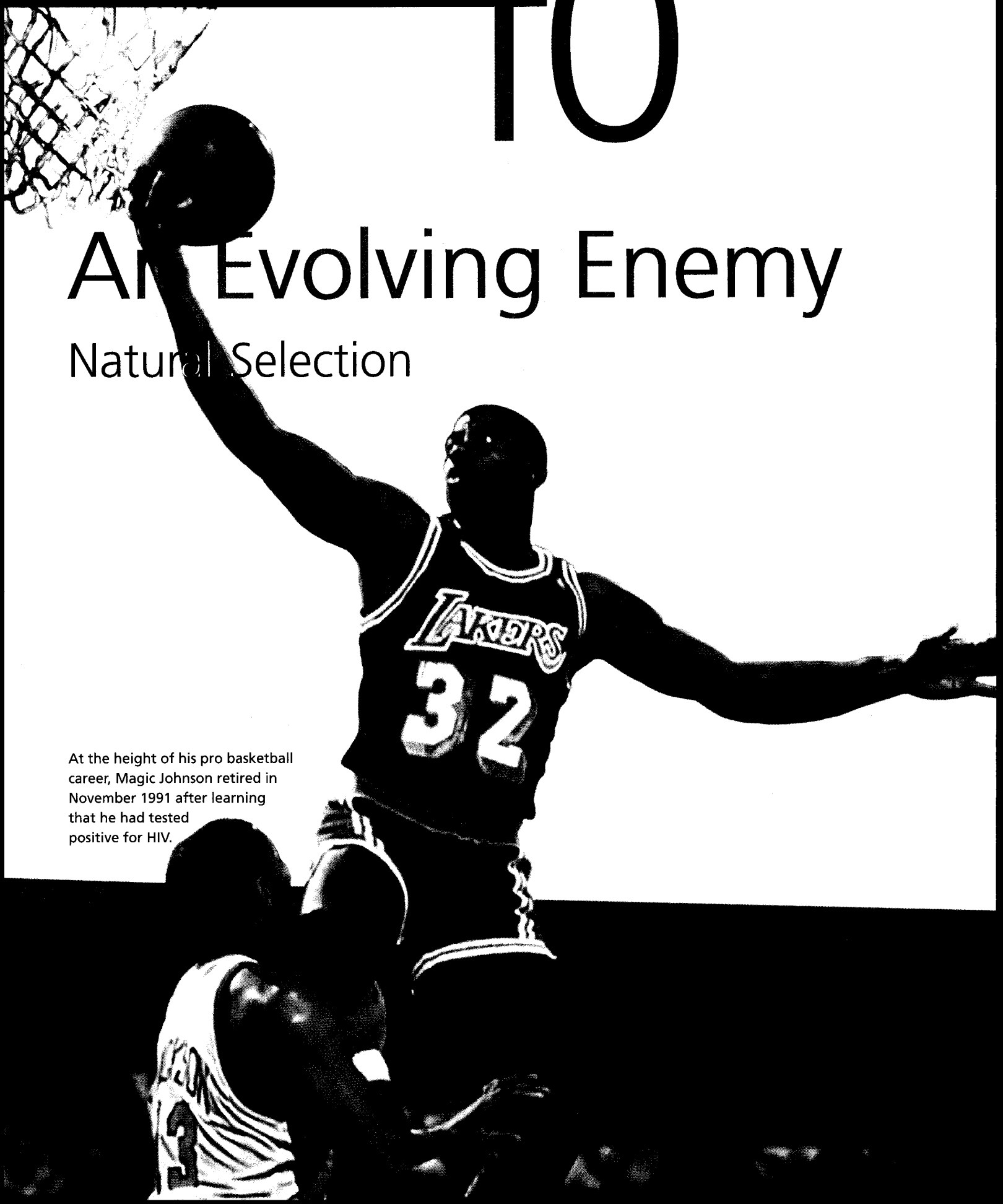
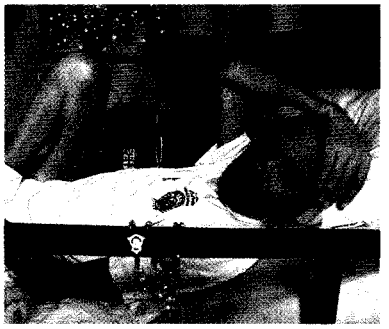
CHAPTER 10

An Evolving Enemy

Natural Selection



At the height of his pro basketball career, Magic Johnson retired in November 1991 after learning that he had tested positive for HIV.



At the time of his retirement, fans expected that Magic would meet the fate of HIV patients such as this man—death from AIDS.

However, Magic Johnson and many other HIV-infected individuals have survived many years without suffering from this debilitating and fatal disease. Why?

In late 1991, basketball fans around the world were hit with devastating news. Earvin "Magic" Johnson, one of the greatest basketball guards ever to play the game, was retiring at age 32, two years after being named the NBA's most valuable player for the third time in 10 seasons. In his relatively short career, Magic broke the record for the most career assists and led the Los Angeles Lakers to five NBA championships. Why was this talented, popular, and successful athlete with a new wife and a baby on the way leaving the game just as he was reaching his physical prime? He had learned only days before that he was infected with HIV, the virus that causes AIDS.

In 1991, a diagnosis of HIV infection was considered to be a death sentence. At that time, the typical length of time between the diagnosis of HIV and death from AIDS was 8 to 10 years. Magic Johnson's fans and other NBA players braced themselves to watch the terrible decline that always occurred with the onset of AIDS.

Now fast forward to November 2005, 14 years after Magic's diagnosis and retirement. The fit and muscular 45-year-old NBA Hall of Fame member is now part owner of the Los Angeles Lakers and head of a company that owns dozens of movie theaters, coffee shops, and a fast-food franchise. In the time since being diagnosed, Magic has won an Olympic gold medal, made two comebacks as an NBA player, coached his former team, celebrated three more

Modern anti-AIDS therapy, consisting of multiple drugs, has disabled a powerful tool of HIV—evolution.

Lakers NBA championships, hosted his own late-night television show, and was inducted into the NBA Hall of Fame. He is about as successful as any former sports star, and just about as healthy. Now many of his friends joke that he will be hit by a bus before he dies of AIDS.

Magic Johnson's survival despite his HIV infection is partly a testament to the huge effort doctors and scientists have invested to control AIDS. The time between the identification of this new disease and the first drug treatments was less than a decade. Although anti-HIV drugs have been available since 1987, five years before Magic's announcement, most people did not remain healthy for long after they started using these drugs. The failure of these early treatment strategies was the result of a single factor—evolution—and the success of current treatments depends on the understanding and management of this powerful process.

In this chapter, we will explore how the process of evolution has shaped HIV and governed our methods for controlling this killer virus. To do so, we must first understand a little of the biology of HIV and AIDS.

10.1 AIDS and HIV

Acquired immune deficiency syndrome, or **AIDS**, was first described in 1981 after dozens of young gay men in New York City and San Francisco were diagnosed with illnesses rarely seen in healthy young people. The types of illnesses seen in affected individuals were more typical of people who had been born with genetic mutations leading to serious defects in the functioning of their immune system. In contrast, this new outbreak of susceptibility to these illnesses appeared to be *acquired* (that is, caused by exposure to some factor) because it was seen suddenly in large numbers of previously normal-functioning people.

AIDS Is a Disease of the Immune System

The increased susceptibility to illness in these young men resulted from a decline in their immune system function. The role of the immune system is to maintain the integrity of the body. The cells of the immune system constantly patrol the tissues and organs of the body for anything that is not clearly produced by the body—that is, anything that is "nonself." Upon encountering a nonself entity, the immune system acts to eliminate it; this is known as an **immune response**.

The virus that causes AIDS primarily kills or disables a particular class of immune system cells called **T4 cells**. T4 cells are also known as helper T cells because they serve as the directors of the immune system's response to specific nonself entities. Thus the loss of T4 cells causes immune deficiency—that is, affected individuals experience diseases that are normally controlled by healthy immune systems. These include infections by organisms commonly found on our bodies in low levels, such as *Pneumocystis carinii*, a fungus that is found in nearly everyone's lungs by age 30. In healthy people, *P. carinii* is held in check by the immune system; but in AIDS patients, this organism often causes pneumonia and extensive lung damage. Diseases like *P. carinii* pneumonia are called opportunistic infections because they occur only when the opportunity arises due to a weakened immune system.

Because individuals with weakened immune systems may have more than one opportunistic infection, each with its own signs and symptoms, there is no single condition that is always associated with AIDS. This is why the disease is called a syndrome—a group of signs and symptoms indicating that an individual has AIDS. Primary among those signs is the depletion of T4 cells.

HIV Causes AIDS

Within months of the initial reports of this new disease, it became clear that AIDS could be transmitted through both sexual intercourse and contact with the blood of affected individuals. By 1983, two independent teams of scientists, led by Luc Montagnier in France and Robert Gallo in the United States, had identified the factor causing the transmission and symptoms of AIDS—the factor was later named the **human immunodeficiency virus**, or **HIV**. The evidence linking HIV to AIDS is outlined in Essay 10.1. Worldwide, most HIV transmission occurs via sexual intercourse without a condom. In the United States, both unprotected sex and the sharing of needles by injection-drug users are primary modes of HIV transmission.

HIV is a virus composed of RNA and proteins, surrounded by a protein coat and membrane envelope. As with all viruses, HIV can reproduce only by using the cellular "machinery" of its **host**, the organism it is infecting, to make copies. The reproductive cycle of HIV is illustrated in Figure 10.1 on page 260.

Essay 10.1 The Evidence Linking HIV to AIDS

Although a small number of scientists have argued that the link between HIV and AIDS is weak, the vast majority of them agree that the statement "HIV causes AIDS" is a fact. Scientists use Koch's postulates, developed by physician Robert Koch in the nineteenth century, as the litmus test for determining the cause of any epidemic disease. The postulates are summarized as follows:

1. *Association:* The suspected infectious agent is found in all individuals suffering from a particular disease.
2. *Isolation:* The supposed infectious agent can be grown outside the host in a pure culture (without any other microorganisms).
3. *Transmission:* Transfer of the suspected pathogen to an uninfected host produces the disease in the new host.
4. *Isolation from new victim:* The same pathogen must be found in the newly infected host.

Does HIV fulfill Koch's postulates as the cause of AIDS? Let us examine the evidence for each assumption.

- *Association:* Studies from around the world show that virtually all AIDS patients carry antibodies that indicate HIV infection.
- *Isolation:* HIV has been isolated from virtually all AIDS patients, as well as in almost all individuals with HIV antibodies. In addition, researchers have documented the presence of HIV genes in both groups of patients.
- *Transmission:* HIV does not readily cause AIDS in other animals, so transmission is difficult to demonstrate. However, this postulate has been fulfilled by a series of tragic incidents. In one case, three laboratory workers with no other risk factors developed AIDS after accidental exposure to concentrated HIV at work. In another case, transmission of HIV from a Florida dentist to six oral surgery patients was documented by genetic analysis of the virus isolated from both the dentist and the patients. The dentist and four of the patients developed AIDS and died. Finally, the Centers for Disease Control (CDC) has documented reports of 57 occupationally-acquired HIV infections among health-care workers, of whom 26 have developed AIDS in the absence of other risk factors.
- *Isolation from new victim:* In the case of the three laboratory workers just described, HIV was isolated from each infected individual, and its RNA sequence was examined. The HIV proved to be the virus that the workers had handled. In the case of the Florida dentist, HIV isolated from his infected patients had very similar RNA sequences, indicating that all of them were infected with the same virus strain.

In short, the link between HIV and AIDS has been firmly established using the standard set of Koch's postulates, and this relationship has been accepted by medical scientists.

