genetic information.

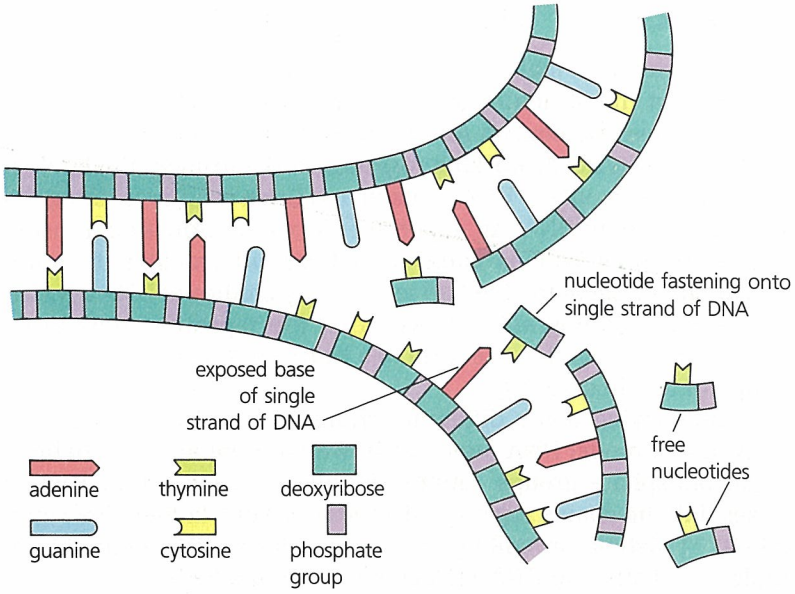
In the double-helix model, the order of bases along one strand determines the matching bases on the other strand. That is, every adenine (A) must be joined to thymine (T), and every guanine (G) must be joined to cytosine (C). No other pairings are possible. Suppose, for example, that the order of bases along one strand is AGGTTAC. The matching order along the second strand must be TCCAATG. The two strands are said to be *complementary.* Each strand is the complement of the other according to the A-T and G-C base pairing rule. The double-helix model of DNA was a great breakthrough in the science of genetics. Watson, Crick, and Wilkins received the Nobel Prize for this work in 1962. Had she lived, Franklin would also have been a recipient.



▲ **Figure 26–10**
Watson-Crick Model of DNA.

Replication of DNA

The double-helix model also explains how an exact copy of each chromosome is made during cell division. The base pairs that form each rung of the model are held together by a weak *hydrogen bond.* Before copying begins, these bonds break, and the two strands of the DNA molecule come apart. This exposes the bases along each strand. The bases of free nucleotides in the nucleus of the cell can then fasten onto the complementary bases on each exposed strand. When the nucleotides join together, they make a complete comple-



▲ **Figure 26–11**

DNA Replication. DNA replication results in the formation of two double-stranded molecules exactly like the original DNA molecule.

mentary strand exactly like the old one. In this way, two double-stranded molecules of DNA exactly like the original molecule are made. See Figure 26–11. Each double-stranded molecule contains one old strand and one new strand of DNA.

Where does replication start and end along the DNA molecule? Through experiments, scientists determined that replication does not begin at one end and continue to the other. Instead, replication begins at the same time at many points along the molecule. Enzymes then link the small segments of DNA into one long strand. In this way, a DNA molecule replicates much more rapidly than if there were only one starting point.

26-2 Section Review

1. What type of particles did Hershey and Chase use to show that DNA is the genetic material?
2. Which three chemical groups make up a nucleotide?
3. What is the shape of a DNA molecule?
4. How are the base pairs in a DNA molecule held together?

Critical Thinking

5. Suppose that a strand of DNA were to have the following base sequence: TGGCAATCTG. What would be the base sequence along the complementary strand? (*Ordering*)

26-3 Gene Expression

Section Objectives:

- *Describe* the one gene-one polypeptide hypothesis.
- *Explain* how the order of nucleotides in DNA codes for different amino acids and how this code is transcribed into RNA.
- *Compare* the structures and functions of mRNA, tRNA, and rRNA.
- *Describe* how a polypeptide is assembled.


Concept Laboratory: *Gain* an understanding of DNA structure by creating a model (p. 533).

