GLOBAL EDITION

Campbell Essential Biology with Physiology

SIXTH EDITION

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Brief Contents

THE PROCESS OF SCIENCE **Deadly Viruses**

Can DNA and RNA Vaccines Protect Against Viruses?

BACKGROUND

West Nile virus first appeared in the United States in 1999. Most people with the virus do not become ill. But in some cases, the virus causes a potentially fatal swelling of the central nervous system. The virus is spread by mosquitoes. There is no vaccine and no cure for those who become ill.

Medical researchers are hoping to improve our arsenal against West Nile virus by developing DNA and RNA vaccines. Vaccines trigger an immune response to a harmless molecule that mimics some part of the attacking pathogen. Once exposed, the immune system is primed to fight the disease if it detects the real pathogen in the future. A traditional vaccine contains the trigger protein. An RNA or DNA vaccine contains a copy of a viral gene and lets the patient's body make the specific trigger protein.

METHOD

Researchers tested an RNA vaccine containing a gene from West Nile virus using cats and dogs, which, like most mammals, are susceptible to the virus **(Figure 10.29a)**. The cats were given high doses of the vaccine, low doses, or placebos (ineffective treatments that serve as a control). The dogs received only low doses or placebos. All animals received booster vaccines 28 days after their first dose. After that time, the animals were exposed to mosquitoes carrying the virus and tested for the presence of infection.

RESULTS

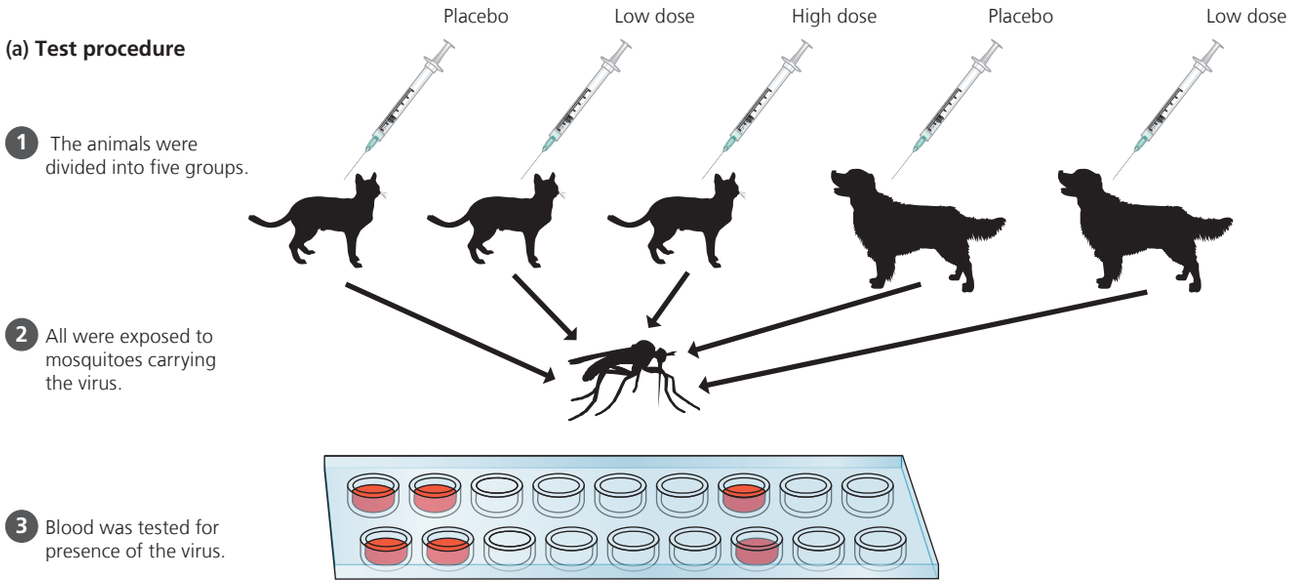
The results were striking **(Figure 10.29b)**. No animals became infected with the virus after a high dose of vaccine. Clearly, the new vaccine was quite effective, at least among cats and dogs. Although no DNA or RNA vaccines have yet been approved for human use, this type of research suggests that they may became a standard tool in the near future.

