12-1 DNA

How do genes work? What are they made of, and how do they determine the characteristics of organisms? Are genes single molecules, or are they longer structures made up of many molecules? In the middle of the 1900s, questions like these were on the minds of biologists everywhere.

To truly understand genetics, biologists first had to discover the chemical nature of the gene. If the structures that carry genetic information could be identified, it might be possible to understand how genes control the inherited characteristics of living things.

Griffith and Transformation

Like many stories in science, the discovery of the molecular nature of the gene began with an investigator who was actually looking for something else. In 1928, British scientist Frederick Griffith was trying to figure out how bacteria make people sick. More specifically, Griffith wanted to learn how certain types of bacteria produce a serious lung disease known as pneumonia.

Griffith had isolated two slightly different strains, or types, of pneumonia bacteria from mice. Both strains grew very well in culture plates in his lab, but only one of the strains caused pneumonia. The disease-causing strain of bacteria grew into smooth colonies on culture plates, whereas the harmless strain produced colonies with rough edges. The differences in appearance made the two strains easy to distinguish.

Guide for Reading

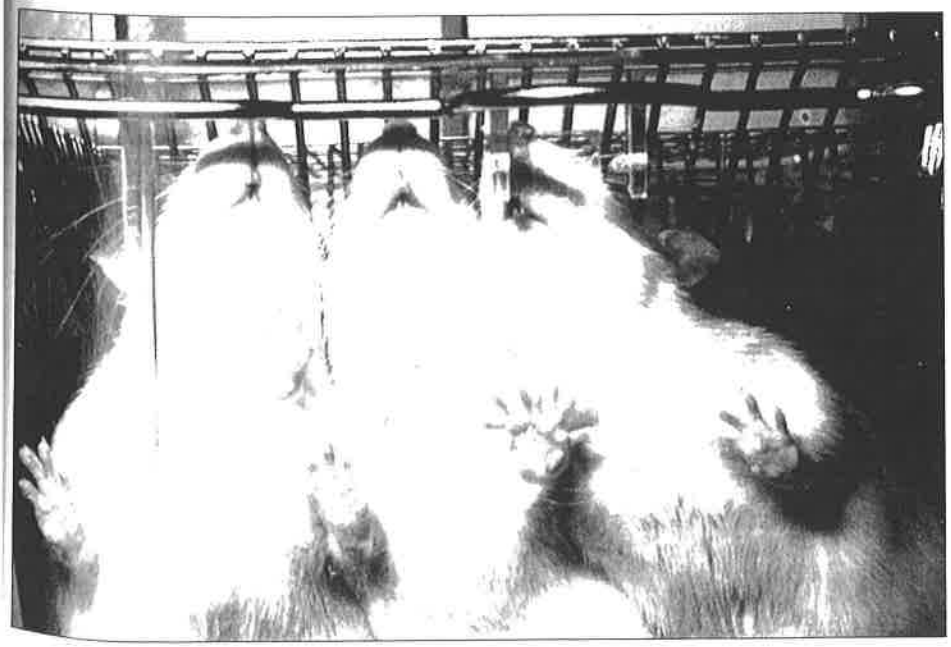
Key Concepts

- What did scientists discover about the relationship between genes and DNA?
- What is the overall structure of the DNA molecule?