Genes and Enzymes

The idea that hereditary material controls the synthesis of enzymes was suggested in the early 1900s. Sir Archibald Garrod, an English physician, studied certain diseases that he called "inborn errors of metabolism." He hypothesized that these diseases are caused by the body's inability to make a certain enzyme. He also hypothesized that this inability was inherited. Garrod published his ideas in 1909, but they were ignored at the time. It was not until the 1930s and 1940s that scientists realized their importance.

The best evidence that genes control the production of enzymes came from the experiments of George Beadle and Edward Tatum, two American scientists, in 1941. In their experiments, Beadle and Tatum used the red bread mold *Neurospora crassa.* From the results of their experiments, Beadle and Tatum were able to conclude that each gene produces its effects by controlling the synthesis of a single enzyme. This is known as the *one gene-one enzyme hypothesis.*

One Gene-One Polypeptide Hypothesis

It is now known that genes control the synthesis of all proteins. Some proteins are enzymes. Some are hormones. Some form the structures of the cell.

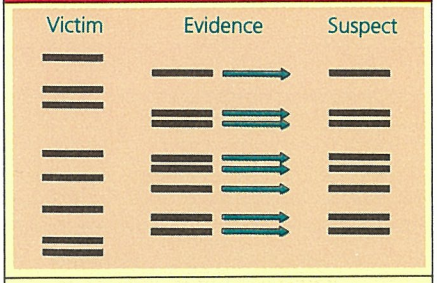
As you may recall, proteins are made of polypeptides—long chains of amino acids (see Chapter 4). Some proteins consist of two or more polypeptides linked and twisted around each other. Hemoglobin, for example, is a protein made of two different polypeptide chains.

It was found that the synthesis of each polypeptide is controlled by a different gene. Because of this fact, the one gene-one enzyme hypothesis was changed to the **one gene-one polypeptide hypothesis.** According to this hypothesis, each gene directs the synthesis of a particular polypeptide chain.

The DNA Code

To direct the synthesis of a polypeptide, a gene must be able to direct the order in which amino acids are put together. It was not clear from the Watson-Crick model of DNA how this could be done.

Science, Technology and Society



Technology: DNA Fingerprinting

Science has recently added a weapon to the crime lab's arsenal. From a drop of blood, strands of hair, or other biological material found at a crime scene, scientists can produce a "fingerprint" of a person's DNA. As with regular fingerprints, everyone, except identical twins, has a unique set of DNA.

To produce a DNA fingerprint, scientists isolate DNA from the blood or other organic evidence found at the scene of a crime. They also isolate DNA from a blood sample taken from a suspect. Both samples are treated with enzymes that cut the DNA into small fragments. The length of the fragments depends on the sequence of nitrogeneous bases in the DNA—which differs from person to person.

The DNA fragments in both samples are subjected to electrophoresis (see page 26) and treated to produce a black-and-white picture. The fragments in each sample create a pattern of black bands (see above). If the two patterns match, it is almost certain that the evidence came from the suspect.

■ ***Imagine you are on a jury and DNA fingerprinting evidence is introduced. How would you regard such evidence? Explain.***

Among the ideas put forward was the idea that the order of bases along the DNA strands is a code that specifies the order of the amino acids.

There are 20 amino acids in the proteins of humans and most other organisms. Therefore, there must be at least 20 different code "words" to specify these amino acids. As you have read, there are 4 different bases in DNA: adenine (A), guanine (G), cytosine (C), and thymine (T). Using a 2-letter code, only 16 different 2-letter code sequences can be made from 4 bases: AA, AT, AG, AC, TT, TA, TG, TC, and so forth. This is not enough, so the code "words" must be at least 3 bases long. From 4 bases, 64 different 3-base sequences can be made—more than are needed. Research has shown that the code for specifying an amino acid is made of 3-base "words." Most amino acids are specified by more than one code "word."