TREATMENT	% OF CATS INFECTED	% OF DOGS INFECTED
Placebo	82	93
Low vaccine dose	12.5	0
High vaccine dose	0	(no dose given)

(b) Effects of the RNA vaccine on cats and dogs

▶ Figure 10.29 **Testing an RNA vaccine against West Nile virus.**

(a) Test procedure



Thinking Like a Scientist

Why was it important for some dogs and cats to be given placebo injections?

For the answer, see Appendix D.

HIV, the AIDS Virus

The devastating disease **AIDS** (acquired immunodeficiency syndrome) is caused by **HIV** (human immunodeficiency virus), an RNA virus with some nasty twists. In outward appearance, HIV **(Figure 10.30)** resembles the mumps or flu virus. Its envelope enables HIV to enter and leave a cell much the way the mumps virus does. But HIV has a different mode of reproduction. It is a **retrovirus**, an RNA virus that reproduces by means of a DNA molecule, the reverse of the usual DNA → RNA flow of genetic information. These viruses carry molecules of an enzyme called **reverse transcriptase**, which catalyzes reverse transcription: the synthesis of DNA on an RNA template.

▼ Figure 10.30 HIV, the AIDS virus.

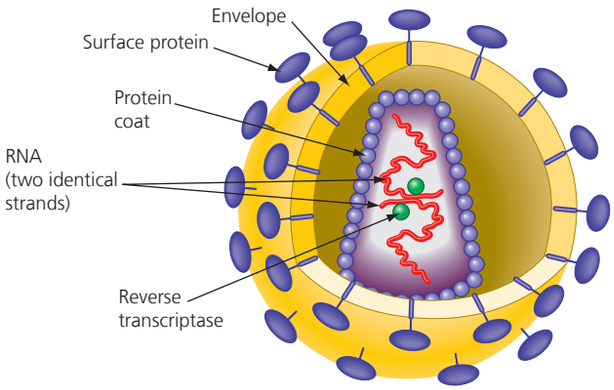


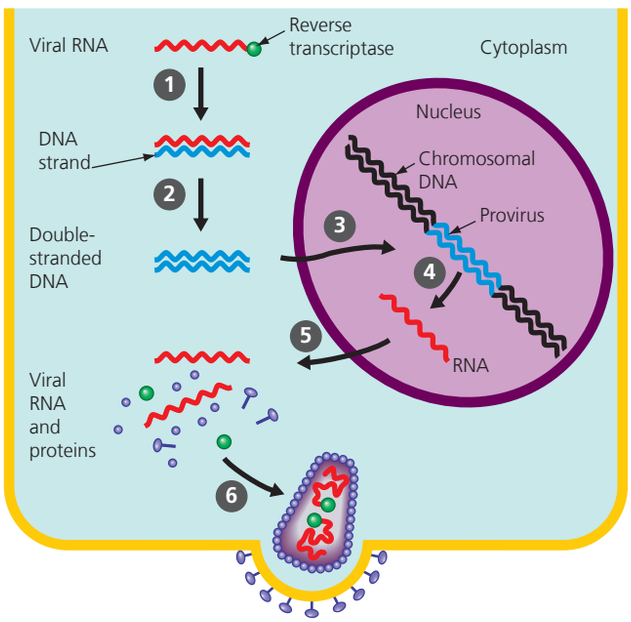
Figure 10.31 illustrates what happens after HIV RNA is uncoated in the cytoplasm of a cell. The reverse transcriptase (green) ❶ uses the RNA as a template to make a DNA strand and then ❷ adds a second, complementary DNA strand. ❸ The resulting double-stranded viral DNA then enters the cell nucleus and inserts itself into the chromosomal DNA, becoming a **provirus**. Occasionally, the provirus is ❹ transcribed into RNA ❺ and translated into viral proteins. ❻ New viruses assembled from these components eventually leave the cell and can then infect other cells. This is the standard reproductive cycle for retroviruses.