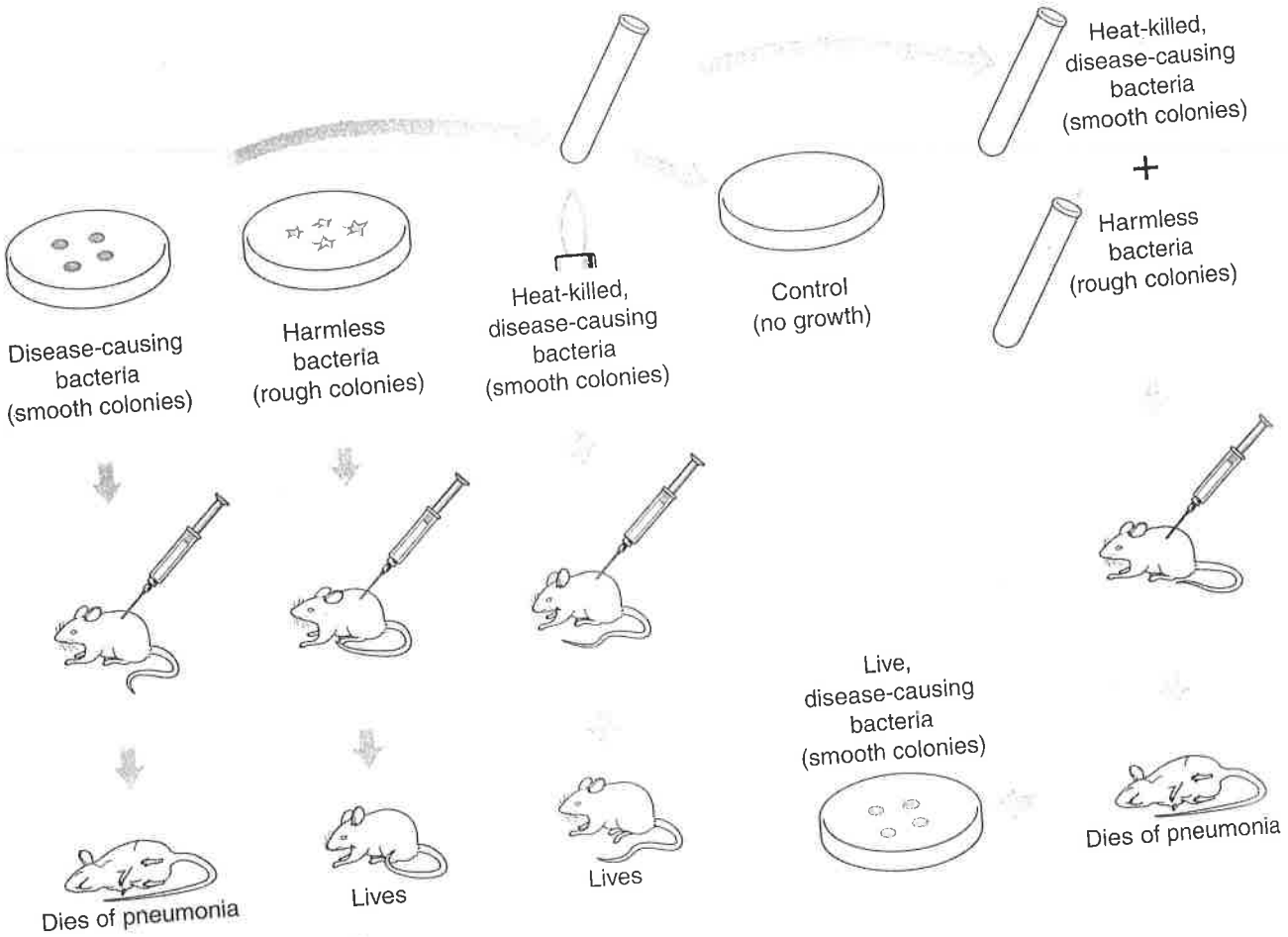
Vocabulary

transformation
bacteriophage
nucleotide
base pairing

Reading Strategy: Summarizing As you read, find the key ideas for the text under each blue heading. Write down a few key words from each main idea. Then, use the key words in your summary. Revise your summary, keeping only the most important ideas.



◀ **Figure 12-1** White mice like these are commonly used in scientific experiments.



▲ **Figure 12–2** Griffith injected mice with four different samples of bacteria. When injected separately, neither heat-killed, disease-causing bacteria nor live, harmless bacteria killed the mice. The two types injected together, however, caused fatal pneumonia. From this experiment, biologists inferred that genetic information could be transferred from one bacterium to another. **Inferring** *After heating the disease-causing bacteria, why did Griffith test whether material from the bacterial culture would produce new colonies in a petri dish?*

Griffith's Experiments When Griffith injected mice with the disease-causing strain of bacteria, the mice developed pneumonia and died. When mice were injected with the harmless strain, they didn't get sick at all. Griffith wondered if the disease-causing bacteria might produce a poison.