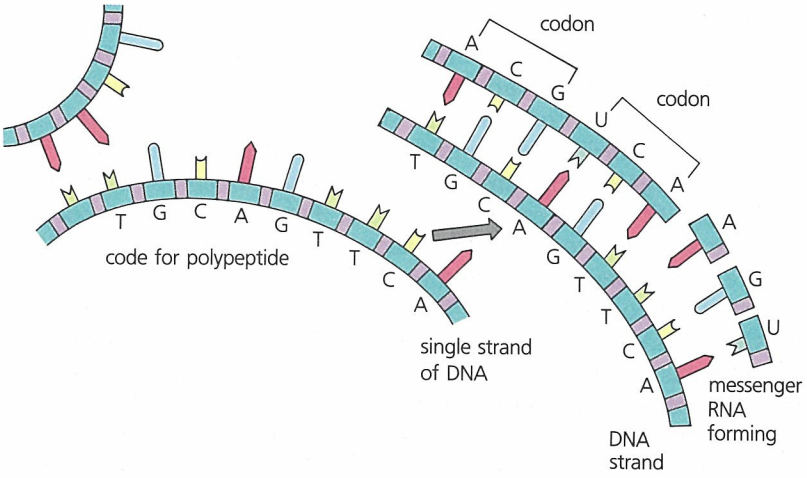
Today, scientists know that a gene is made of many nucleotides. The order of the bases of three adjacent nucleotides is the code that specifies a particular amino acid to be added to a polypeptide chain. The code also contains "punctuation"—code "words" that tell where a polypeptide begins and ends. In most cases, these points are also the beginning and end of a gene.

RNA and Protein Synthesis

In cells with nuclei, the genes are found within the nucleus. Yet, protein synthesis takes place outside the nucleus. How, then, does DNA direct the synthesis of proteins? DNA does this with the help of RNA, or ribonucleic acid. The chemical makeup of RNA is similar to the chemical makeup of DNA, with two differences. In RNA, the 5-carbon sugar is ribose, and the nitrogen-containing base **uracil** (U) takes the place of thymine. Thus, the four bases found in RNA are adenine, guanine, cytosine, and uracil. The structure of RNA is also a little different. Unlike DNA, which is double-stranded, RNA is made of only a single strand of nucleotides.

Messenger RNA

The first step in directing protein synthesis is to copy the DNA code for a polypeptide into a molecule of RNA. To copy the code, the DNA strands separate for a short time and serve as a pattern, or *template,* for RNA. See Figure 26–12. Complementary RNA nucleotides take their places along the exposed strands by matching up complementary bases. When the assembled RNA sequence reaches the DNA "stop" code, it leaves the DNA strand. The RNA strand is now a separate molecule that carries the complete message for a single polypeptide in complementary form. That is, each A of the DNA is represented by a U in the RNA, each T by an A, each G by a C, and each C by a G. A strand of RNA that copies a genetic message from DNA in this way is called **messenger RNA,** or mRNA. The copying of a genetic message into a molecule of mRNA is called **transcription.** Each group of three bases on the mRNA that specifies an amino acid is called a **codon** (KOH dahn).



▲ **Figure 26–12**

Transcription of a Gene. The code for each polypeptide is copied from one of the DNA strands into a strand of messenger RNA. The copying process is similar to DNA replication, except that uracil replaces thymine as a complement for adenine.

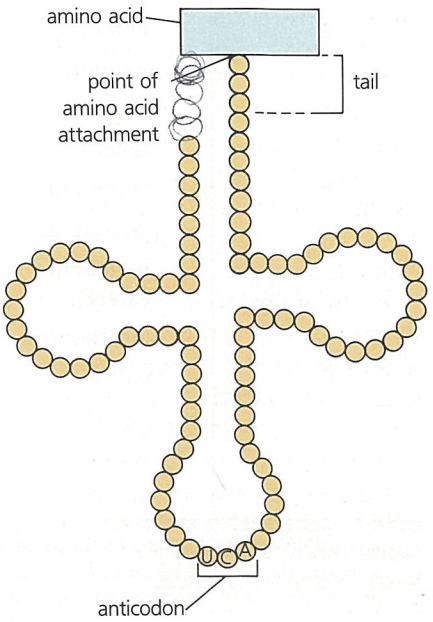
Transfer RNA

Messenger RNA is only one of three kinds of RNA that are found in the cell. A second kind is called **transfer RNA,** or tRNA. While mRNA may have thousands of nucleotides along its length, tRNA has only about 80. The molecule of tRNA has an odd shape, as shown in Figure 26–13. At one end there is a short tail. A particular amino acid can become attached to this tail.