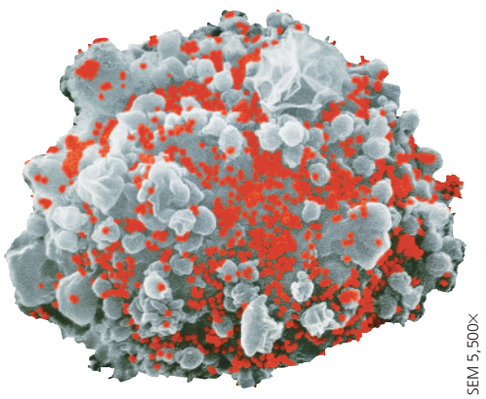
HIV infects and eventually kills several kinds of white blood cells that are important in the body's immune system. The loss of such cells causes the body to become susceptible to other infections that it would normally be able to fight off. Such secondary infections cause the syndrome (a collection of symptoms) that eventually kills AIDS patients. Since it was first recognized in 1981, HIV has infected tens of millions of people worldwide, resulting in millions of deaths.

Although there is as yet no cure for AIDS, its progression can be slowed by two categories of anti-HIV drugs. Both types of medicine interfere with the reproduction of the virus. The first type inhibits the action of enzymes called proteases, which help produce the final versions of HIV proteins. The second type, which includes the drug AZT, inhibits the action of the HIV enzyme reverse transcriptase. The key to AZT's effectiveness is its shape. The shape of a molecule of AZT is very similar to the shape of part of the T (thymine) nucleotide **(Figure 10.32)**. In fact, AZT's shape is so similar to the T nucleotide that AZT can bind to reverse transcriptase, essentially taking the place of T. But unlike thymine, AZT cannot be incorporated into a growing DNA chain. Thus, AZT "gums up the works," interfering with the synthesis of HIV DNA. Because this synthesis is an essential step in the reproductive cycle of HIV, AZT may block the spread of the virus within the body.

Many HIV-infected people in the United States and other industrialized countries take a "drug cocktail" that contains both reverse transcriptase inhibitors and protease inhibitors, and the combination seems to be much more effective than the individual drugs in keeping the virus at bay and extending patients' lives. In fact, the death rate from HIV infection can be lowered by 80% with proper treatment. However, even in combination, the drugs do not completely rid the body of the virus. Typically, HIV reproduction and the symptoms of AIDS return if a patient discontinues the medications. Because AIDS has no cure yet, prevention (namely, avoiding unprotected sex and staying away from needle sharing) is the only healthy option. ✅

▼ Figure 10.31 The behavior of HIV nucleic acid in an infected cell.





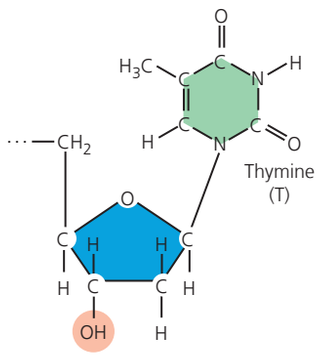
HIV (red dots) infecting a white blood cell

✅ CHECKPOINT

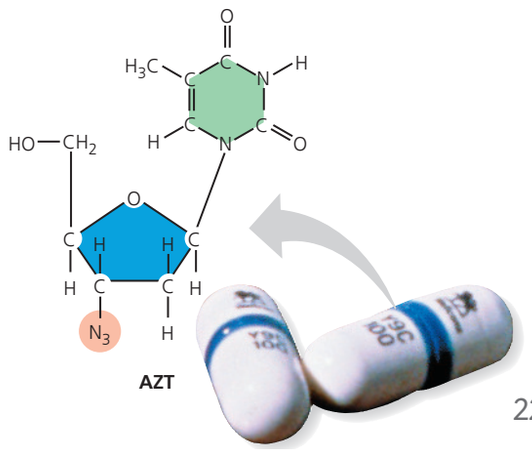
Why is HIV called a retrovirus?

■ *Answer: Because it synthesizes DNA from its RNA genome. This is the reverse ("retro") of the usual DNA → RNA information flow.*

▼ Figure 10.32 AZT and the T nucleotide. The anti-HIV drug AZT (right) has a chemical shape very similar to part of the T (thymine) nucleotide of DNA.