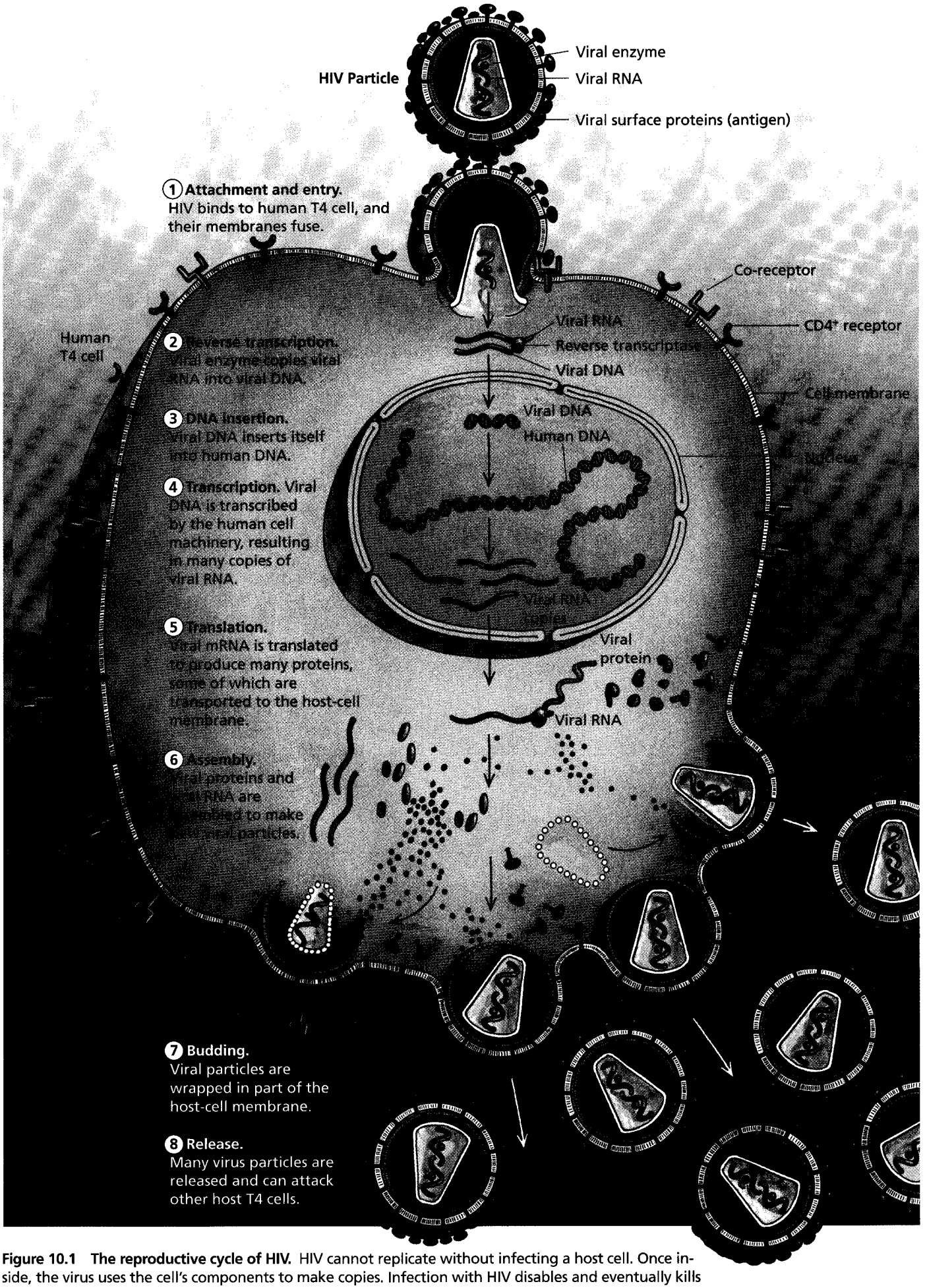


Figure 10.1 The reproductive cycle of HIV. HIV cannot replicate without infecting a host cell. Once inside, the virus uses the cell's components to make copies. Infection with HIV disables and eventually kills the host cell.

HIV initially binds to proteins on the surface of a cell (the $CD4^+$ receptor and a co-receptor) and then releases its own RNA and proteins into the cell (step ①). Once inside the cell, the viral RNA is reverse transcribed into viral DNA by the action of one of the viral proteins, the enzyme called reverse transcriptase (step ②). Transcription is the process in all cells that rewrites the information in DNA into the language of RNA; reverse transcription is simply the converse of that process, in which a strand of RNA is rewritten in the language of DNA.

With the help of another viral enzyme, the viral DNA produced by reverse transcription inserts itself into the cell's genome (step ③), where it commandeers the proteins and cell organelles required for copying genetic material and producing proteins. The cell now makes new copies of the viral RNA (step ④), translates the genes on the viral DNA into the proteins that make up the coat, enzymes, and membrane surface proteins (step ⑤), and assembles new viruses (step ⑥). Then the newly made copies of the virus are released from the cell by budding off the cell membrane and go on to infect other cells that possess the $CD4^+$ receptor and an appropriate co-receptor (steps ⑦ and ⑧). Infection with HIV usually either disables or kills the host cell. Most of the cells infected with HIV are T4 cells, but other cells that carry the $CD4^+$ receptor are susceptible to HIV as well.

The Course of HIV Infection

Early symptoms of HIV infection resemble the flu in about 70% of infected individuals; there are no noticeable symptoms in the remaining 30%. This generalized feeling of fatigue and illness is caused by the initial nonspecific immune response to any viral invader—the same factors that are responsible for the run-down feeling you experience before the onset of a head cold. Because HIV is killing off immune system cells that protect people from a variety of infectious organisms, the run-down feeling may last for a number of weeks. Most people infected with HIV begin to control the virus within 6 to 12 weeks and therefore recover from these flu-like symptoms. This seeming recovery from the infection occurs once the immune system develops a specific response to HIV.

A specific response to a virus or other disease-causing organism develops because the immune system can produce cells and proteins that effectively destroy invaders once the system is exposed to these invaders. Among the billions of cells that make up the immune system, a few individual cells belonging to a particular class (called **B cells**) are capable of recognizing some of the unique proteins that are present in and on HIV particles. A protein or other molecule that is recognized as nonself by immune system cells is called an **antigen**. Proteins called antigen receptors, found on the surface of B cells, bind to an antigen and begin a specific immune system response. In the presence of fragments of HIV, the B cells that have an HIV-antigen receptor are stimulated to divide; these daughter cells will produce HIV **antibodies**, proteins that bind to and help eliminate the virus (Figure 10.2). Within 3 months of initial contact with the virus, 95% of infected individuals have high levels of HIV antibodies circulating in their blood. As a result, the level of HIV in the infected person's bloodstream is greatly reduced.

Once a specific immune response to HIV is fully developed and the number of viruses in the blood has dropped, the levels of T4 cells in an infected individual rebound. At this point, the person is asymptomatic and has a mostly normal immune response. The asymptomatic phase of HIV infection may last for as long as 10 years.

In nearly all HIV-infected individuals who are not receiving drug treatment, the immune system eventually loses control over the virus. At some point, virus levels begin to increase and T4 cell numbers decline, signaling the

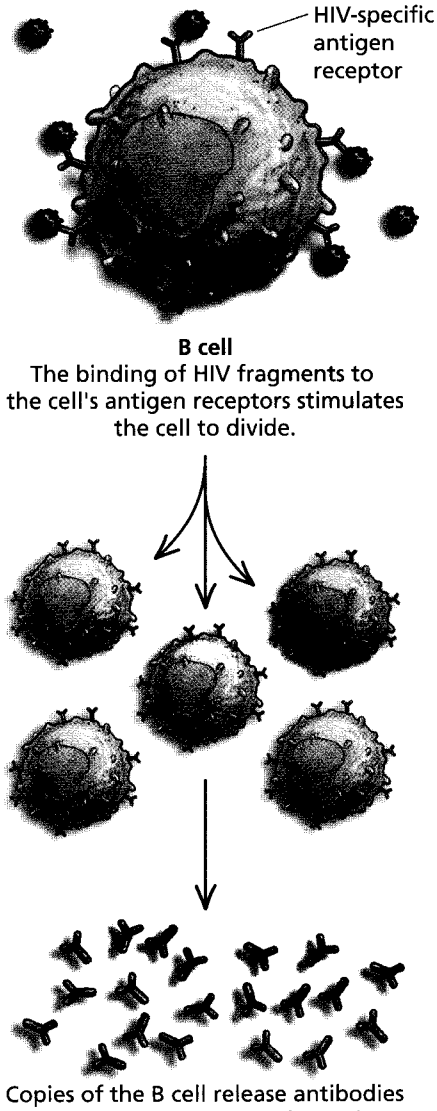


Figure 10.2 The immune response to HIV. The presence of HIV in the body stimulates the multiplication of immune system cells, some of which produce anti-HIV antibodies. These antibodies help reduce levels of HIV in the bloodstream.

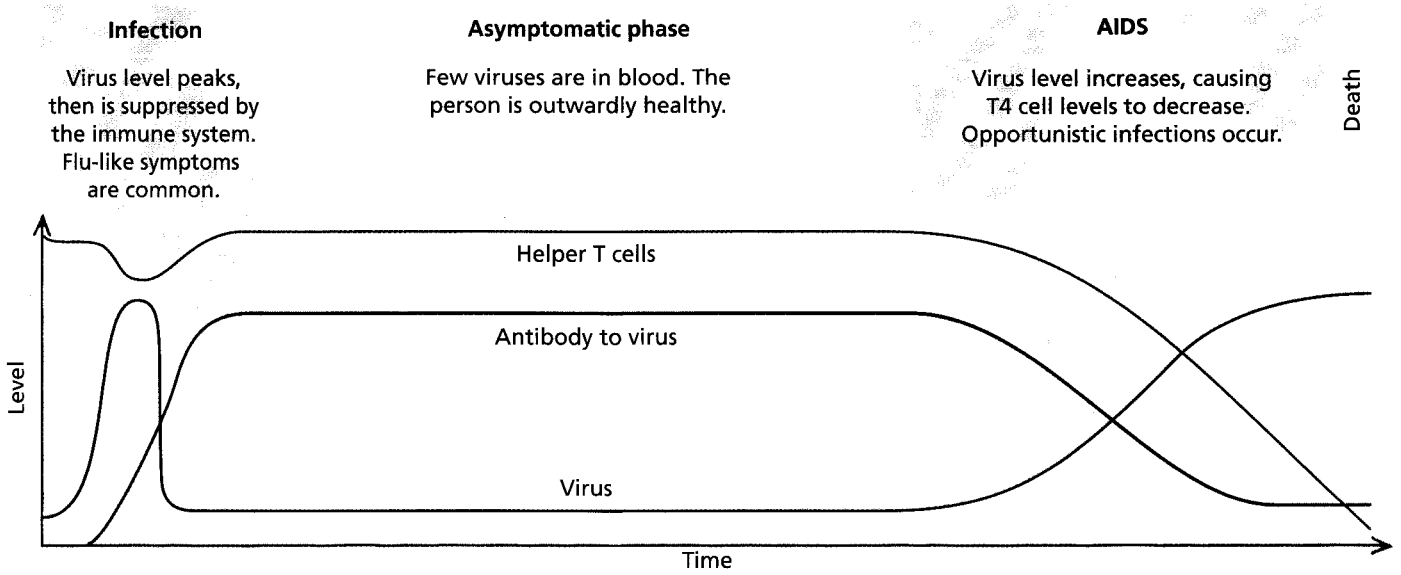


Figure 10.3 The typical course of HIV infection. This graph illustrates the change in HIV levels in the blood, the level of antibodies present, and the level of T4 cells over time. After initial infection, most patients produce enough antibodies to control virus levels for months or years. Eventually, however, nearly all HIV-infected people develop AIDS when the body fails to maintain antibodies to the virus.

onset of AIDS (Figure 10.3). Why does HIV eventually win its battle with the immune system? Primarily due to the evolution of HIV within its host.

Evolution is most simply defined as a change in the genetic characteristics of a population over time. Often these changes occur due to the differential survival of individuals in a population made up of individuals who vary in their traits—that is, by the process of **natural selection**. The natural selection of HIV particles within an infected person's body causes the HIV population within the body to evolve and eventually escape immune system control. Understanding why most people infected with HIV eventually fail to control this virus requires an understanding of this very important idea in biology—any population, whether plant, animal, bacteria, or virus, has the potential to adapt to its environment if it is given enough time and possesses a mechanism to generate variation. Charles Darwin first elaborated the theory of natural selection in the middle of the nineteenth century. That theory has since become one of the most powerful ideas in science.