Each tRNA molecule will pick up only one kind of amino acid. There are 20 different forms of tRNA, one for each of the 20 different amino acids. At the other end of the tRNA molecule, there is a loop of exposed nucleotides. In this loop, there is a sequence of 3 bases, called an **anticodon,** that are complements of an mRNA codon. The codon that this anticodon matches is one that specifies the amino acid that each tRNA carries. Thus, tRNA is a device for bringing a certain amino acid to a certain place specified by mRNA.

Figure 26–13

Transfer RNA. The mRNA codon that matches the anticodon of the tRNA calls for the particular amino acid that is attached to the tail end of the tRNA. ▼



Ribosomal RNA

Ribosomal RNA, or rRNA, is formed in the nucleoli of the cell. A ribosome consists of protein and rRNA. The ribosomal protein is made in the cytoplasm and then travels into the nucleus. In the nucleoli, the protein and the rRNA join together to form complete ribosomes. The ribosome is where a polypeptide is assembled during protein synthesis.

Assembly of a Polypeptide

The synthesis of the three kinds of RNA, as well as the assembly of ribosomes, occurs in the cell nucleus. The RNA and complete ribosomes migrate separately through the nuclear pores to the

cytoplasm. Within the cytoplasm, there is contained a supply of all the amino acids that are needed to make the cell's proteins. Figure 26–14 lists all codons and the amino acids each codes for. This is called the genetic code. Within the cytoplasm polypeptides are assembled according to the instructions carried by mRNA.

In the cytoplasm, amino acid molecules become attached to their specific varieties of tRNA. See Figure 26–15. Ribosomes become attached to different places along each strand of mRNA. Where a ribosome is attached to mRNA, a molecule of tRNA with the right anticodon temporarily joins with the corresponding codon on the mRNA. The amino acid brought into position by the tRNA joins the last amino acid in the chain and separates from tRNA. The ribosome then moves along to the next codon. A new tRNA takes its place on the mRNA strand, and its amino acid joins the polypeptide chain. As the ribosome moves along, the tRNA that has delivered its amino acid is released. It is now free to pick up another amino acid and deliver it to the right place for assembly into the chain. Amino

Figure 26–14
The Genetic Code. Most of the amino acids are specified by more than one codon. For example, GCU, GCC, GCA, and GCG all code for the amino acid alanine. ▼

The Genetic Code

First Base in Codon	Second Base in Codon				Third Base in Codon
	U	C	A	G	
U	phenylalanine	serine	tyrosine	cysteine	U
	phenylalanine	serine	tyrosine	cysteine	C
	leucine	serine	stop	stop	A
	leucine	serine	stop	tryptophan	G
C	leucine	proline	histidine	arginine	U
	leucine	proline	histidine	arginine	C
	leucine	proline	glutamine	arginine	A
	leucine	proline	glutamine	arginine	G
A	isoleucine	threonine	asparagine	serine	U
	isoleucine	threonine	asparagine	serine	C
	isoleucine (start);	threonine	lysine	arginine	A
	methionine	threonine	lysine	arginine	G
G	valine	alanine	aspartate	glycine	U
	valine	alanine	aspartate	glycine	C
	valine	alanine	glutamate	glycine	A
	valine	alanine	glutamate	glycine	G

An mRNA codon consists of three nucleotides. For example ACU codes threonine. The first letter, A, is read in the first column; the second letter C, from the second letter column; and the third letter, U, from the third letter column. Most amino acids are specified by more than one codon.