Part of a T nucleotide



AZT

MAD COW DISEASE IS CAUSED BY ODDLY SHAPED PROTEINS.

Prions

Prions are infectious proteins that cause brain diseases in several animal species. While a virus contains DNA or RNA, a prion consists solely of a misfolded form of a normal brain protein. When the prion gets into a cell containing the normal form of the protein, the prion somehow converts normal protein molecules to misfolded versions. The misfolded proteins then clump together, disrupting brain functions.

Diseases caused by prions include scrapie in sheep; chronic wasting disease in deer and elk; mad cow disease, which infected more than 2 million cattle in the United Kingdom in the 1980s; and Creutzfeldt-Jakob disease in humans, an incurable and inevitably fatal deterioration of the brain. An early 1900s New Guinea epidemic of kuru, another human disease caused by prions, was halted after anthropologists identified the cause—ritualistic cannibalism of the brain—and convinced locals to stop that practice.

Prions incubate at least 10 years before symptoms develop. This can prevent timely identification of sources of infection. Additionally, prions are not destroyed in food by normal heating. The only hope for developing effective treatments lies in understanding the process of infection.

To close the chapter, let's revisit some other noncellular threats to human health: emerging viruses. ✓

✓ CHECKPOINT

What makes prions so unusual as pathogens?

■ *Answer: Prions, unlike any other infectious agent, have no nucleic acid (DNA or RNA).*

EVOLUTION CONNECTION **Deadly Viruses**

Emerging Viruses

Viruses that suddenly come to the attention of medical scientists are called **emerging viruses** (Figure 10.33). We've already explored Zika virus (first recognized in Brazil in 2015) and West Nile virus (which first appeared in North America in 1999). Although each virus had persisted at low levels for many years, each became a much greater threat quite suddenly.

How do viruses give rise to new diseases? First, they can evolve into more dangerous forms. Although viruses are not alive, they are subject to natural selection, which is accelerated by high mutation rates. Unlike DNA, RNA has no mechanisms to repair copying errors, so RNA viruses can mutate rapidly. Some mutations enable viruses to infect people who had developed resistance to the ancestral strain. This is why we need yearly flu vaccines: Mutations create new influenza virus strains to which people have no immunity.

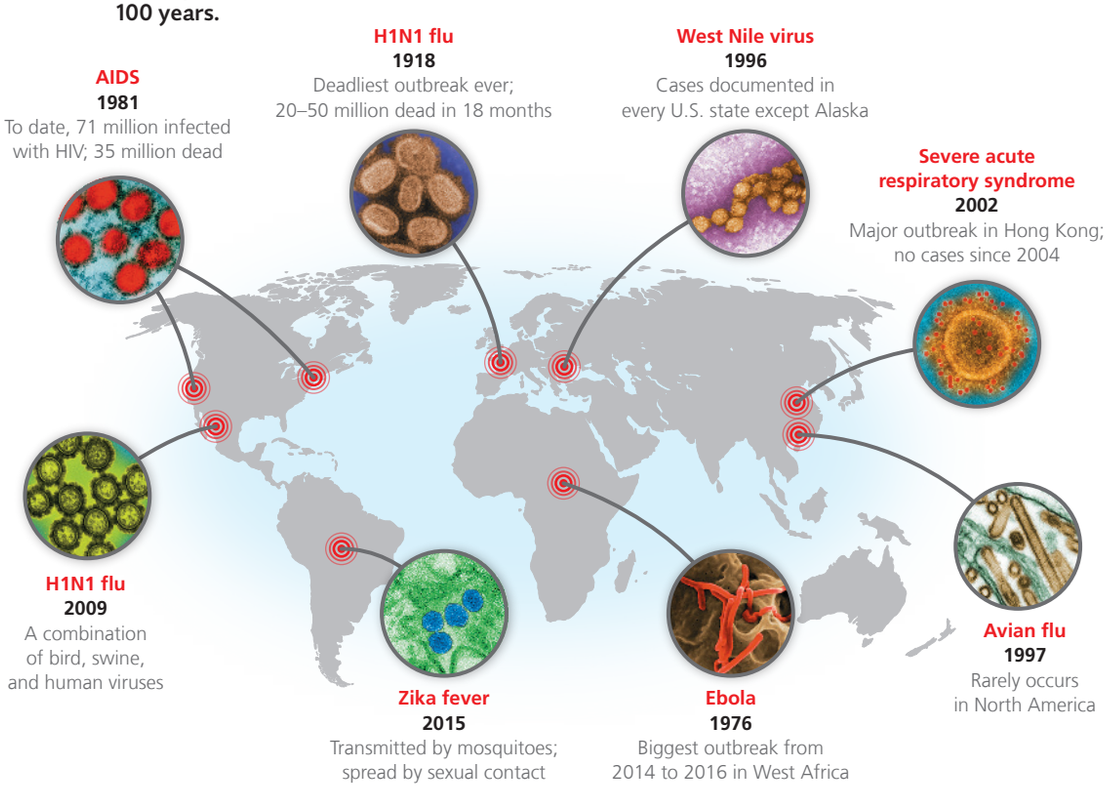
Second, viral diseases can spread from one host species to another. Scientists estimate that about three-quarters of new human diseases originated in other animals. When humans hunt, live, or raise livestock in new habitats, the risk increases. HIV (which causes AIDS) may have started as a slightly different virus in chimpanzees. Human hunters were probably infected when they butchered infected animals. As the virus mutated in the human hosts, strains that out-competed other varieties for human host cells became increasingly common.