10.2 The Theory of Natural Selection

In *The Origin of Species*, Charles Darwin put forth two major ideas: the theory of common descent and the theory of natural selection. We discussed the theory of common descent in detail in Chapter 9 and learned that all species living today appear to have descended from a single ancestor that arose in the distant past. Darwin's presentation of this theory was thorough and convincing. Within 20 years of his book's publication, Darwin's principle that all living organisms are related to each other through common descent had been accepted by most scientists. However, it was another 60 years before the scientific community accepted Darwin's ideas about *how* the great variety of living organisms had come about—the process he called natural selection. Today, natural selection is considered one of the most important causes of evolution; although others, such as the processes of genetic drift and sexual selection as described in Chapter 11, also cause populations to change over time.

(a) Variation in coat color

(b) Variation in blooming time

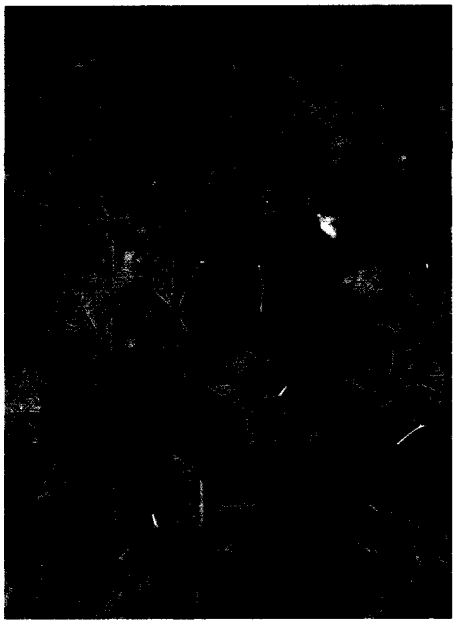


Figure 10.4 Observation 1: Individuals within populations vary. (a) Gray wolves vary in coat color, even within a single litter of animals. (b) Flowers may vary in blooming time, with some individual plants blooming much earlier than others of the same species.

Four Observations and an Inference

The theory of natural selection is elegantly simple. It is an inference based on four general observations:

1. Individuals within Populations Vary. Observations of groups of humans support this statement—people do come in an enormous variety of shapes, sizes, colors, and facial features. It may be less obvious that there is variation in nonhuman populations as well. For example, within a litter of gray wolves born to a single female, some individuals may be black, tawny, or reddish in color (Figure 10.4a); or within a single population of flowers, some individuals will bloom earlier than the majority, and some will bloom later (Figure 10.4b). We can add all kinds of less obvious differences to this visible variation; for example, the amount of caffeine produced in the seeds of a coffee plant varies among individuals in a wild population. Each different type of individual in a population is termed a **variant**.

2. Some of the Variation Among Individuals Can Be Passed on to Their Offspring. Although Darwin did not understand how it occurred, he observed many examples of the general resemblance between parents and offspring. Farmers regularly take advantage of the inheritance of certain variations. For example, some chickens produce more eggs than others do, and their offspring often produce more eggs than do the offspring of less productive chickens. This variation enables a farmer to select only the offspring of the best-laying hens as the new flock of egg producers. Darwin noticed that pigeon breeders took advantage of the inheritance of variation when they produced fancy birds—pigeons with fan-shaped tails were more likely to produce offspring with fan-shaped tails than were pigeons with straight tails (Figure 10.5). Darwin hypothesized that offspring tend to have the same characteristics as their parents in natural populations as well.

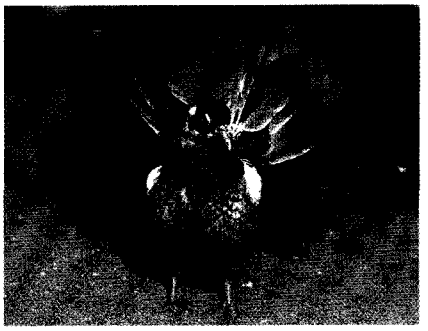


Figure 10.5 Observation 2: Some of the variation among individuals can be passed on to their offspring. Darwin noted that breeders could create flocks of pigeons with fantastic traits by using as parents of the next generation only those individuals that displayed these traits.

For several decades after *The Origin of Species* was published, the observation that some variations were inherited was the most controversial part of the theory of natural selection. Since scientists could not adequately explain the origin and inheritance of variation, many were unwilling to accept that natural selection could be a mechanism for evolutionary change. When Gregor Mendel's work on inheritance in pea plants (discussed in Essay 6.1) was rediscovered in the 1900s, the mechanism for this observation became clear—natural selection operates on genetic variation that can be passed from one generation to the next.

3. Populations of Organisms Produce More Offspring than Will Survive. This observation is clear to most of us—the trees in the local park make literally millions of seeds every summer, but only a few of the much smaller number that sprout live for more than a few years. In *The Origin of Species*, Darwin gave a graphic example of the difference between offspring production and survival. In his example, he used elephants, animals that live long lives and are very slow breeders. A female elephant does not begin breeding until age 30, and she produces about one calf every 10 years until around age 90. Darwin calculated that even at this very low rate of reproduction, if all the descendants of a single pair of African elephants survived and lived full, fertile lives, after about 500 years their family would have more than 15 million members—many more than can be supported by all the available food resources on the African continent (Figure 10.6)! Clearly, only a subset of the elephants born in every generation survives long enough to reproduce. The same is true for nearly every species; the capacity for reproduction far outstrips the resources of the environment, and so many individuals do not survive to maturity.

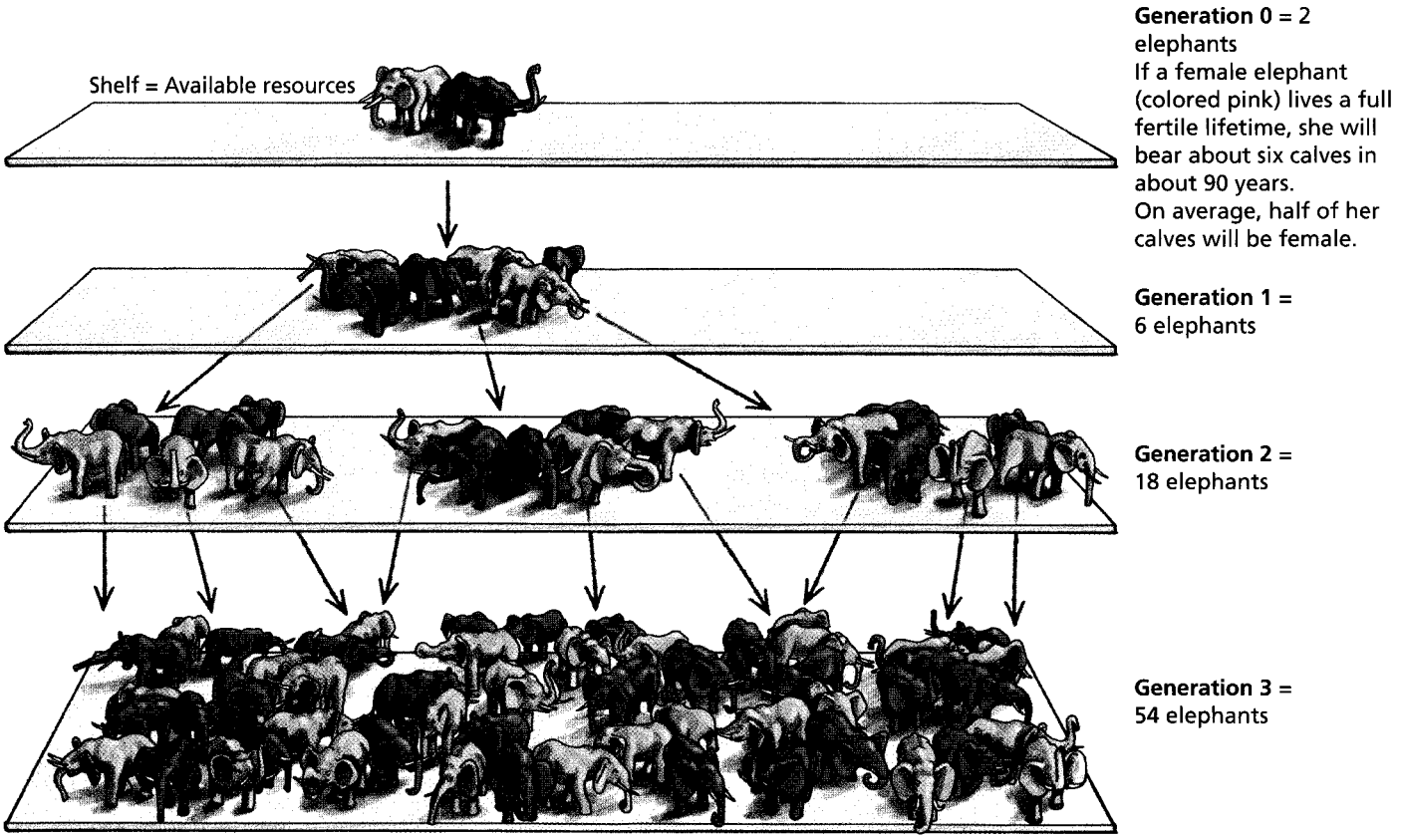


Figure 10.6 Observation 3: Populations of organisms produce more offspring than will survive. Even slow-breeding animals like elephants are capable of producing huge populations relatively quickly. Limited resources prevent this breeding from happening.

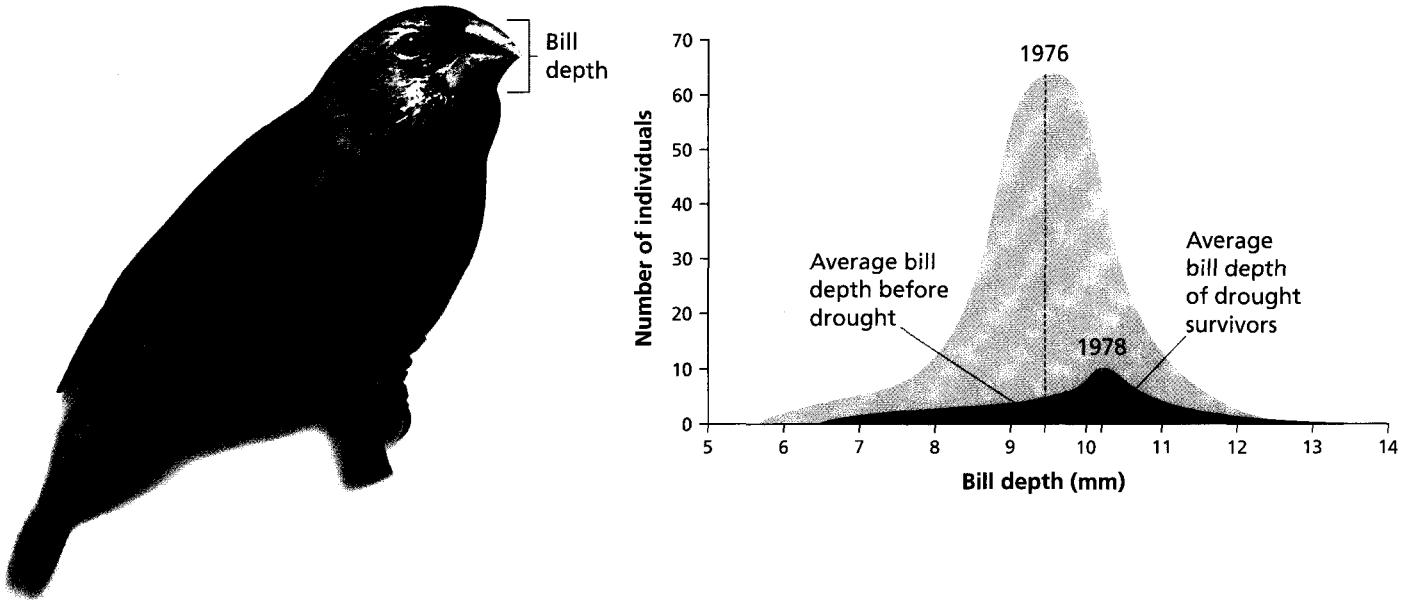


Figure 10.7 Observation 4: Survival and reproduction are not random. Darwin's finches on the Galápagos Islands did not have equal chances of surviving a severe drought. The pale purple curve summarizes bill depth in these birds before the drought. The same population after the drought of 1976 and 1977 (dark purple curve) had an average bill depth of approximately 0.5 mm greater. This illustrates that during the drought years of 1976 and 1977, finches with larger-than-average bills that could crack larger seeds—the only food available during the drought—had higher fitness than did small-billed birds.