To find out, he took a culture of these cells, heated the bacteria to kill them, and injected the heat-killed bacteria into mice. The mice survived, suggesting that the cause of pneumonia was not a chemical poison released by the disease-causing bacteria. Griffith's experiments are shown in **Figure 12–2.**

Transformation Griffith's next experiment produced an amazing result. He mixed his heat-killed, disease-causing bacteria with live, harmless ones and injected the mixture into mice. By themselves, neither should have made the mice sick. But to Griffith's amazement, the mice developed pneumonia and many died. When he examined the lungs of the mice, he found them filled not with the harmless bacteria, but with the disease-causing bacteria. Somehow the heat-killed bacteria had passed their disease-causing ability to the harmless strain. Griffith called this process **transformation** because one strain of bacteria (the harmless strain) had apparently been changed permanently into another (the disease-causing strain).

Griffith hypothesized that when the live, harmless bacteria and the heat-killed bacteria were mixed, some factor was transferred from the heat-killed cells into the live cells. That factor, he hypothesized, must contain information that could change harmless bacteria into disease-causing ones. Furthermore, since the ability to cause disease was inherited by the transformed bacteria's offspring, the transforming factor might be a gene.

Avery and DNA

In 1944, a group of scientists led by Canadian biologist Oswald Avery at the Rockefeller Institute in New York decided to repeat Griffith's work. They did so to determine which molecule in the heat-killed bacteria was most important for transformation. If transformation required just one particular molecule, that might well be the molecule of the gene.

Avery and his colleagues made an extract, or juice, from the heat-killed bacteria. They then carefully treated the extract with enzymes that destroyed proteins, lipids, carbohydrates, and other molecules, including the nucleic acid RNA. Transformation still occurred. Obviously, since these molecules had been destroyed, they were not responsible for the transformation.

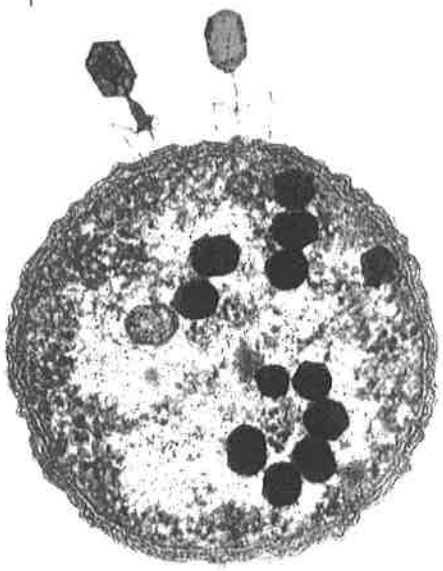
Avery and the other scientists repeated the experiment, this time using enzymes that would break down DNA. When they destroyed the nucleic acid DNA in the extract, transformation did not occur. There was just one possible conclusion. DNA was the transforming factor. **Avery and other scientists discovered that the nucleic acid DNA stores and transmits the genetic information from one generation of an organism to the next.**

The Hershey-Chase Experiment

Scientists are a skeptical group. It usually takes several experiments to convince them of something as important as the chemical nature of the gene. The most important of these experiments was performed in 1952 by two American scientists, Alfred Hershey and Martha Chase. They collaborated in studying viruses, nonliving particles smaller than a cell that can infect living organisms.