Third, viral diseases from a small, isolated population can spread, leading to an epidemic. AIDS went unnamed and virtually ignored for decades. Several factors, including international travel, intravenous drug use, sexual activity, and delayed effective action allowed it to become a global scourge.

Nobel Prize winner Joshua Lederberg warned: "We live in evolutionary competition with microbes. There is no guarantee that we will be the survivors." If we are to be victorious in the fight against emerging viruses, we must understand molecular biology and evolutionary processes.

VISUALIZING THE DATA

▼ Figure 10.33
A sample of major emerging virus outbreaks of the past 100 years.

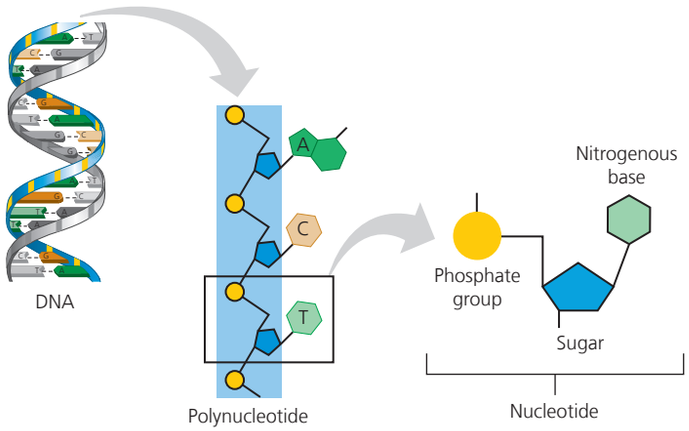


Chapter Review

SUMMARY OF KEY CONCEPTS

DNA: Structure and Replication

DNA and RNA Structure



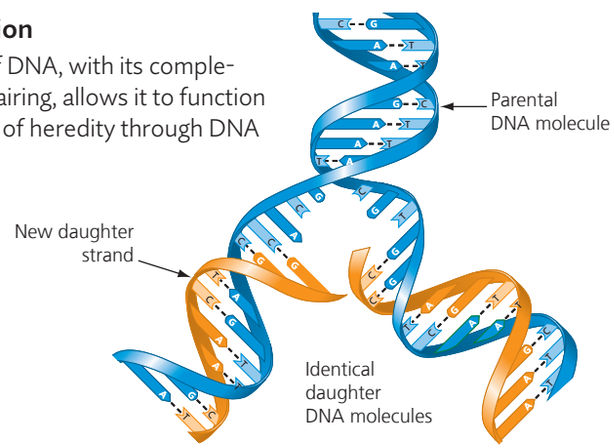
	DNA	RNA
Nitrogenous base	C G A T	C G A U
Sugar	Deoxy-ribose	Ribose
Number of strands	2	1

Watson and Crick's Discovery of the Double Helix

Watson and Crick worked out the three-dimensional structure of DNA: two polynucleotide strands wrapped around each other in a double helix. Hydrogen bonds between bases hold the strands together. Each base pairs with a complementary partner: A with T, and G with C.