4. Survival and Reproduction Are Not Random. In other words, the subset of individuals that survive long enough to reproduce is not an arbitrary group. Some variants in a population have a higher likelihood of survival and reproduction than other variants do. The relative survival and reproduction of one variant compared to others in the same population is referred to as its **fitness**. Traits that increase an individual's fitness in a particular environment are called **adaptations**. Individuals with adaptations to a particular environment are more likely to survive and reproduce than are individuals lacking such adaptations.

Darwin referred to the results of differential survival and reproduction as natural selection. Although Darwin used the word *selection*, which implies some active choice, you should note that natural selection is a passive process. Adaptations are "selected for" in the sense that individuals possessing them survive and contribute offspring to the next generation. For example, among the birds called Darwin's finches, scientists have observed that when rainfall is scarce, a large bill is an adaptation. This is because birds with larger bills are able to crack open large, tough seeds—the only food available during severe droughts. As shown in Figure 10.7, the 300 survivors of a 1977 drought had an average bill depth that was 6% greater than the average bill depth of the original population of 1300 birds.

Adaptations are not only traits that increase survival. Any trait that increases the number of offspring produced relative to others in a population is also an adaptation. For example, flowers in a crowded mountain meadow may have a relatively limited number of potential insect pollinators. More pollinator visits generally results in more seeds being produced by a single flower, and so any trait that increases a flower's attractiveness to pollinators, such as a brighter color or greater nectar production, should be favored by natural selection (Figure 10.8).

You may have heard natural selection described as "survival of the fittest;" however, it is important to recognize that natural selection results in

Figure 10.8 Adaptations are not about survival only. The number of seeds a flowering plant produces depends, in part, on the number of pollinators that visit it. Variations that increase flower's attractiveness to a pollinator can increase its "reproductive success."

the survival and reproduction of those individuals that are best adapted to the current environment given the current variants in the population. The survivors are not "fittest" in an absolute sense, only relatively, meaning that the variants with the highest rates of survival and reproduction are simply better adapted to local conditions than are others in the same population.

Darwin's Inference: Natural Selection Causes Evolution. The result of natural selection is that favorable inherited variations tend to increase in frequency in a population over time, while unfavorable variations tend to be lost. In other words, adaptations become more common in a population as those individuals who possess them contribute larger numbers of their offspring to the succeeding generation. Natural selection results in a change in the traits of individuals in a population over the course of generations—voilà, evolution.

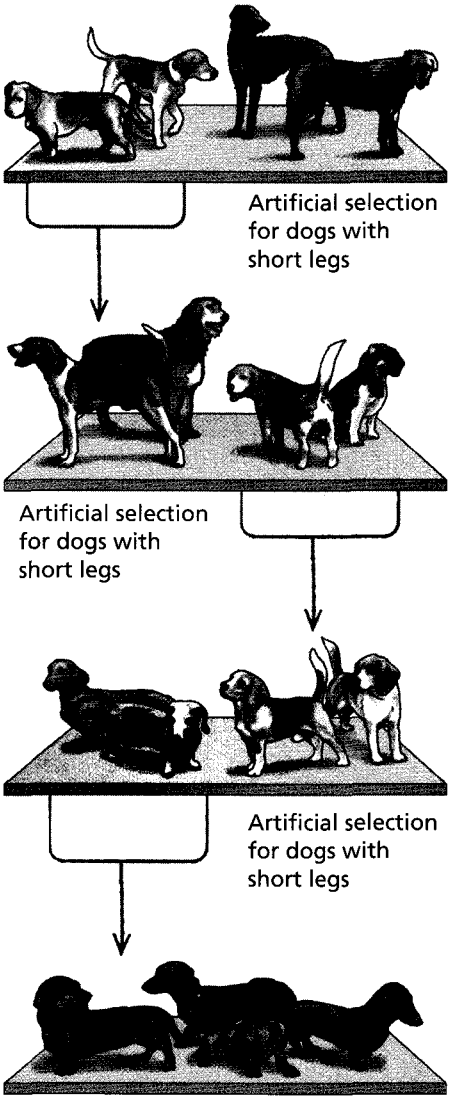


Figure 10.9 Artificial selection can cause evolution. When breeders select dogs with certain traits to produce the next generation of animals, they increase the frequency of that trait in the population. Over generations, the trait can become quite exaggerated. Dachshunds are descendants of dogs that were selected for the production of very short legs.

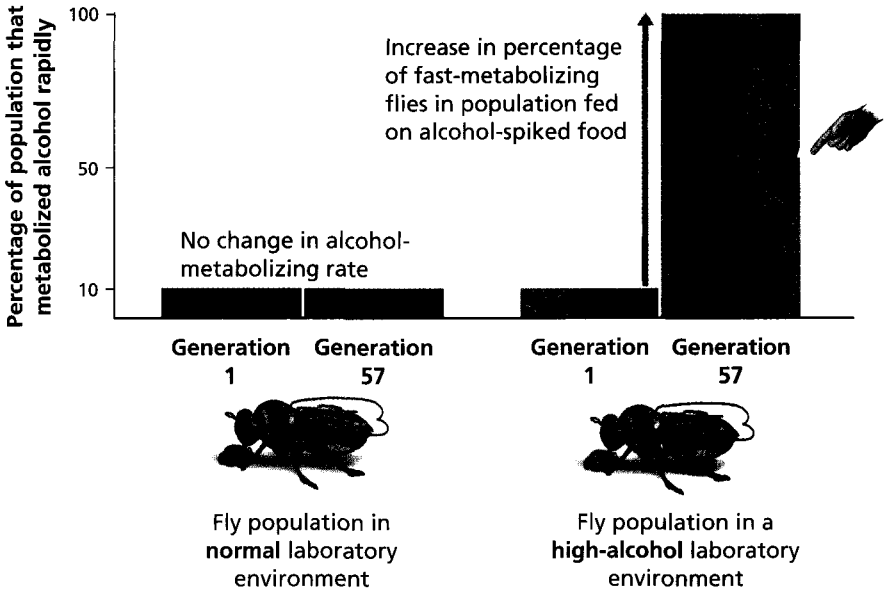
Testing Natural Selection

Darwin proposed a scientific explanation of how evolution occurs, and like all good hypotheses, it needed to be tested. As Darwin noted in *The Origin of Species*, humans have been testing the hypothesis that selection causes evolution for thousands of years. By imposing selection on domestic animals and plants, humans have changed the characteristics of populations of these organisms.

Artificial Selection. Selection imposed by human choice is called **artificial selection**. It is artificial in the sense that humans control the survival and reproduction of individual plants and animals with favorable characteristics in order to change the characteristics of the population. Dog varieties resulted from artificial selection; they evolved through selection by breeders for various traits (Figure 10.9). Most of the fruits and vegetables we are familiar with also developed as a result of artificial selection. However, due to the direct intervention of humans on the survival and reproduction of these organisms, artificial selection is not exactly equivalent to natural selection.

Natural Selection in the Lab. Scientists have also observed selection occurring among organisms that are intentionally exposed to different environments. An example of this kind of experiment is one performed on fruit flies placed in environments containing different concentrations of alcohol. High concentrations of alcohol cause cell death. Many organisms, including fruit flies and humans, produce enzymes that metabolize alcohol—that is, they break it down, extract energy from it, and modify it into less-toxic chemicals. There is variation among fruit flies in the rate at which they metabolize alcohol. In a typical laboratory environment, most flies process alcohol relatively slowly, but about 10% of the population possesses an enzyme variant that allows those flies to metabolize alcohol twice as rapidly as the more common variant.

In their experiment, scientists divided a population of fruit flies into two random groups. Initially, these two groups had the same percentage of fast and slow alcohol metabolizers. One group of flies was placed in an environment containing typical food sources; the other group was placed in an environment containing the same food spiked with alcohol. After 57 generations, the percentage of fast-metabolizing flies in the normal environment was the same as at the beginning of the experiment—10%. But after the same number of generations, 100% of the flies in the alcohol-spiked environment were the fast-metabolizing variety (Figure 10.10). Because all of the flies in this environment were now the fast-metabolizing variety, the *average* rate of alcohol



After 57 generations, all flies in the population are fast processors of alcohol. As a result, the **average** rate of alcohol metabolism in this population is twice the rate measured in the unmodified population.

Figure 10.10 An observation of natural selection. When fruit flies are placed in an alcohol-spiked environment, the percentage of flies that can rapidly metabolize alcohol increases over many generations because of natural selection. This causes the average speed of alcohol metabolism in the population to increase as well. In the normal laboratory environment, there is no selection for faster alcohol processing, so the average rate of alcohol metabolism does not change.

metabolism in the population was much higher in generation 57 than in generation 1. The population had evolved.

The evolution of the fruit flies in this experiment was a result of natural selection. In an environment where alcohol concentrations were high, individuals that were able to metabolize alcohol relatively rapidly had higher fitness. Since they lived longer and were less affected by alcohol, they left more offspring than the slow metabolizers did. Thus, each generation had a higher frequency of fast-metabolizing individuals than the previous generation did. After many generations, flies that could metabolize alcohol rapidly predominated in the population.

Natural Selection in Wild Populations. The effects of natural selection have been observed in dozens of wild populations as well. A classic example of natural selection in action is the evolution of bill size in Galápagos finches in response to drought. Figure 10.7 illustrated that a nonrandom subset of the finch population survived a 1977 drought—the survivors tended to be those with the largest bills, which could more easily handle the tough seeds produced by the plants that survived the drought. The survival of this nonrandom subset of birds resulted in a change in the next generation. The population of birds that hatched from eggs in 1978—the descendants of the drought survivors—had an average bill depth of 4% to 5% larger than that of the pre-drought population. Bill size in this population of birds evolved in response to natural selection occurring in a setting uninfluenced by humans.

The Modern Understanding of Natural Selection

One barrier to the acceptance of Darwin's theory of natural selection was a lack of understanding of the origins of variation among individuals and of the mechanism by which variations were passed to the next generation. Without this understanding, it was difficult to see how natural selection could cause a change in the frequency of particular traits in a population. It was not until the early twentieth century, when they began to understand the nature of genes, that most biologists fully accepted the theory of natural selection.

As we discussed in Chapter 6, genes are segments of genetic material (typically DNA, but RNA in some viruses) that contain information about

the structure of molecules called proteins. The actions of proteins within an organism help determine its physical traits. Different versions of the same gene are called alleles, and variation in traits among individuals in a population is often due to variation in the alleles they carry.

We can apply these genetic principles to the fruit flies exposed to a high-alcohol environment. In this population there are two variants, or alleles, of the gene that controls alcohol processing. One allele produces an enzyme we will refer to as "fast," and the other produces an enzyme we will call "slow." Flies that make the fast enzyme can metabolize alcohol rapidly. To make this enzyme, they must carry 2 copies of the fast allele. As described in detail in Chapter 6, half of the alleles carried by a parent are passed to their offspring via their eggs or sperm. In the high-alcohol environment, flies with the fast enzyme had more offspring than did flies with the slow enzyme. Since they carry 2 copies of the fast allele, each of the offspring of a fast metabolizer received a copy of this allele. Therefore, in the next generation, a higher percentage of individuals carried the fast allele. We can now describe the evolution of a population as an increase or decrease in the *frequency of an allele* for a particular gene.

Understanding the nature of genes also explains the origin of their variations. Different alleles for the same gene arise through mutation—changes in the DNA sequence. As described in Unit Two, mutations that can be passed on to offspring occur by chance when DNA is copied during the production of eggs and sperm. These mutations can occur anywhere in an organism's genome. If one occurs in noncoding DNA, it may have little effect, but a mutation that occurs in a gene can cause a change in the function of the protein that the gene codes for. If a mutation results in an allele that has a function different from that of the original allele, the resulting variation could become subject to the process of natural selection. The existence of two different alleles for alcohol metabolism in fruit flies suggests that one of these alleles is a mutated version of the other. In the normal laboratory environment, neither of these alleles appears to have a strong effect on fitness. Since the slow metabolizers are more numerous than the fast metabolizers, it appears that there might be a slight disadvantage to carrying the fast enzyme. However, in a different environment, the mutation resulting in the fast allele gives an advantage, and its presence in the population allows for the population's evolution (Figure 10.11).