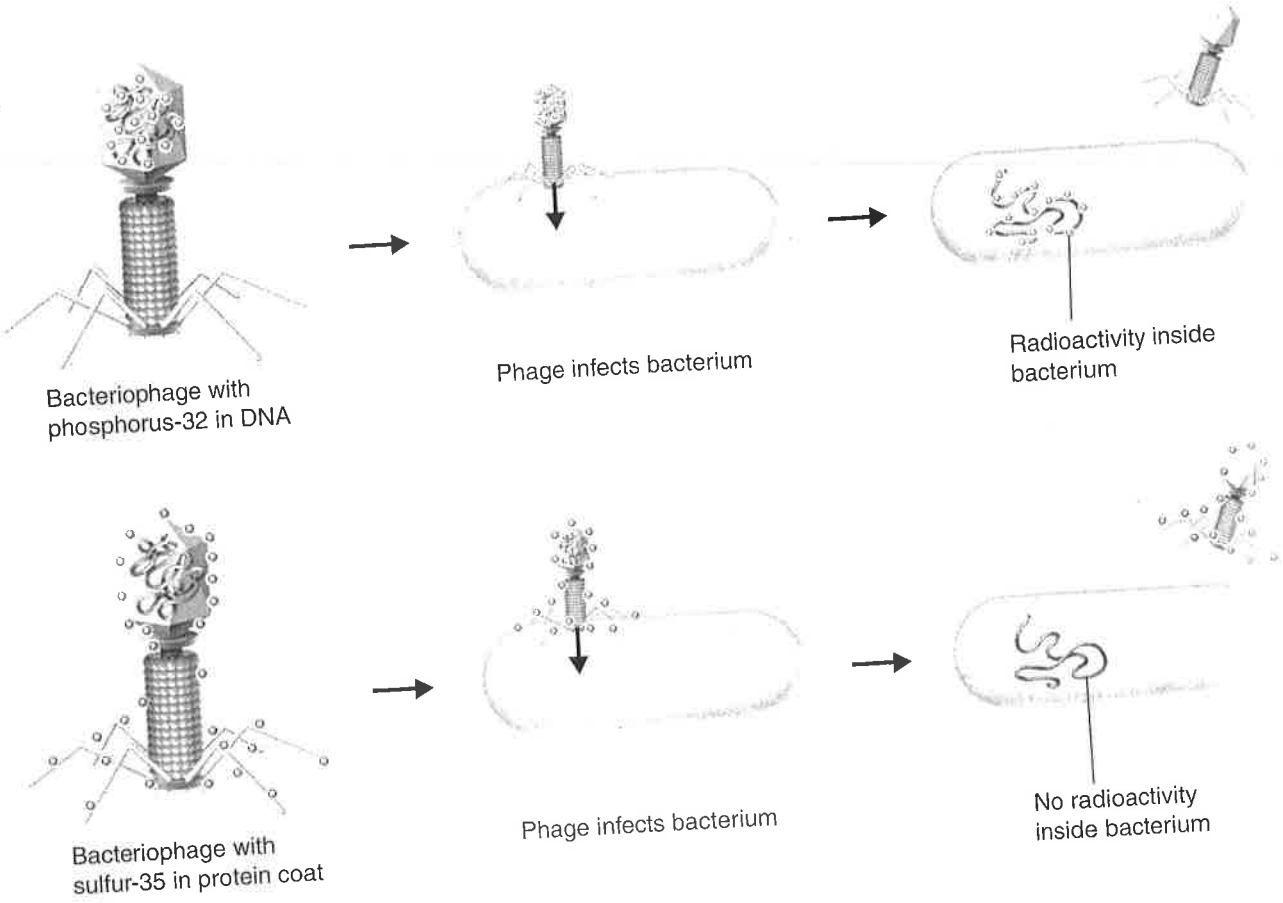
Bacteriophages One kind of virus that infects bacteria is known as a **bacteriophage** (bak-TEER-ee-uh-fayj), which means "bacteria eater." **Figure 12–3** shows typical bacteriophages. Bacteriophages are composed of a DNA or RNA core and a protein coat. When a bacteriophage enters a bacterium, the virus attaches to the surface of the cell and injects its genetic information into it. The viral genes act to produce many new bacteriophages, and they gradually destroy the bacterium. When the cell splits open, hundreds of new viruses burst out.

CHECKPOINT *What is a bacteriophage?*



(magnification: 25,000×)

▼ **Figure 12–3** A bacteriophage is a type of virus that infects and kills bacteria. This image shows two T2 bacteriophages (purple) invading an *E. coli* cell (green).
Comparing and Contrasting *How large are viruses compared with bacteria?*



▲ **Figure 12–4** Alfred Hershey and Martha Chase used different radioactive markers to label the DNA and proteins of bacteriophages. The bacteriophages injected only DNA into the bacteria, not proteins. **From these results, Hershey and Chase concluded that the genetic material of the bacteriophage was DNA.**

Radioactive Markers Hershey and Chase reasoned that if they could determine which part of the virus—the protein coat or the DNA core—entered the infected cell, they would learn whether genes were made of protein or DNA. To do this, they grew viruses in cultures containing radioactive isotopes of phosphorus-32 (^{32}P) and sulfur-35 (^{35}S). This was a clever strategy because proteins contain almost no phosphorus and DNA contains no sulfur. The radioactive substances could be used as markers. If ^{35}S was found in the bacteria, it would mean that the viruses' protein had been injected into the bacteria. If ^{32}P was found in the bacteria, then it was the DNA that had been injected.