DNA Replication

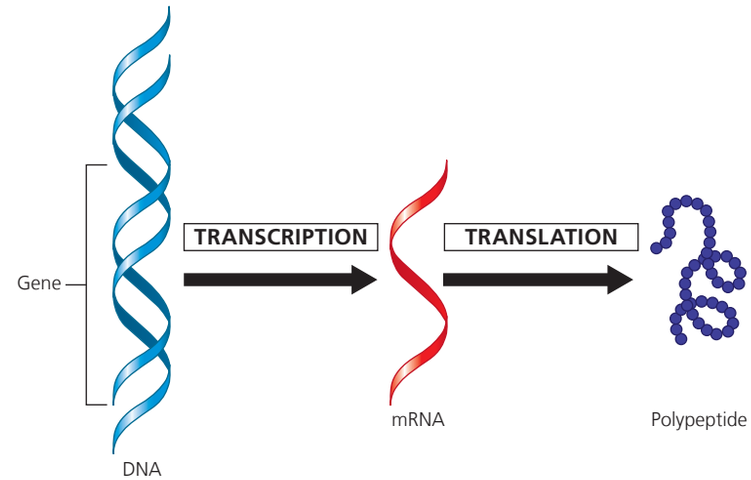
The structure of DNA, with its complementary base pairing, allows it to function as the molecule of heredity through DNA replication.



From DNA to RNA to Protein

How an Organism's Genotype Determines Its Phenotype

The information constituting an organism's genotype is carried in the sequence of its DNA bases. The genotype controls phenotype through the expression of proteins.



From Nucleotides to Amino Acids: An Overview

The DNA of a gene is transcribed into RNA using the usual base-pairing rules, except that an A in DNA pairs with U in RNA. In the translation of a genetic message, each triplet of nucleotide bases in the RNA, called a codon, specifies one amino acid in the polypeptide.

The Genetic Code

In addition to codons that specify amino acids, the genetic code has one codon that is a start signal and three that are stop signals for translation.

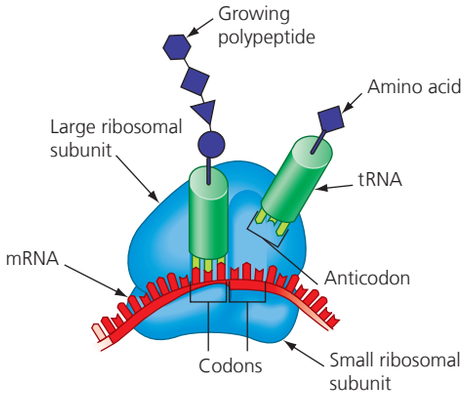
Transcription: From DNA to RNA

In transcription, RNA polymerase binds to the promoter of a gene, opens the DNA double helix there, and catalyzes the synthesis of an RNA molecule using one DNA strand as a template. As the single-stranded RNA transcript peels away from the gene, the DNA strands rejoin.

The Processing of Eukaryotic RNA

The RNA transcribed from a eukaryotic gene is processed before leaving the nucleus to serve as messenger RNA (mRNA). Introns are spliced out, and a cap and tail are added.

Translation: The Players



Translation: The Process

In initiation, a ribosome assembles with the mRNA and the initiator tRNA bearing the first amino acid. Beginning at the start codon, the codons of the mRNA are recognized one by one by tRNAs bearing succeeding amino acids. The ribosome bonds the amino acids together. With each addition, the mRNA moves by one codon through the ribosome. When a stop codon is reached, the completed polypeptide is released.

Review: DNA → RNA → Protein

The sequence of codons in DNA, through the sequence of codons in mRNA, spells out the primary structure of a polypeptide.