Scientists now understand that the random process of gene mutation generates the raw material—variations—for evolution, and that natural selection acts as a filter that selects for or against new alleles produced by mutation. We can also see that variation within a population can help ensure the survival of that population when the environment changes—if no individuals in the experiment carried the fast allele, it is possible that no flies would have survived in the alcohol-spiked environment. In Chapter 14, we discuss the importance of genetic variation for the long-term survival of species.

Subtleties of Natural Selection

Natural selection is a fairly simple idea, but it is surprisingly easy to misunderstand. Common misunderstandings of this idea fall into three categories: the relationship between the individual and the population, the limitations on the traits that can be selected, and the ultimate result of selection.

Natural Selection Acts on the Inherited Traits of Individuals. A common misconception about natural selection can be illustrated by the following erroneous statement: "The Dodo could not adapt to human hunters, so it went extinct." This assertion seems to presume that individuals must change within their lifetimes in order to survive environmental changes. However, evolution can occur only when traits that influence survival are present in a population and have a genetic basis. Again, the example of the

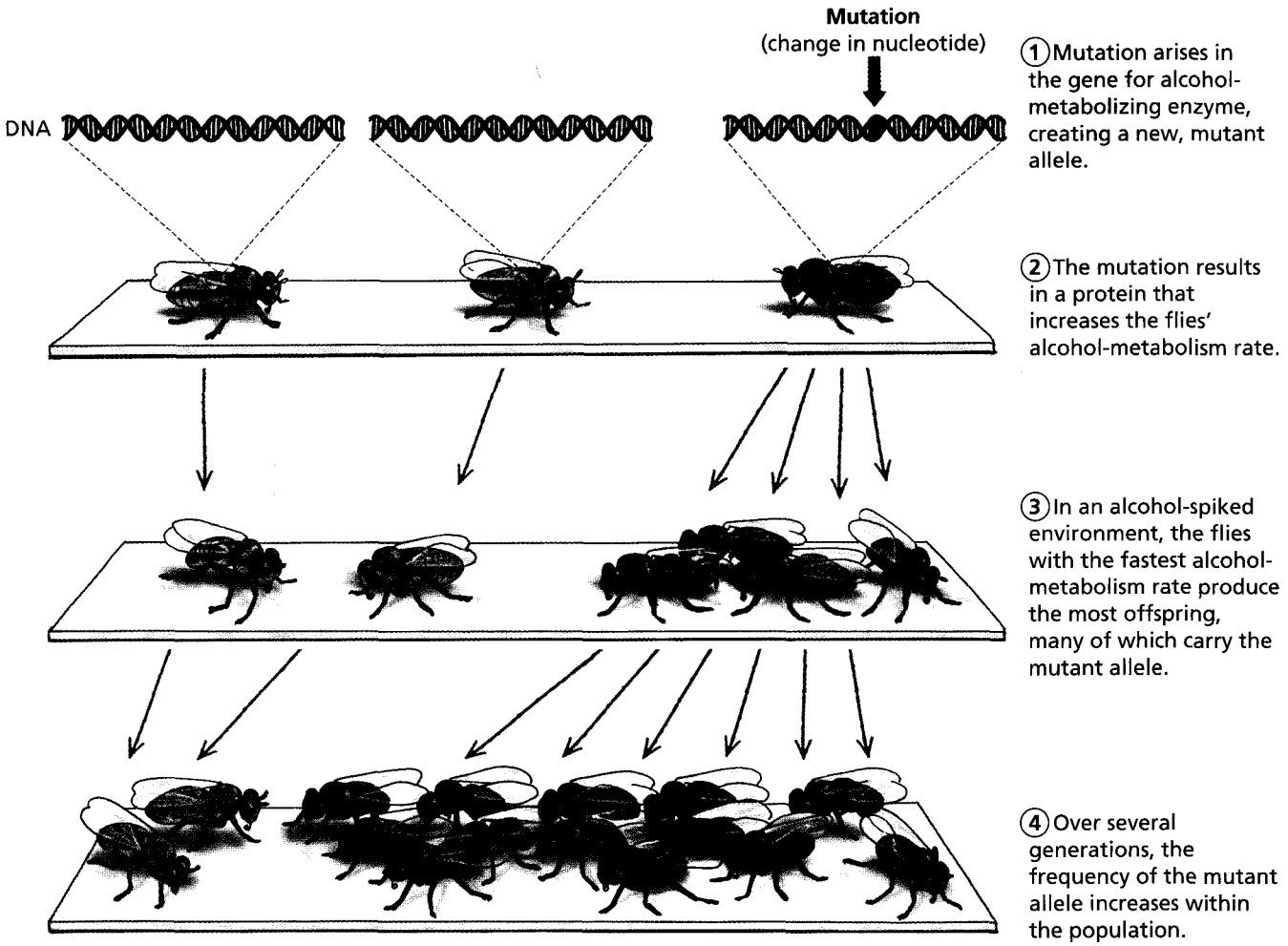


Figure 10.11 Mutation and natural selection. When a gene has mutated, its product may have a slightly different activity. If this new activity leads to increased fitness in individuals carrying the mutated gene, it will become more common in the population through the process of natural selection.

alcohol-metabolizing fruit flies illustrates this point. Selection did not cause change in individual flies; either a fly could rapidly metabolize alcohol, or it could not. It was the differential survival and reproduction of these types of flies in an alcohol-laced environment that caused the population to change.

Natural Selection Does Not Result in Perfection. Natural selection does cause populations to become better fit to their environment, but the result of that process is not necessarily "better" organisms—simply ones that are better adapted to the current situation. Changes in traits that increase survival and reproduction in one environment may be liabilities in another environment. For example, Richard Lenski and his coworkers at Michigan State University found that certain populations of bacteria would adapt to an environment where food levels were low by evolving the production of chemicals that were deadly to other bacteria. Individual bacteria that produced this chemical had an advantage over those that did not; by killing off their nearby competitors, the poisonous bacteria had more of the very limited food available to them and thus became prevalent in the population. However, when the poisonous bacteria were grown in a food-rich environment, they did not grow as well as nonpoisonous bacteria did. This was probably because the poisonous bacteria were using energy to produce their toxin—energy that could have been used for growth and reproduction. Nonpoisonous bacteria in a food-rich environment that

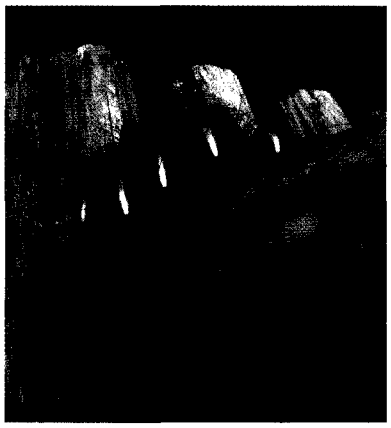


Figure 10.12 The panda's thumb. In addition to the 5 digits on its paw, the giant panda has an opposable "thumb." The thumb is made up of wrist bones that are adapted to help these animals strip leaves from bamboo shoots, their primary food source.

expended the maximum amount of energy on growth had more offspring and thus were better adapted when food was abundant. With nearly all adaptations, there is a trade-off such as this, where increased success in one environment or in one aspect of survival leads to decreased success in another environment or aspect of survival.

The process of natural selection also acts only on the variants that are available within a population. While it might increase our survival and reproduction to have two arms, two legs, and a set of wings, it is not possible to evolve this set of limbs because no such variant exists in the human population. The fact that the adaptations of organisms are constrained by their underlying biology is apparent throughout nature in what evolutionary biologists call *jury-rigged design*, meaning "made using whatever is available." The late Stephen Jay Gould described one of the most famous examples of jury-rigged design—the "thumb" found on a giant panda's front paws (Figure 10.12). These animals apparently have 6 digits: 5 fingers composed of the same bones as our fingers, and a thumb constructed from an enlarged bone equivalent to one found in our wrist. The muscles that operate this opposable thumb are rerouted hand muscles. This structure in pandas appears to be an adaptation that increases their ability to strip leaves from bamboo shoots, their primary food source. A more effective design for an opposable thumb is our own, adapted from one of the basic 5 digits. However, in the panda population, this variation did not exist. Individuals with enlarged wrist bones did exist, so what evolved in giant pandas was a jury-rigged thumb that does its job but is not as flexible as our own thumb.

Natural Selection Results from Current Environmental Conditions. Selection does not result in the "progress" of a population toward a particular predetermined goal; instead, it is situational. The example of the alcohol-metabolizing flies helps to illustrate this point. Only the population of flies in the high-alcohol environment evolved a faster rate of alcohol metabolism. Without a change in the environment, the alcohol-metabolizing rate of the population of flies in the normal environment did not evolve.

The situational nature of natural selection can lead to evolutionary patterns that defy our sense that species are evolving toward a "more perfect" condition. For example, flowering plants evolved from nonflowering plants; and the flower is, in part, an adaptation to attract bees and other pollinators in order to increase seed production. However, some species of flowering plants, especially grasses, have adapted to environments where wind pollination is particularly effective and the need to attract insect pollinators is much reduced. In these plants, natural selection has favored individuals that have very reduced flower parts and generate primarily pollen-producing and egg-producing structures—much like the reproductive structures of their distant nonflowering ancestors (Figure 10.13). Grasses have not regressed but instead have simply adapted to the environment they experience.

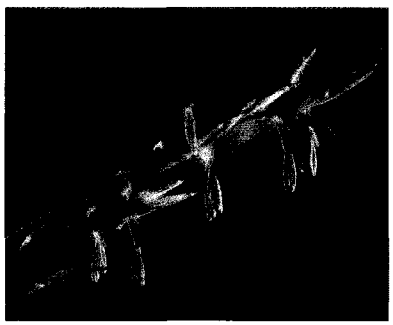


Figure 10.13 Natural selection does not imply progression. Grasses are flowering plants that evolved from ancestors with much showier flowers. The reduction of their flowers as a result of their adaptation to wind pollination does not represent an evolutionary "regression" but instead illustrates the situational nature of natural selection.

While natural selection is often considered a force that causes the traits in a population to change, under certain conditions, selection can cause a population's traits to remain very stable or to split into two species. The type of natural selection experienced by the flies in the alcohol-laden environment is called **directional selection** because it causes the population traits to move in a particular direction, in this case toward higher rates of alcohol metabolism (Figure 10.14a). In certain environments, however, the average variant in the population may have the highest fitness. This results in **stabilizing selection**, in which the extreme variants in a population are selected against and the traits of the population stay the same (Figure 10.14b). For example, in humans, the survival of newborns is correlated to birth weight—both extremely small and extremely large babies