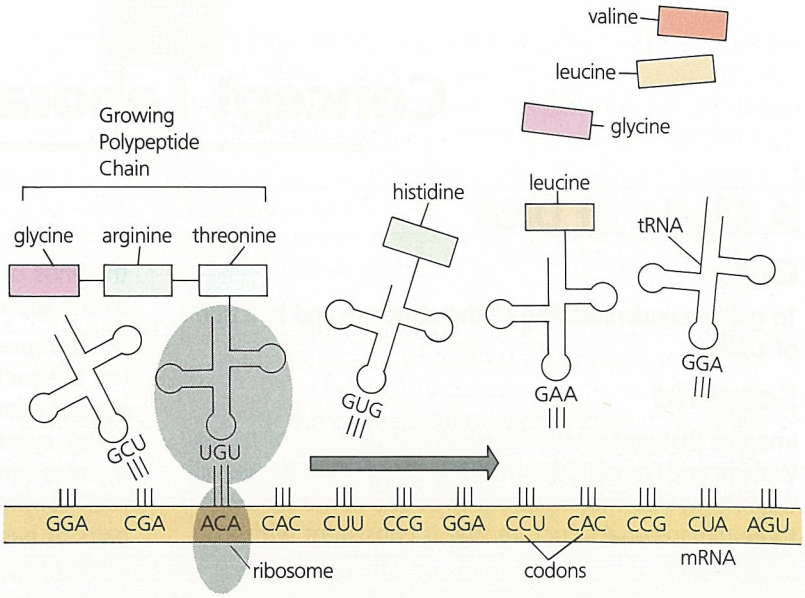


Figure 26–15

Protein Synthesis. As a ribosome moves into position at a codon of a messenger RNA, a transfer RNA with the complementary anticodon temporarily bonds to the codon. The tRNA adds its amino acid to the polypeptide chain, then detaches and moves away. ▶

acids are added to the growing polypeptide chain until the ribosome reaches a "stop" codon. The polypeptide is then let go, and it forms itself into a complete protein molecule.

Every step in the process of translating the genetic message into a polypeptide chain is helped by a specific enzyme. There are enzymes that attach amino acids to tRNA. There are enzymes that attach tRNA to mRNA. There are enzymes that join the amino acids to the polypeptide chain. There are also enzymes in the nucleus that open the DNA molecule for transcription, and others that help in the assembly of RNA. All of these enzymes must be specified by genes.

The process by which the information coded in RNA is used for the assembly of a particular amino acid sequence is known as **translation.** Figure 26–16 shows how a genetic message is first

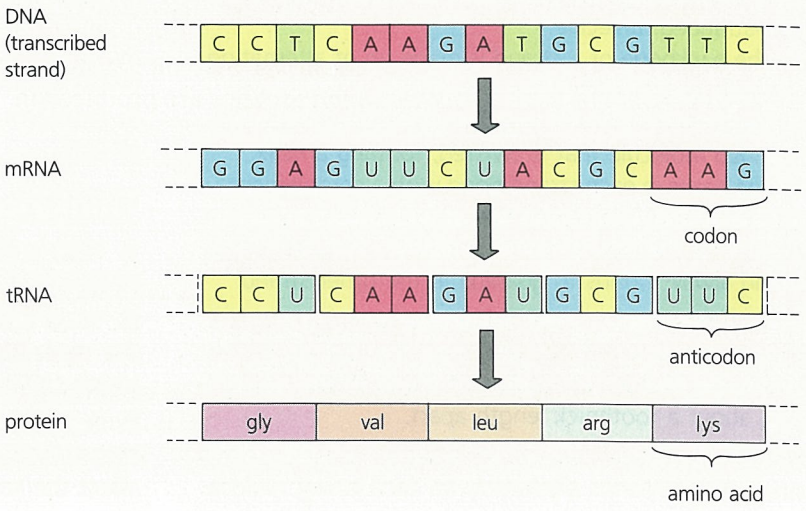


Figure 26–16

From DNA to Proteins. In transcription, the genetic code of DNA is copied into a molecule of mRNA. In translation, the information coded in mRNA is used to assemble a specific amino acid sequence, forming a polypeptide. This is done with the help of tRNA. ▶

transcribed from DNA to RNA and then translated into a polypeptide. By this remarkable system, all the cell's proteins are synthesized in the cytoplasm, while the chromosomes carrying the hereditary instructions for this synthesis remain in the nucleus.

26-3 Section Review

1. Which hypothesis states that each gene directs the synthesis of a particular chain of a protein?
2. How is information encoded in a gene?
3. What is the process by which genetic messages are copied into an RNA molecule?
4. Where in the cell are proteins made?

Critical Thinking

5. Suppose that, instead of the correct sequence AGC, an error occurred that changed the sequence to ATC. What would happen upon transcription? What would happen upon translation? (*Predicting*)