Mutations

Mutations are changes in the DNA base sequence, caused by errors in DNA replication, recombination, or mutagens. Substituting, deleting, or inserting nucleotides in a gene has varying effects on the polypeptide and organism.

Type of Mutation	Effect
Substitution of one DNA base for another	**Silent** mutations result in no change to amino acids.
	Missense mutations swap one amino acid for another.
	Nonsense mutations change an amino acid codon to a stop codon.
Insertions or **deletions** of DNA nucleotides	**Frameshift** mutations can alter the triplet grouping of codons and greatly change the amino acid sequence.

Viruses and Other Noncellular Infectious Agents

Viruses are infectious particles consisting of genes packaged in protein.

Bacteriophages

When phage DNA enters a lytic cycle inside a bacterium, it is replicated, transcribed, and translated. The new viral DNA and protein molecules then assemble into new phages, which burst from the cell. In the lysogenic cycle, phage DNA inserts into the cell's chromosome and is passed on to generations of daughter cells. Much later, it may initiate phage production.

Plant Viruses

Viruses that infect plants can be a serious agricultural problem. Most have RNA genomes. Viruses enter plants through breaks in the plant's outer layers.

Animal Viruses

Many animal viruses, such as flu viruses, have RNA genomes; others, such as hepatitis viruses, have DNA. Some animal viruses "steal" a bit of cell membrane as a protective envelope. Some, such as the herpesvirus, can remain latent inside cells for long periods.

HIV, the AIDS Virus

HIV is a retrovirus. Inside a cell it uses its RNA as a template for making DNA, which is then inserted into a chromosome.

Prions

Prions are infectious proteins that cause a number of degenerative brain diseases in humans and other animals.

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SELF-QUIZ

1. A molecule of DNA contains two polymer strands called _____, made by bonding together many monomers called _____.
2. Name the three parts of every nucleotide.
3. List these terms in order of size from largest to smallest: chromosome, codon, gene, nucleotide.
4. A scientist inserts a radioactively labeled DNA molecule into a bacterium. The bacterium replicates this DNA molecule and distributes one daughter molecule (double helix) to each of two daughter cells. How much radioactivity will the DNA in each of the two daughter cells contain? Why?
5. Which mRNA nucleotide triplet encodes the amino acid tryptophan (see Figure 10.10)? During translation, an amino-acid-conjugated tRNA binds to an mRNA nucleotide triplet via its anticodon. What is the nucleotide sequence of the tryptophan's tRNA anticodon? What is the corresponding original codon on the DNA molecule that the mRNA is transcribed from?
6. Describe the process by which the information in a gene is transcribed and translated into a protein. Correctly use these terms in your description: tRNA, amino acid, start codon, transcription, mRNA, gene, codon, RNA polymerase, ribosome, translation, anticodon, peptide bond, stop codon.
7. Match the following molecules with the cellular process or processes in which they are primarily involved.

a. ribosomes	1. DNA replication
b. tRNA	2. transcription
c. DNA polymerases	3. translation
d. RNA polymerase	
e. mRNA	

8. A geneticist finds that a particular mutation has no effect on the polypeptide encoded by the gene. This mutation probably involves
   a. deletion of one nucleotide.
   b. alteration of the start codon.
   c. insertion of one nucleotide.
   d. substitution of one nucleotide.
9. Scientists have discovered how to put together a bacteriophage with the protein coat of phage A and the DNA of phage B. If this composite phage were allowed to infect a bacterium, the phages produced in the cell would have
   a. the protein of A and the DNA of B.
   b. the protein of B and the DNA of A.
   c. the protein and DNA of A.
   d. the protein and DNA of B.
10. How do some viruses reproduce without ever having DNA?
11. HIV requires an enzyme called _____ to convert its RNA genome to a DNA version. Why is this enzyme a particularly good target for anti-AIDS drugs? (*Hint*: Would you expect such a drug to harm the human host?)

For answers to the Self Quiz, see Appendix D.