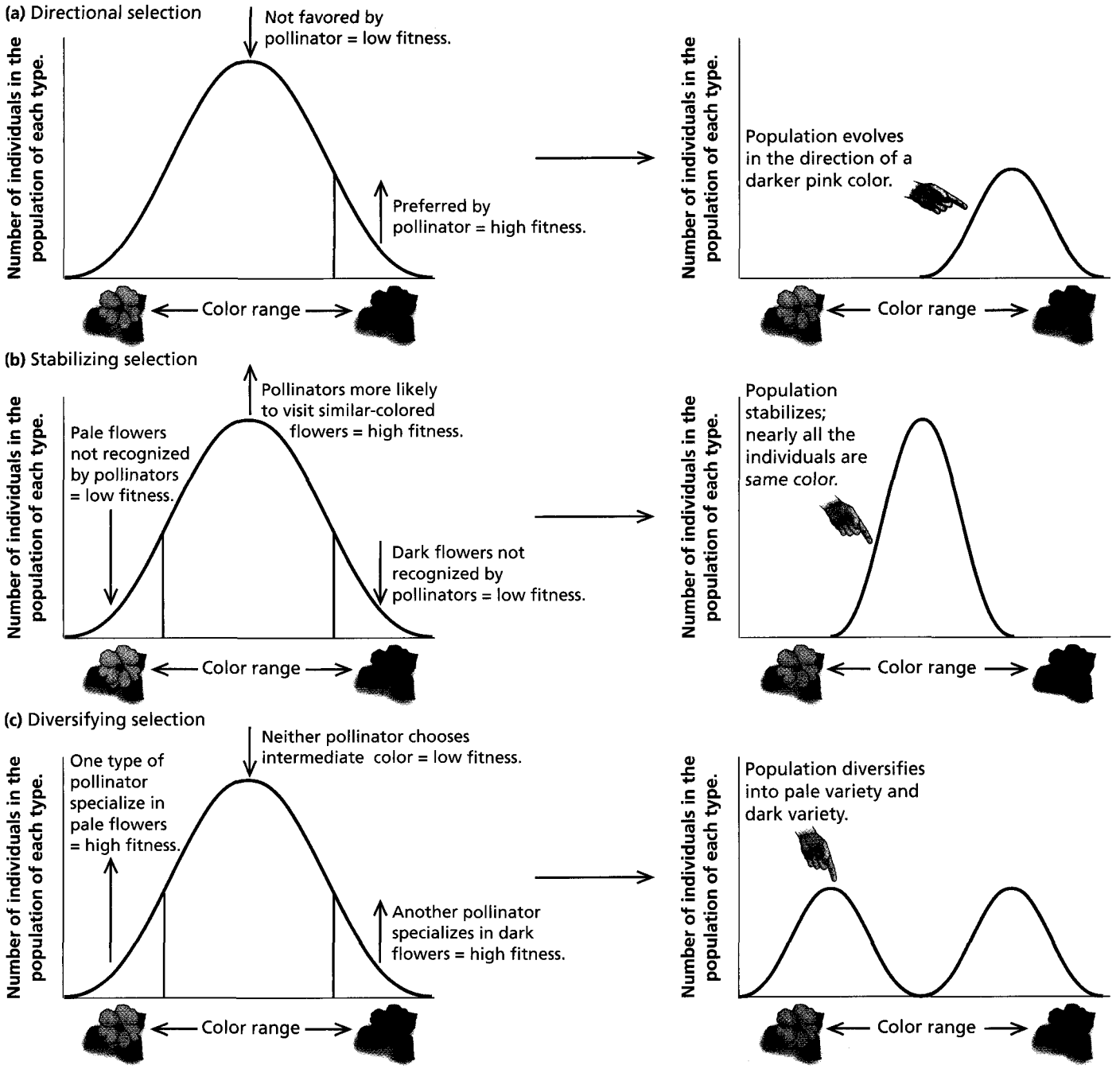


Figure 10.14 Directional, stabilizing, and diversifying selection. Imagine a variable population of pink flowers. If effective pollinators prefer darker-colored flowers as in (a), the population as a whole would be expected to become redder. This is directional selection. (b) If the most "average" color receives the greatest number of pollinator visits, then any extreme variants will likely be lost from the population. This is stabilizing selection. (c) If two populations of pollinators specialize in different ends of the range of colors, the diversity of color in the flower population is expected to increase.

are selected against, causing the average birth weight of babies to be relatively stable over time. Finally, in certain populations, the most common variant may have the lowest fitness, resulting in **diversifying** selection. Diversifying selection causes the evolution of a population consisting of two or more variants (Figure 10.14c). Diversifying selection may contribute to the diversity of HIV particles found in an infected person, a diversity which eventually overwhelms his or her immune system.

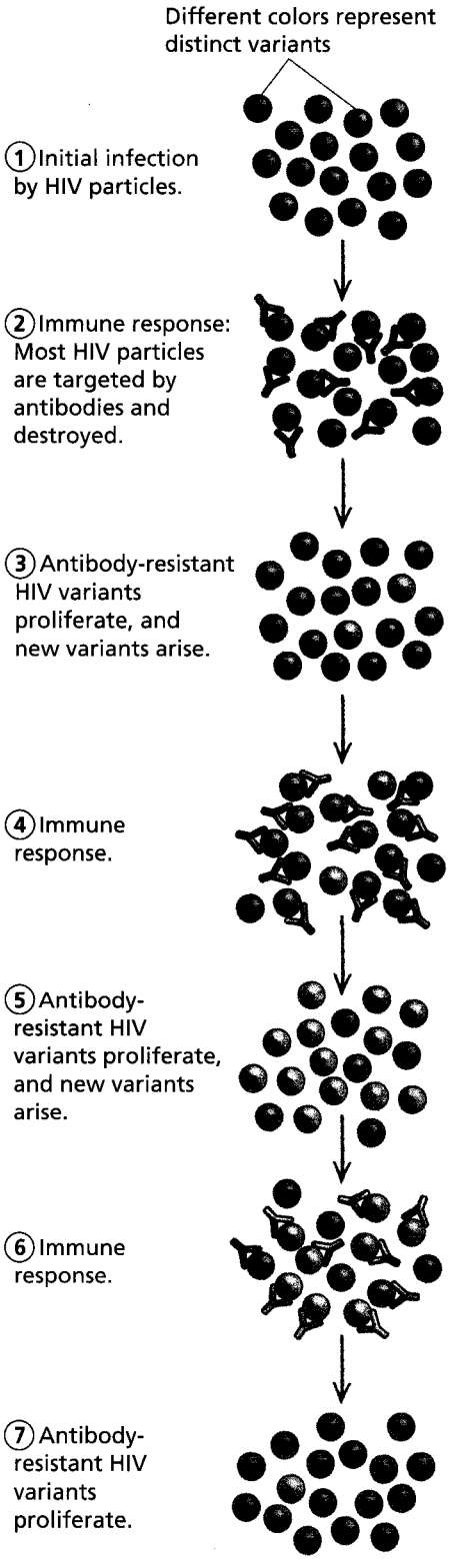


Figure 10.15 The evolution of HIV. HIV populations evolve in response to changes in the immune system. When the immune system develops a specific response to a strain of HIV, mutants that escape this response proliferate until the immune system develops a response to the mutant strain.

10.3 Natural Selection and HIV

Our understanding of how natural selection causes evolutionary change can help us understand why, before effective drug therapy became available, most people infected with HIV eventually died of AIDS. During the asymptomatic period of HIV infection, the number of HIV virus particles in an infected person's bloodstream is relatively low. However, the immune response to HIV does not completely eliminate the virus. HIV persists inside immune system structures called lymph nodes, where it continues to infect and kill T4 cells. The dying T4 cells release the virus into the bloodstream, where anti-HIV antibodies quickly eliminate them. At the same time, the infected individual maintains a high rate of T4 cell production to replace those lost to HIV. In a sense, the virus and the immune system maintain a balance of power during this period.

HIV Fits Darwin's Observations

The population of HIV is not unchanging during the asymptomatic period; instead, it is evolving in response to the environment created by the infected individual's immune system. HIV will evolve via natural selection because it fulfills all of Darwin's observations.

1. **Viruses in the bloodstream vary.** HIV particles are constantly being reproduced because they continue to infect cells in the lymph nodes; any time there is reproduction, mutation can occur. As a result, during the asymptomatic period, new variants of HIV continually arise. Some of these HIV variants have mutated antigens.
2. **The variation among viruses can be passed on to offspring.** The antigens present on a virus particle are coded for by the particle's RNA. When the virus infects a cell, the RNA is reproduced by the host cell and passed on to a new generation of virus particles.
3. **More viruses are produced than survive.** The HIV antibodies produced by the infected host can eliminate most of the viruses that are produced by infected cells.
4. **Virus survival is not random.** The change in antigens that results from mutation can be great enough that the earlier HIV antibodies do not recognize the new variants. Due to their longer survival in the bloodstream, these new virus variants have higher fitness than do the older variants.

Because of the increased fitness of particular variants, subsequent virus generations consist of a greater percentage of virus particles that possess a new antigen. The population evolves to become resistant to a particular antibody produced by the host.

The Evolutionary Arms Race

At the same time the virus population is evolving, the immune system of the host, and thus the environment to which the virus is exposed, is continually changing. As a new HIV variant becomes more common in an infected person's bloodstream, his or her immune system develops an antibody to the variant's unique antigens. HIV again begins to be cleared from the bloodstream—that is, until the next new HIV antigen variant arises through mutation. In other words, the population of HIV inside the host is continually evolving as natural selection by the host's immune system favors variants with unrecognizable antigens (Figure 10.15).

The evolutionary arms race between HIV and the immune system is somewhat similar to the ongoing battles between computer security professionals and

hackers. When a hacker succeeds in accessing protected information, security professionals create a "patch" to cover the flaw that the hacker exploited. A patch keeps hackers at bay until they develop another strategy for breaking into the system—causing the security team to come up with another patch in a seemingly endless cycle. In the case of HIV and the immune system, the patch already exists in the form of one or a few randomly generated B cells that can recognize the new HIV antigens. However, the development of a specific immune response to this new variant by division of these B cells and the production of new antibodies takes several hours to days, and so the overall effect is the same.

Like other RNA viruses that require reverse transcriptase, HIV has a high rate of mutation. Some scientists estimate that every single HIV particle produced has at least one difference from the HIV from which it arose. In addition, HIV has an enormously high rate of reproduction. As the host's immune system focuses its resources on the most common variants, less common types proliferate. The frequent mutation and rapid reproduction of HIV, along with the diversifying selection imposed by the host's immune system, result in a population of the virus within an asymptomatic host that contains about 1 billion distinct variants. With this many variants, it is almost assured that one or more has antigens that are not immediately recognized by the host's immune system. Because these variants avoid the host's antibodies, they can grow to large populations very quickly. Evolution of the HIV population within an infected individual can be extremely fast.

HIV's rapid evolution appears to be the cause of the eventual end of the asymptomatic period in an infected person. The immune system is able to produce antibodies to many different HIV antigen variants, but eventually the sheer number of different HIV variants that the immune system must respond to becomes overwhelming. Finally, one variant arises that escapes immune system control for a long period; large numbers of T4 cells become infected with this variant and are killed or disabled, and the infected individual becomes increasingly immune-deficient. This change initiates the onset of AIDS. In our analogy, imagine millions of hackers, each trying slightly different ways of bypassing the security of a single computer system. As the security team's resources become stretched, the likelihood of one hacker breaking through and crashing the system increases. The relentless evolution of HIV within an infected person's body eventually exhausts his or her ability to control this deadly virus.

10.4 How Understanding Evolution Can Help Prevent AIDS

Immediately after scientists identified and characterized HIV as the virus that causes AIDS, a search began for drugs that would interfere with HIV's ability to replicate. Early drug therapies had rapid failure rates; it was only until scientists incorporated their understanding of natural selection into anti-AIDS treatments that effective, long-term therapies were developed.

Single Drug Therapy Selects for Drug Resistance

One target of anti-HIV drugs is the process of reverse transcription, the rewriting of HIV's genetic information from RNA into DNA. Reverse transcription does not occur in uninfected human cells, and drugs that target this process have the potential for zeroing in on HIV replication without harming normal functions of the human body. One class of drugs used to inhibit reverse transcription is known as the nucleoside analogs. These drugs are similar in structure to one of the four DNA nucleotides described in Chapter 5—A, C, G, and T. Nucleoside analogs inhibit reverse transcription because reverse transcriptase adds one of these analogs to a growing HIV DNA strand in place of the real

nucleotide. Once a nucleoside analog is added to a growing DNA strand, replication halts because additional nucleotides cannot be attached to the analog (Figure 10.16a).

One of the first nucleoside analogs approved as treatment for AIDS is known as Azidothymidine, or AZT. While it is not free of side effects, some very severe, AZT first appeared to be a wonder drug—nearly eliminating HIV from the blood of patients who had already progressed to AIDS. However, in all cases, AZT failed to keep virus populations low for an extended period of time. The failure of AZT over time occurred due to the evolution of HIV. Among the virus variants present in an infected person, there are some that do not mistake AZT for a normal nucleotide and never incorporate it into growing HIV DNA strands. These variants are therefore favored by natural selection; they continue to replicate and become the predominant HIV variants in an AZT-treated individual (Figure 10.16b). As a result of natural selection in the presence of AZT, the HIV population evolves to become **drug resistant**—that is, not susceptible to the effects of AZT. The evolution of drug resistance in disease-causing organisms is not new. However, the speed at which AZT resistance arose in AIDS patients was an early clue to HIV's amazing capacity to evolve.