The Hershey-Chase experiment is shown in **Figure 12–4.** The two scientists mixed the marked viruses with bacteria. Then, they waited a few minutes for the viruses to inject their genetic material. Next, they separated the viruses from the bacteria and tested the bacteria for radioactivity. Nearly all the radioactivity in the bacteria was from phosphorus (^{32}P), the marker found in DNA. **Hershey and Chase concluded that the genetic material of the bacteriophage was DNA, not protein.**

CHECKPOINT *What part of the virus did the Hershey-Chase experiment show had entered the bacteria?*

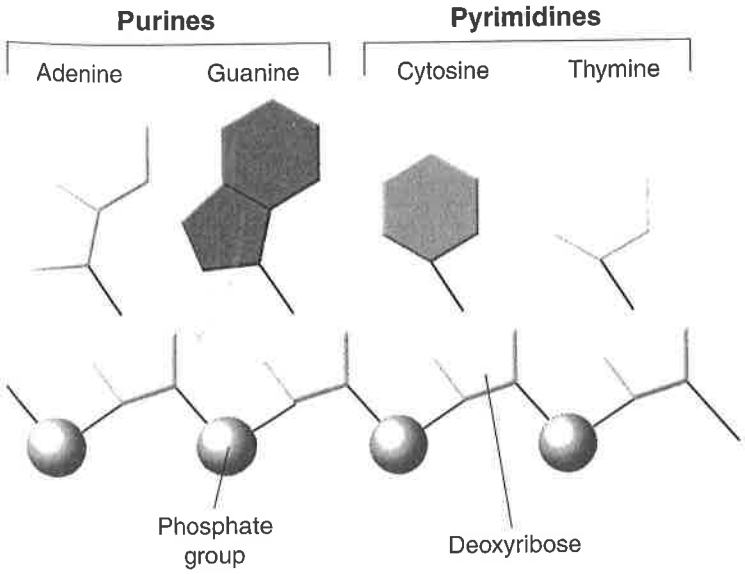
The Components and Structure of DNA

You might think that knowing genes were made of DNA would have satisfied scientists, but that was not the case at all. Instead, they wondered how DNA, or any molecule for that matter, could do the three critical things that genes were known to do: First, genes had to carry information from one generation to the next; second, they had to put that information to work by determining the heritable characteristics of organisms; and third, genes had to be easily copied, because all of a cell's genetic information is replicated every time a cell divides. For DNA to do all of that, it would have to be a very special molecule indeed.

DNA is a long molecule made up of units called **nucleotides.** As **Figure 12–5** shows, each nucleotide is made up of three basic components: a 5-carbon sugar called deoxyribose, a phosphate group, and a nitrogenous (nitrogen-containing) base. There are four kinds of nitrogenous bases in DNA. Two of the nitrogenous bases, adenine (AD-uh-neen) and guanine (GWAH-neen), belong to a group of compounds known as purines. The remaining two bases, cytosine (SY-tuh-zeen) and thymine (THY-meen), are known as pyrimidines. Purines have two rings in their structures, whereas pyrimidines have one ring.

The backbone of a DNA chain is formed by sugar and phosphate groups of each nucleotide. The nitrogenous bases stick out sideways from the chain. The nucleotides can be joined together in any order, meaning that any sequence of bases is possible.

If you don't see much in **Figure 12–5** that could explain the remarkable properties of the gene, don't be surprised. In the 1940s and early 1950s, the leading biologists in the world thought of DNA as little more than a string of nucleotides. They were baffled, too. The four different nucleotides, like the 26 letters of the alphabet, could be strung together in many different ways, so it was possible they could carry coded genetic information. However, so could many other molecules, at least in principle. Was there something more to the structure of DNA?