26-4 Control of Gene Expression

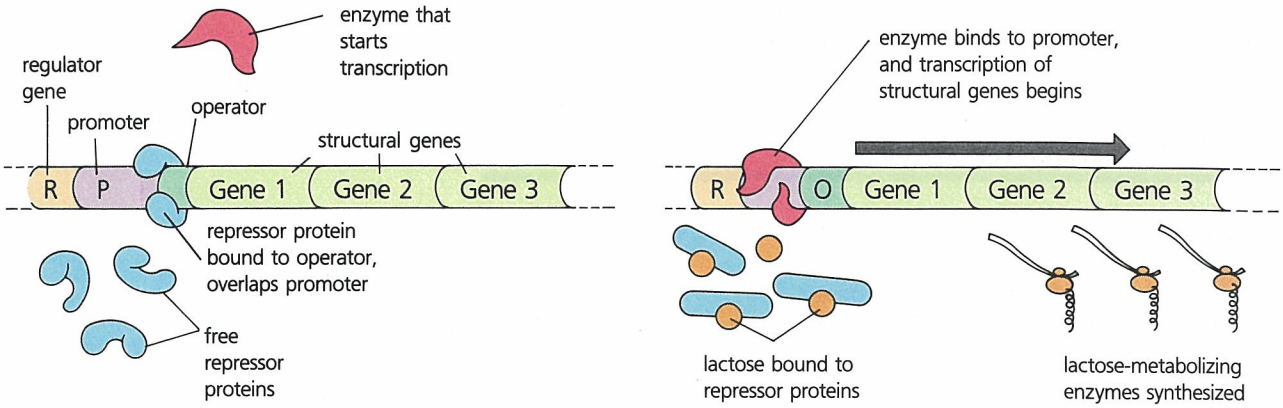
Section Objectives:

- *Explain* how gene expression is regulated in prokaryotes and in eukaryotes.
- *Compare* the operon of prokaryotes with the genes and control sections of DNA in eukaryotes.
- *Describe* homeotic genes and oncogenes.

Every cell in an organism has the complete set of genes characteristic of that organism. But, even though all the cells of an organism have the same genes, different cells perform different functions and produce different proteins. Why is a particular set of genes activated in one cell, while a different set is activated in another cell of the same organism? One of the major questions that biologists are trying to answer is what determines which proteins are produced in a given cell.

Gene Expression in Bacteria

In the early 1960s, three French biologists, François Jacob, Jacques Monod, and André Lwoff, discovered how the transcription of certain genes is controlled in the bacterium *E. coli.* They were awarded a Nobel Prize in 1965 for their work. Jacob, Monod, and Lwoff studied the production of the three enzymes the bacteria use to digest lactose, a sugar. They found that the enzymes are produced by the bacteria only when they are needed. That is, the bacteria produce the lactose-digesting enzymes when lactose is



▲ **Figure 26–17**

Synthesis of Lactose-Digesting Enzymes in Bacteria. (A) When lactose is not present, repressor proteins bind to the operator of the operon. Because the repressor protein is much larger than the operator gene, it overlaps the promoter gene as well. The enzyme that starts transcription of the structural genes cannot bind to the promoter. No lactose-digesting enzymes are produced.

(B) When lactose is present, the lactose binds to the repressor protein. This means that the lactose-repressor complex cannot bind to the operator. Therefore, the enzyme that starts transcription is able to bind to the promoter, which means that lactose-digesting enzymes are produced.

present and other sources of energy are not available. Thus, enzyme production is turned on and off, depending on the needs of the cell.

Jacob, Monod, and Lwoff determined that production of the lactose-digesting enzymes is controlled by a cluster of genes. The amino acid sequences of the enzymes are determined by three structural genes. A *structural gene* is a DNA segment that codes for the production of a particular polypeptide.

The investigators found that the activity of the structural genes is controlled by an *operator gene,* a sequence of nucleotides found next to the structural genes. The structural genes cannot be transcribed unless the operator gene is in an active state. We can think of the operator as being switched "on" to cause transcription or switched "off" to prevent transcription. See Figure 26–17.

The activity of the operator is controlled by a protein called a *repressor protein.* The repressor protein is the product of another gene, called a *regulator gene.* When the repressor protein binds to the operator gene, transcription of the structural genes cannot start. The repressor protein is always present in the cell, and it is normally bound to the operator gene so that the operator is off. When lactose binds to the repressor protein, the protein changes shape. This makes it unable to bind to the operator gene. Therefore, when lactose is present, the operator gene is turned on. Then, transcription of the structural genes proceeds, and lactose-digesting enzymes are produced.