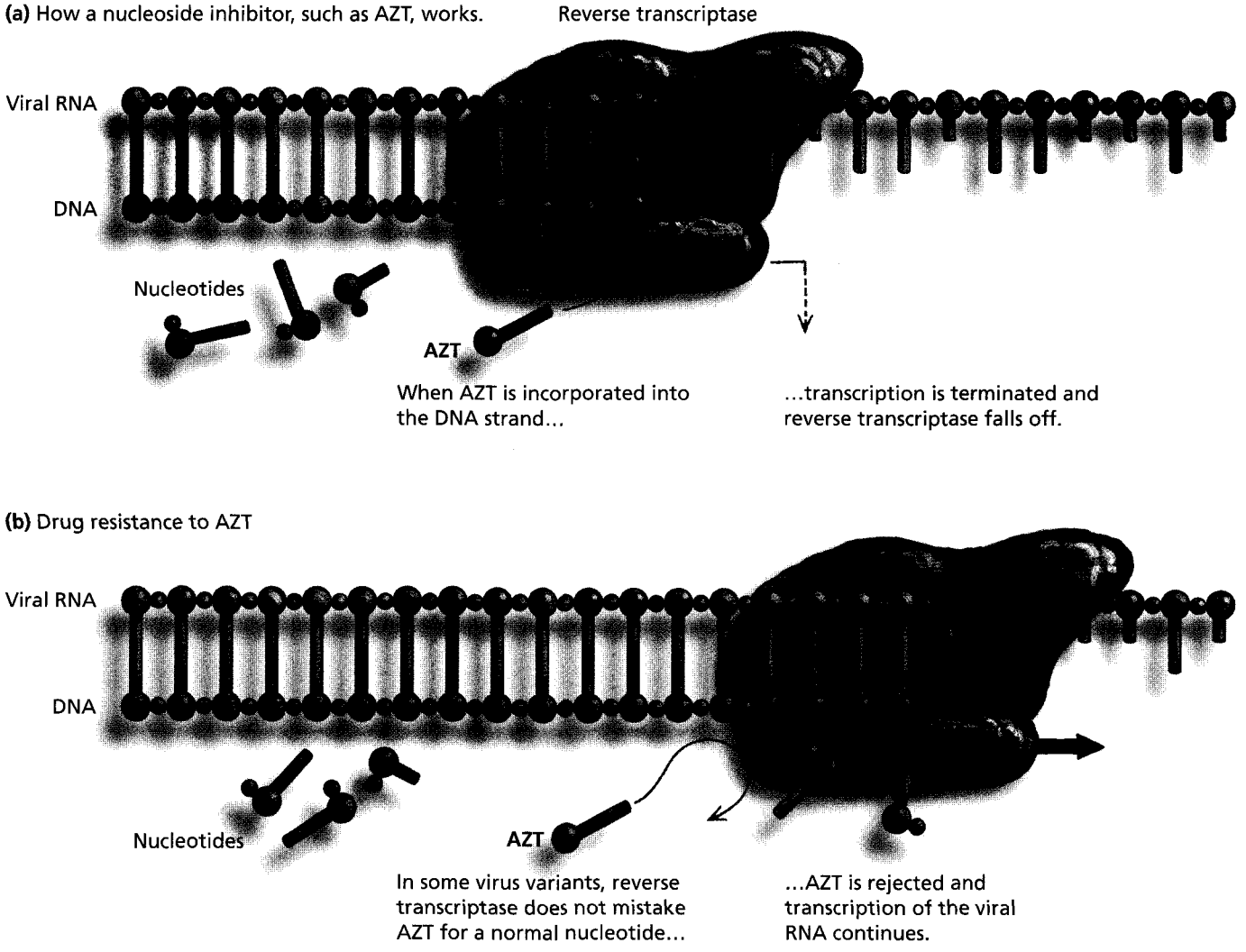


Figure 10.16 AZT and drug resistance. (a) AZT and other nucleoside inhibitors interfere with HIV replication by tricking reverse transcriptase into adding AZT to the growing DNA strand, stopping replication. (b) Some variants of HIV are resistant to AZT because their reverse transcriptase is mutated and does not mistake AZT for a nucleotide.

Combination Drug Therapy Can Slow HIV Evolution

Since the development of AZT, dozens of new anti-HIV drugs have been made available. In addition to more types of nucleoside analogs, other non-nucleoside analogs that interfere with reverse transcription are now in use. Among these are a powerful class of drugs, called protease inhibitors, that stop HIV replication by interfering with the process that converts inactive viral proteins to active enzymes. In 2003, another class of drugs, called entry inhibitors because they block the HIV receptors on cell membranes, was added to the drug arsenal. However, there are still fewer than 30 anti-HIV drugs available. When patients take only one of any of these drugs, HIV quickly develops resistance to it.

Resistance to Multiple Drugs Is Uncommon. Understanding that the rapid rate of HIV evolution decreases the effectiveness of these drugs has led doctors to a new standard of care for the infection. This standard is the use of **combination drug therapy**, also commonly called drug cocktail therapy—a combination of at least two reverse transcription inhibitors and a protease inhibitor. This approach has dramatically decreased the number of AIDS cases and deaths due to AIDS in the United States. The effectiveness of combination therapy is based on the following fact: The greater the number of drugs used, the greater the number of changes are required in the virus's genetic material in order for resistance to develop. The likelihood of a virus variant arising that is resistant to a single drug is relatively small but still very possible in a patient with 1 billion different HIV variants. However, the likelihood of a virus variant arising with resistance to all three drugs in a cocktail is extremely small. The chance that an HIV particle exists that is resistant to a single drug is analogous to the likelihood that in 1 billion lottery ticket holders, one person will hold the winning combination—in other words, almost certain. The likelihood of a variant being resistant to several different drugs is analogous to that same ticket holder winning the lottery three times in a row—incredibly unlikely. Just as it is very difficult to win the lottery three times in a row, it is very difficult for HIV to adapt to an environment where it faces three "killer drugs" at once.

Reducing HIV Replication Decreases the Rate of Evolution. Another key to the effectiveness of combination drug therapy is that when HIV replication is suppressed, new HIV variants arise more slowly. If replication represents the main route by which mutations occur, fewer rounds of replication mean fewer possible mutants. With fewer variants produced, the likelihood also decreases that one contains the combination of mutations that make it resistant to multiple drugs.

Thus, drug cocktails control HIV populations within people by creating an environment that is difficult to adapt to and by slowing the rate at which new adaptations appear. Understanding how HIV evolves to defeat the immune system has allowed scientists to devise ways to interfere with this evolutionary process and prevent HIV infection from progressing into AIDS in most of the treated individuals (Figure 10.17 on page 276). To return to the analogy of computer security professionals and their hacker foes, combination drug therapy not only is equivalent to designing several layers of electronic security around protected information, making it difficult to circumvent all of them at once, but also serves to reduce the number of hackers who are working on ways to defeat the system.

Multiple-Drug-Resistant HIV May Be Less Deadly. Combination drug therapy greatly reduces the chance of an HIV variant that is resistant to multiple drugs appearing in an infected person, but in about 15% of patients, populations of multiple-drug-resistant variants do evolve. In these cases, HIV infection develops into AIDS and leads to death. However, in 30% to 40% of HIV-infected individuals who host HIV populations resistant to multiple drugs and who thus have high levels of HIV in their blood, there is no decrease in T4 cells. In these patients, the drug-resistant HIV variant in their

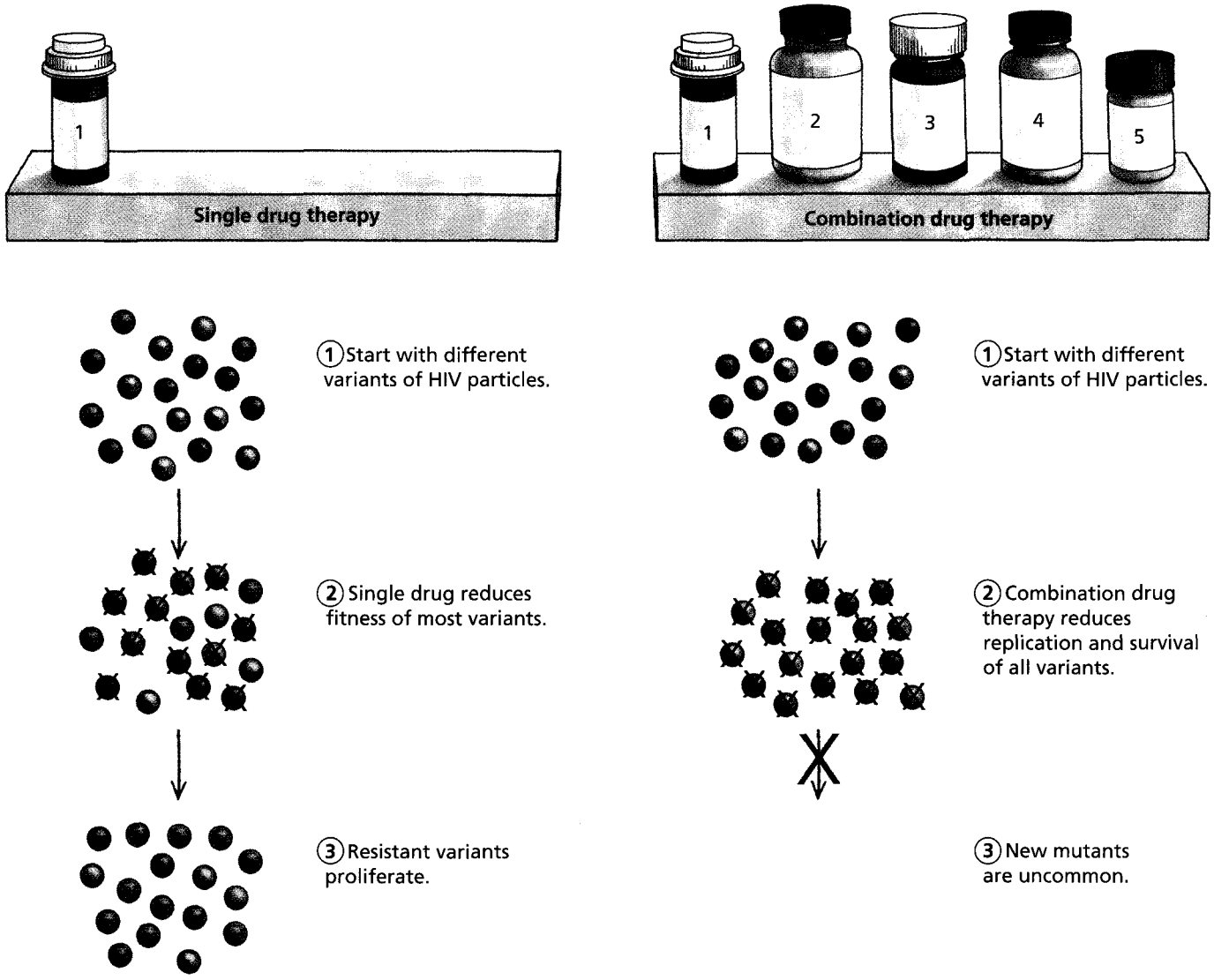


Figure 10.17 Combination drug therapy slows HIV evolution. Using multiple anti-HIV drugs makes the environment much harsher for the virus and decreases the likelihood that a variant with multiple resistances will evolve.

bodies appears to be unable to kill these cells. Patients infected with these meeker HIV variants may live for 3 years or more with high loads of the virus in their bloodstream before progressing to AIDS—much longer than for most people who have high loads of non-drug-resistant HIV. The virus population in this group of patients demonstrates one of the subtleties of natural selection—it rarely results in an organism that is well-adapted for all environments. Recall that for nearly all mutations, there exists a trade-off. In the case of drug-resistant HIV, the mutations that confer this resistance appear to also interfere with the virus's ability to infect large numbers of cells. In some patients with multiple-drug-resistant HIV variants, combination drug therapy has led to the evolution in their bodies of a less deadly virus and has prolonged their lives.

Problems with Combination Drug Therapy

Despite the good news about increased health and prolonged lives of HIV-infected people undergoing combination drug therapy, there are some problems with this approach. Combination drug therapy is expensive;

it often results in severe and unpleasant side effects; and most important, it is difficult to follow. Patients may have to take dozens of pills per day, some of which have very different requirements (for instance, some pills must be taken on an empty stomach, while others need to be taken with food or significant amounts of water). All of this effort is taken to control an infection that initially may not seem any more severe than a mild flu.