◀ **Figure 12–5** DNA is made up of nucleotides. Each nucleotide has three parts: a deoxyribose molecule, a phosphate group, and a nitrogenous base. There are four different bases in DNA: adenine, guanine, cytosine, and thymine. **Interpreting Graphics** *How are the nucleotides joined together to form the DNA chain?*

Percentages of Bases in Four Organisms

Source of DNA	A	T	G	C
Streptococcus	29.8	31.6	20.5	18.0
Yeast	31.3	32.9	18.7	17.1
Herring	27.8	27.5	22.2	22.6
Human	30.9	29.4	19.9	19.8

▲ **Figure 12–6** Erwin Chargaff showed that the percentages of guanine and cytosine in DNA are almost equal. The same is true for adenine and thymine. **Interpreting Graphics** *Which organism has the highest percentage of adenine?*

Chargaff's Rules One of the puzzling facts about DNA was a curious relationship between its nucleotides. Years earlier, Erwin Chargaff, an American biochemist, had discovered that the percentages of guanine [G] and cytosine [C] bases are almost equal in any sample of DNA. The same thing is true for the other two nucleotides, adenine [A] and thymine [T], as shown in **Figure 12–6.** The observation that [A] = [T] and [G] = [C] became known as Chargaff's rules. Despite the fact that DNA samples from organisms as different as bacteria and humans obeyed this rule, neither Chargaff nor anyone else had the faintest idea why.

X-Ray Evidence In the early 1950s, a British scientist named Rosalind Franklin began to study DNA. She used a technique called X-ray diffraction to get information about the structure of the DNA molecule. Aiming a powerful X-ray beam at concentrated DNA samples, she recorded the scattering pattern of the X-rays on film. Franklin worked hard to make better and better patterns from DNA until the patterns became clear.

Biology and History

Discovering the Role of DNA

Genes and the laws of heredity were discovered before scientists identified the molecules that genes are made of. With the discovery of DNA, scientists have been able to explain how genes are replicated and how they function.

1928
Frederick Griffith
Griffith discovers that a factor in heat-killed, disease-causing bacteria can "transform" harmless bacteria into ones that can cause disease.

1944
Oswald Avery
Avery's team determines that genes are composed of DNA.

1951
Linus Pauling
Robert Corey
Pauling and Corey determine that the structure of a class of proteins is a helix.

1952
Rosalind Franklin
Franklin studies the DNA molecule using a technique called X-ray diffraction.

1900 — 1925 — 1950

By itself, Franklin's X-ray pattern does not reveal the structure of DNA, but it does carry some very important clues. The X-shaped pattern in the photograph in the time line shows that the strands in DNA are twisted around each other like the coils of a spring, a shape known as a helix. The angle of the *X* suggests that there are two strands in the structure. Other clues suggest that the nitrogenous bases are near the center of the molecule.

CHECKPOINT *What technique did Franklin use to study DNA?*

The Double Helix At the same time that Franklin was continuing her research, Francis Crick, a British physicist, and James Watson, an American biologist, were trying to understand the structure of DNA by building three-dimensional models of the molecule. Their models were made of cardboard and wire. They twisted and stretched the models in various ways, but their best efforts did nothing to explain DNA's properties.

Then, early in 1953, Watson was shown a copy of Franklin's remarkable X-ray pattern. The effect was immediate. In his book *The Double Helix,* Watson wrote: "The instant I saw the picture my mouth fell open and my pulse began to race." Using clues from Franklin's pattern, within weeks Watson and Crick had built a structural model that explained the puzzle of how DNA could carry information, and how it could be copied. They published their results in a historic one-page paper in April of 1953.

Watson and Crick's model of DNA was a double helix, in which two strands were wound around each other.

Writing in Science

Do research in the library or on the Internet to find out what James Watson or Francis Crick has worked on since discovering the structure of DNA. Organize your findings about the scientist's work and write a short essay describing it.

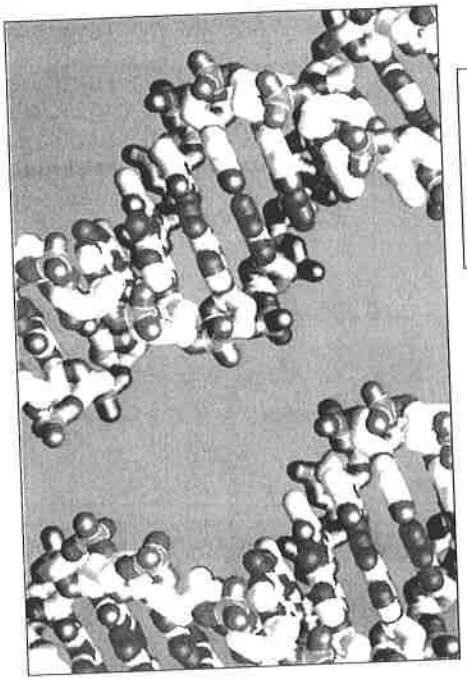
1953
James Watson
Francis Crick
Watson and Crick develop the double-helix model of the structure of DNA.