There is another control gene, called a *promoter,* that also plays a role in gene expression in bacteria. The promoter attracts and binds the enzyme that starts transcription. If the enzyme cannot bind to the promoter, transcription of the structural genes will not start. The promoter and the operator control the copying of a cluster of structural genes. In prokaryotes, such as bacteria, the promoter, the operator, and their associated structural genes are called an **operon** (OP er on).

Gene Expression in Higher Organisms

Scientists first thought that the control of gene expression in higher organisms (eukaryotes) would be similar to that in prokaryotes. However, this is not so for several reasons. In the first place, eukaryote genes relating to a certain function are not clustered together. Related genes are far apart from one another on a chromosome. Sometimes, they are on different chromosomes entirely. To further complicate matters, each eukaryote gene is split into parts, called *exons,* that are not next to each other. An **exon** is a segment of DNA that codes for amino acids that will become part of a protein. In between the exons, there are sections of DNA, called *introns.* An **intron** is a segment of DNA that does not code for amino acids of a protein.

When a gene is transcribed, both the introns and exons are made into RNA. The introns are then "edited out." To do this, enzymes cut out the intron RNA and then join, or splice, together the exon RNA pieces. Before this happens, two other strings of RNA nucleotides, one called a cap and the other a tail, are added to the ends of the RNA. See Figure 26–18. Because the enzymes can cut and splice the RNA in different ways, different proteins can be made from the same DNA segment.

Changes in the amount of coiling or in the shape of the DNA also affect the expression of genes in eukaryotes. A change in

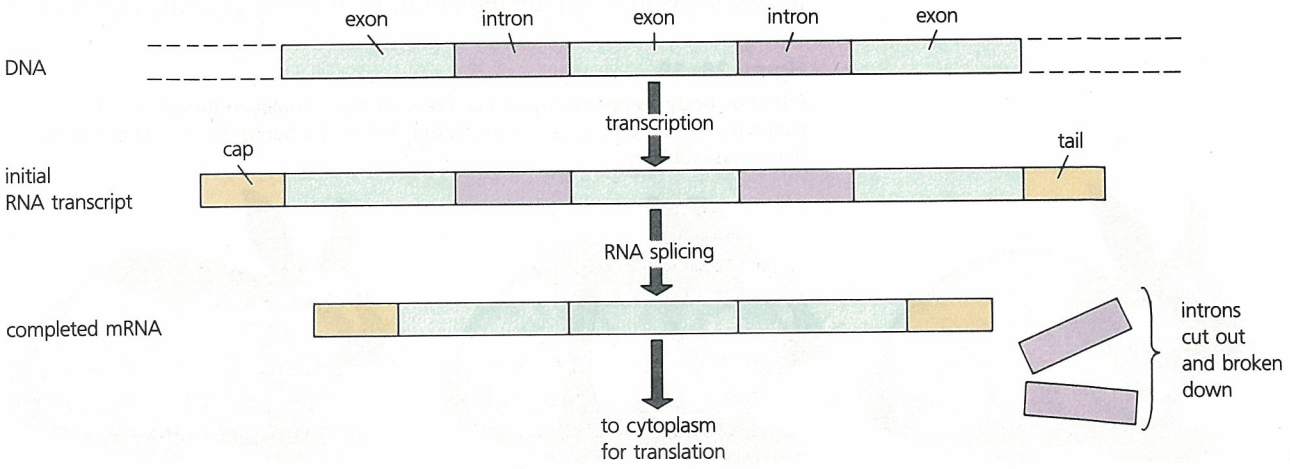


Figure 26–18
mRNA Synthesis in Eukaryotes. Both the exons and introns are transcribed, producing one long RNA molecule. More nucleotides are added to the ends of the RNA. Enzymes then cut out the RNA introns and splice together the exons to form the completed messenger RNA. ▼

coiling or shape determines which parts of the DNA are accessible to enzymes and other proteins and to RNA. In turn, this accessibility influences the process of transcription. As you may recall from the discussion in Chapter 20, chromatin is made up of DNA wound around groups of proteins called histones. It is now thought that histones control the coiling and uncoiling of DNA in chromatin. Tightly packed DNA is not transcribed. Loosely packed DNA is transcribed. Finally, in some eukaryotes, certain chemical groups can attach to sections of DNA, changing its shape and reducing transcription.