IDENTIFYING MAJOR THEMES

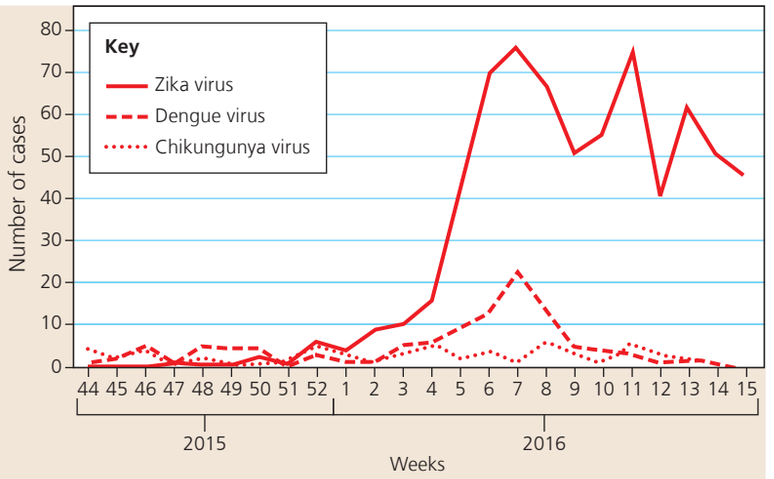
For each statement, identify which major theme is evident (the relationship of structure to function, information flow, pathways that transform energy and matter, interactions within biological systems, or evolution) and explain how the statement relates to the theme. If necessary, review the themes (see Chapter 1) and review the examples highlighted in blue in this chapter.

12. Nearly every organism on Earth shares the identical genetic code, indicating that this scheme arose very early in the history of life.
13. The shape of a tRNA molecule, with its anticodon on one end and amino acid attachment site at the other end, hints at how the molecule acts during translation.
14. Genes carry the instructions needed to build an RNA and then a protein.

For answers to Identifying Major Themes, see Appendix D.

THE PROCESS OF SCIENCE

15. *Acetabularia* are enormously large (2—4 cm long), single-celled green algae that look somewhat like mushrooms. They consist of a cap, a stalk, and a root-like structure called "rhizoid" that contains the large cell nucleus. In 1943, Joachim Hämmerling exchanged the nuclei of an *Acetabularia mediterranea* (which forms a flat cap) with that of an *Acetabularia crenulata* (which forms a castellated cap). What result would you expect from this experiment? Which basic concept does it confirm?
16. In 1958, Matthew Meselson and Franklin Stahl grew bacteria in a medium enriched with the rare, heavy nitrogen isotope ^{15}N. The DNA extracted from these bacteria can be separated from the DNA extracted from the bacteria grown in normal, mostly ^{14}N-containing medium by density gradient ultracentrifugation—the two DNA fractions separate into distinct layers within the gradient. What did Meselson and Stahl observe when they transferred bacteria that were initially cultured in ^{15}N medium to ^{14}N medium just long enough for one more round of cell division? What does this experiment demonstrate?
17. **Interpreting Data** The graph shows the number of cases per week of Zika, Dengue, and Chikungunya virus in Puerto Rico during the period from November 1, 2015 to April 14, 2016. The same mosquitoes spread all three viruses. Did all three diseases show a similar pattern during this time period? Explain.



Source: Centers for Disease Control and Prevention

BIOLOGY AND SOCIETY

18. Scientists at the National Institutes of Health (NIH) have worked out thousands of sequences of genes and the proteins they encode, and similar analyses are being carried out at universities and private companies. Knowledge of the nucleotide sequences of genes might be used to treat genetic defects or produce lifesaving medicines. The NIH and some U.S. biotechnology companies have applied for patents on their discoveries. In Britain, the courts have ruled that a naturally occurring gene cannot be patented. Do you think individuals and companies should be able to patent genes and gene products? Before answering, consider the following: What are the purposes of a patent? How might the discoverer of a gene benefit from a patent? How might the public benefit? What negative effects might result from patenting genes?
19. Your college roommate seeks to improve her appearance by visiting a tanning salon. How would you explain the dangers of this to her?
20. Flu vaccines have been shown to be safe, are very reliable at reducing the risk of hospitalization or death from influenza, and are inexpensive. Should children be required to obtain a flu vaccine before going to school? What about hospital workers before reporting to work? Defend your answers to these questions.