1960
Sydney Brenner
Brenner and other scientists show the existence of messenger RNA.

1977
Walter Gilbert
Gilbert, Allan Maxam, and Frederick Sanger develop methods to read the DNA sequence.

2000
Human Genome Project
The Human Genome Project—an attempt to sequence all human DNA—is essentially complete.

1950 1975 2000



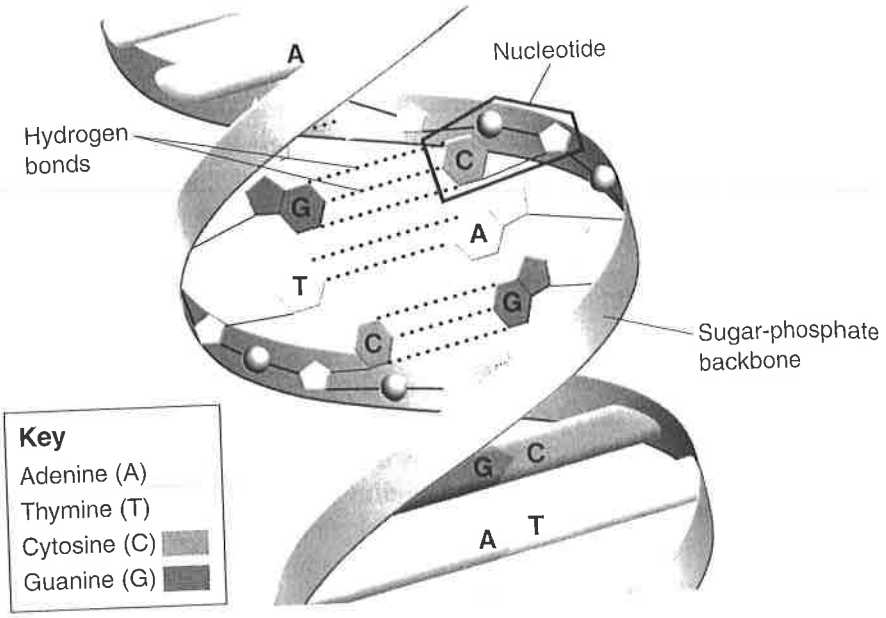


Figure 12–7 **DNA is a double helix in which two strands are wound around each other.** Each strand is made up of a chain of nucleotides. The two strands are held together by hydrogen bonds between adenine and thymine and between guanine and cytosine.

A double helix looks like a twisted ladder or a spiral staircase. When Watson and Crick evaluated their DNA model, they realized that the double helix accounted for many of the features in Franklin's X-ray pattern but did not explain what forces held the two strands together. They then discovered that hydrogen bonds could form between certain nitrogenous bases and provide just enough force to hold the two strands together. As **Figure 12–7** shows, hydrogen bonds can form only between certain base pairs—adenine and thymine, and guanine and cytosine. Once they saw this, they realized that this principle, called **base pairing,** explained Chargaff's rules. Now there was a reason that [A] = [T] and [G] = [C]. For every adenine in a double-stranded DNA molecule, there had to be exactly one thymine molecule; for each cytosine molecule, there was one guanine molecule.

12–1 Section Assessment

1. **Key Concept** List the conclusions Griffith, Avery, Hershey, and Chase drew from their experiments.
2. **Key Concept** Describe Watson and Crick's model of the DNA molecule.
3. What are the four kinds of bases found in DNA?
4. Did Watson and Crick's model account for the equal amounts of thymine and adenine in DNA? Explain.
5. **Critical Thinking Inferring** Why did Hershey and Chase grow viruses in cultures that contained both radioactive phosphorus and radioactive sulfur? What might have happened if they had used only one radioactive substance?

Connecting Concepts

Scientific Methods

Using the experiments of Griffith, Avery, or Hershey and Chase as an example, develop a flowchart that shows how the scientist or scientists used scientific processes. Be sure to identify each process. *Hint:* You may wish to review Chapter 1, which describes scientific methods.