Like the DNA of prokaryotes, the DNA of eukaryotes has sections that control the copying of genes. The control sections are not part of the gene itself. Instead, they are found elsewhere in the DNA. For example, eukaryotes have promoters that attract and bind the enzyme that starts the copying process. Another section of DNA, called the **enhancer,** controls the access of the enzyme to the promoter. Unlike the case in prokaryotes, in eukaryotes, control sections, such as enhancers, are usually far away from the genes they affect.

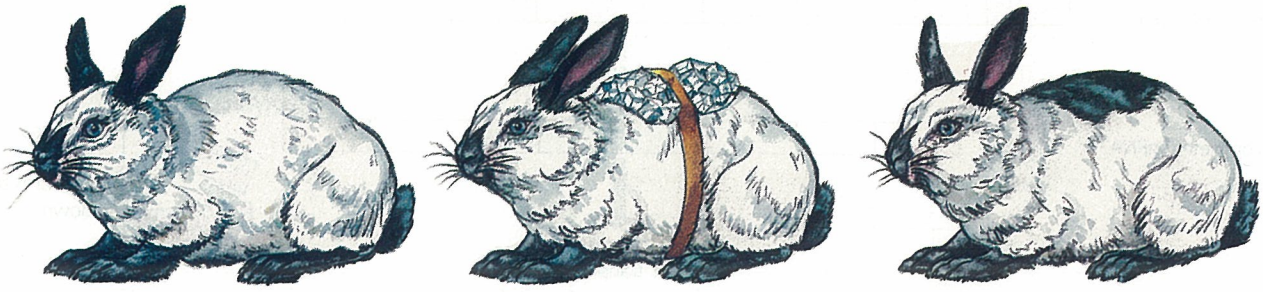
Gene Expression and the Environment

Some environmental factors also can switch genes on and off. You have already read about bacteria producing an enzyme when a certain sugar is present. In green plants, some development genes are switched on and off by light. Changes in temperature cause changes in the expression of the genes governing fur color in the Himalayan rabbit.

The Himalayan rabbit has white fur over most of its body, with black fur on the ear, nose, feet, and tail. See Figure 26–19. This pattern is produced by differences in temperature in certain parts of the body. A gene controls the production of black pigment. Black pigment is deposited in the fur over parts of the body in which the temperature falls below 33°C. This can be shown by placing an ice pack on a shaved area on the back of a Himalayan rabbit. Where the ice pack has lowered the temperature, the new growth of fur will be

Figure 26–19

Effect of Body Temperature on Fur Color of the Himalayan Rabbit. Cold temperatures turn on the gene that controls the production of black pigment in the Himalayan rabbit. ▼



black. Genes carry the basic information for all traits, but the phenotypes of organisms often can be changed by environmental factors that switch genes on and off.

In some reptiles, the incubation temperature of the eggs determines the sex of the offspring. In painted turtles, for example, high incubation temperatures tend to produce females, while low incubation temperatures produce mostly males.

Gene Expression in Development

During the development of an organism, different genes must be active at different times in its life cycle. The question of how genes are switched on and off during development has been studied thoroughly in the fruit fly *Drosophila.* Within the embryo of the fruit fly, scientists have discovered a group of genes, called **homeotic** (ho mee OH tik) **genes.** These genes control the key events in the development of a fruit fly. Homeotic genes switch other genes on and off. They do this by coding for homeotic proteins. It is thought that the homeotic proteins bind certain parts of the DNA and thus control the process of transcription. Similar sequences of DNA, known as *homeoboxes,* have also been found in many other animals, including humans.

Oncogenes and Cancer

Understanding the expression of genes may someday lead to a cure for cancer. **Oncogenes** (ON koh genes) are genes that cause some kinds of cancer. Oncogenes are present in most human cells, but usually they are switched off, or they are expressed in a way that does not cause cancer. When oncogenes are switched on, or when they begin to operate in an abnormal way, they lead to the uncontrolled growth of cells that we call cancer. If scientists can find a way to switch the oncogenes off, they may be able to develop a cure for many cancers.

26-4 Section Review

1. What is the term for the promoter, the operator, and the associated structural genes in prokaryotes?
2. What are the pieces of a split gene called in eukaryotes?
3. In what organism were homeotic genes first identified?
4. What environmental factor determines whether or not a Himalayan rabbit has black fur?

Critical Thinking

5. List some enviromental hazards that might cause oncogenes to be switched on. (*Identifying Causes*)