The Difficulty of Therapy Creates Drug Resistance. Due to the difficulty of undergoing combination drug therapy, individuals commonly skip doses or take themselves off the drugs for a period of time. The effect of these breaks in treatment is an increase in HIV replication, which increases the risk of developing drug-resistant varieties. Patients who do not follow the drug treatment schedule carefully can find themselves with large virus populations that are resistant to multiple drugs. Even if this resistant virus is less able to infect cells, few people can live with high levels of HIV for long. To control the virus over the long term, individuals with multiple-drug-resistant variants must change and perhaps increase the number of drugs in their cocktail. For example, some patients take 10 to 15 different drugs several times per day. Many scientists fear that the rapid rate of HIV evolution will eventually outpace their ability to both develop new drugs and prolong the asymptomatic period of HIV infection.

Drug Therapy Makes HIV Seem Less Serious. Perhaps more troublesome than the evolution of HIV within a patient is the potential evolution of the HIV epidemic in response to combination drug therapy. The rate of transmission of HIV has not significantly changed in the United States for a decade; about 40,000 new infections are reported every year. However, from 10% to 30% of these new infections involve HIV that is already drug resistant. This means that potentially as many as one-third of newly infected people have fewer options for controlling their virus. As the transmission of drug-resistant HIV increases, our ability to control AIDS in the U.S. population will decline. Worse yet, there is some evidence that combination drug therapy has made HIV and AIDS appear to be less of a threat, leading to decreased prevention efforts and an upswing in infection rates. Combination drug therapy does not cure HIV infection; at best, it is an expensive and long-term commitment that increases an individual's ability to live with this disease. Increases in transmission and drug resistance will erode the benefits of this powerful therapy over time.

Drug Therapy Is Expensive. Combination drug therapy is not available to all of the 42 million HIV-infected individuals around the world. Currently, combination drug therapy costs $1000 to $2000 per month. Worldwide, only about 440,000 of the estimated 6 million people who are in immediate need of anti-HIV therapy receive these drugs. Even in the United States, about 30% of those who take combination drug therapy are subsidized by state and federally funded programs, which are susceptible to budget cuts when tax revenues drop. HIV continues to disproportionately affect the poorest and most vulnerable members of our society and the global community. The gap between the resources of the most-affected populations and the cost of this promising therapy means that for years to come, AIDS will continue to kill people by the millions.

Preventing AIDS

Can Humans Evolve Resistance to HIV? Scientists have known for many years that a small percentage of people fail to develop an HIV infection despite chronic exposure to the virus. Most of these individuals carry a mutation in the gene for CCR5, one co-receptor for HIV. This variant prevents HIV from binding to immune system cells and thus prohibits its

reproduction. About 1% of European-descended whites are homozygous for this mutation and are HIV resistant. Given the existence of this heritable variation and differences in survival among those exposed to this killer virus, can we expect natural selection to cause the human population to evolve resistance to HIV? Eventually, perhaps—but remember that natural selection occurs because of differential survival and reproduction of individuals over time. In short, in order for the human population as a whole to become resistant to this virus, nonresistant variants must die out of the population. Even without anti-HIV drugs, this process would take many generations. Because most nonresistant people will never contract HIV and thus will continue to survive and reproduce, the nonresistant allele will persist for a very long time.

Allowing natural selection to take its course in the human population in order for widespread resistance to evolve would require elimination of all anti-HIV therapy—a prospect unthinkable to most people. The relatively high frequency of the HIV-resistant CCR5 mutation in European populations may itself be a result of unimpeded natural selection. Some scientists have hypothesized that this mutation, which is nearly absent in Asian and African populations, became prevalent in Europeans approximately 700 years ago. The most dramatic event of this time period in Europe was the "Black Death," a plague that killed 33% of the European population in a period of three years from 1347 to 1350. It may be that the CCR5 mutation also confers resistance to infection by the bacteria that causes plague. The death and devastation in Europe caused by the Black Death is nearly unimaginable to us, and yet only 20% of the descendants of that event carry even one copy of the CCR5 mutation. The percentage of people who must die of HIV infection in order to result in a population where 100% carry this mutation is even more dramatic, and it is likely to cause even more serious devastation. Clearly, human evolution is not an acceptable solution to the problem of AIDS.

Preventing Infection. Despite the success of combination drug therapy, the best "treatment" for AIDS is to avoid becoming infected with HIV at all. HIV is a fragile virus that is transmitted only through direct contact with bodily fluids—primarily blood, semen, vaginal fluid, or occasionally to newborns via breast milk. There is no evidence that the virus is spread by tears, sweat, coughing, or sneezing. It is not spread by contact with an infected person's clothes, phone, or toilet seat. It is not transmitted by an insect bite. And it is unlikely to be transmitted by kissing (although any kissing that allows the commingling of blood could lead to HIV transmission). HIV is frequently spread through needle sharing among injection-drug users, but the primary mode of HIV transmission is via unprotected sex, including oral sex, with an infected partner. So, what is the best way to avoid HIV infection? Do not use addictive injection drugs and avoid sexual activity. If you are sexually active, know your partner's HIV status, drug habits, and sexual activities. The safest relationship is one that is monogamous, where there is no sexual activity outside of the relationship. According to the Centers for Disease Control (CDC), about one-quarter of the approximately 1 million people infected with HIV in the United States do not know that they carry this deadly virus. If your partner might be at risk for HIV infection, practice safer sex—that is, use a condom.

Living with HIV. Why has Magic Johnson remained free of AIDS for over 14 years since contracting HIV? He has access to the highest-quality medical care to help maintain the effectiveness of his own immune system and the financial and emotional resources that allow him to maintain

long-term combination drug therapy. These actions have both reduced the reproduction of HIV in his body and increased the challenges that the virus must overcome in order to escape the control of his immune system. In other words, he has so far successfully limited the chance that natural selection will cause the evolution of HIV in his body. Magic is still infected with HIV; no one knows whether drug therapy will help his body finally eliminate it, or if the therapy will eventually fail and he will lose the battle with this killer virus. Magic's ability to survive, and even thrive, for so long since his diagnosis gives us hope that someday HIV will not be a death sentence for anyone.

CHAPTER REVIEW

Summary

10.1 AIDS and HIV

- Infection with HIV eventually leads to collapse of the immune system, resulting in AIDS (p. 258).
- The immune system of an individual infected with HIV can initially control the virus, but the evolution of HIV leads to the eventual loss of immune system cells (pp. 261–262).

Web Tutorial 10.1 HIV: The AIDS Virus

10.2 The Theory of Natural Selection

- Individuals in a population vary, and some of this variation can be passed on to offspring (p. 263).
- Not all individuals born in a population survive to adulthood, and not all adults produce the maximum number of offspring possible (p. 264).
- Advantageous traits, called adaptations, increase an individual's fitness, his or her chance of survival and/or reproduction (p. 265).
- The increased fitness of individuals with particular adaptations causes the adaptation to become more prevalent in a population over generations (pp. 265–266).
- *Natural selection is a mechanism for evolutionary change in* populations (p. 266).
- Artificial selection, when humans control an organism's fitness, causes the evolution of different breeds of animals and varieties of plants (p. 266).
- Populations exposed to environmental changes, both in the lab and in nature, have been shown to evolve traits that make them better fitted to the environment (pp. 266–267).
- The modern definition of evolution is a genetic change in a population of organisms (p. 268).
- The traits of an organism are partially determined by alleles, which arise through the process of mutation (p. 268).
- Alleles that code for adaptations become more common in a population over generations as a result of natural selection (p. 268).
- Natural selection can act only on the variants currently available in the population, results in a population that is better adapted to its environment but usually not perfectly adapted as a result of trade-offs, and does not push a population in the direction of a predetermined "goal" (pp. 268–270).
- Selection can cause the traits in a population to change in a particular direction but in some environments may cause certain traits to resist change and in other environments cause multiple variants to evolve (pp. 270–271).

Web Tutorial 10.2 Natural Selection

10.3 Natural Selection and HIV

- HIV eventually overwhelms the immune system because it consists of multiple variants that have differential survival inside the human body; thus, it continually evolves via natural selection (p. 272).
- HIV variants that are immune to the host's anti-HIV antibodies become more common in the host's body because they survive longer and thus reproduce more. As the HIV population consequently changes in form, the immune system develops antibodies to this new form. Eventually, so many different HIV forms exist that the body's attempts to control the virus are overwhelmed (pp. 272–273).

Web Tutorial 10.3 Drug Resistance and Natural Selection

10.4 How Understanding Evolution Can Help Prevent AIDS

- HIV variants that are resistant to any single HIV drug are likely in an infected individual with a highly variable HIV population. As a result, HIV evolves resistance to a drug very quickly via natural selection (p. 274).

- Mutants to multiple anti-HIV drugs are relatively unlikely, and drug therapy suppresses HIV replication, thereby reducing the production of mutant varieties (p. 275).
- Varieties of HIV that can survive in an environment containing multiple drugs are sometimes less deadly than nonresistant varieties (p. 275).
- Anti-HIV combination drug therapy selects for drug-resistant viruses, both within patients and in the general population (p. 276).
- Anti-HIV combination drug therapy has major disadvantages, including high cost, difficulty in following the treatment schedule, and severe side effects (p. 277).
- Resistance to HIV infection is unlikely to become commonplace soon in the human population as a result of natural selection (p. 278).
- The best treatment for AIDS is the prevention of HIV infection, which is primarily accomplished through safer sex practices (p. 278).

Learning the Basics

1. Define *fitness* as used in the context of evolution and natural selection.

2. Define *artificial selection*, and compare and contrast it with natural selection.

3. Describe how HIV evolves when it is exposed to a drug that interferes with replication.

4. Which of the following observations is *not* part of the theory of natural selection?

   A. Populations of organisms have more offspring than will survive.; **B.** There is variation among individuals in a population.; **C.** Modern organisms descended from a single common ancestor.; **D.** Traits can be passed on from parent to offspring.; **E.** Some variants in a population have a higher probability of survival and reproduction than other variants do.

5. The best definition of *evolutionary fitness* is _____.

   A. physical health; **B.** the ability to attract members of the opposite sex; **C.** the ability to adapt to the environment; **D.** survival and reproduction relative to other members of the population; **E.** overall strength

6. An adaptation is a trait of an organism that increases _____.

   A. its fitness; **B.** its ability to survive and replicate; **C.** in frequency in a population over many generations; **D.** a and b are correct; **E.** a, b, and c are correct

7. The heritable differences among organisms are a result of _____.

   A. differences in their DNA; **B.** mutation; **C.** differences in alleles; **D.** a and b are correct; **E.** a, b, and c are correct

8. The immune system of an HIV-infected individual _____.

   A. can eliminate HIV entirely; **B.** cannot cause HIV populations to decline; **C.** causes selection for HIV variants that escape immune system control; **D.** evolves quickly in response to HIV infection; **E.** cannot make antibodies to HIV

9. HIV evolves rapidly because it _____.

   A. has a very high rate of reproduction; **B.** has a very high mutation rate; **C.** can detoxify anti-HIV drugs; **D.** a and b are correct; **E.** a, b, and c are correct

10. HIV is transmitted via _____.

    A. sexual intercourse with an infected person; **B.** shaking hands with an infected person; **C.** using the same bathroom as an infected person; **D.** a bite from an insect that has previously bitten an infected person; **E.** all of the above

Analyzing and Applying the Basics

1. The wide variety of dog breeds is a result of artificial selection from wolf ancestors. Use your understanding of artificial selection to describe how a dog breed such as the Chihuahua may have evolved.

2. The striped pattern on zebras' coats is considered to be an adaptation that helps reduce the likelihood of a lion or other predator identifying and preying on an individual animal. The ancestors of zebras were probably not striped. Using your understanding of the processes of mutation and natural selection, describe how a population of striped zebras might have evolved from a population of zebras without stripes.

3. Are all features of living organisms adaptations? How could you determine if a trait in an organism is a product of evolution by natural selection?

Connecting the Science

1. The theory of natural selection has been applied to human culture in many different realms. For instance, there is a general belief in the United States that "survival of the fittest" determines which businesses are successful and which go bankrupt. How is the selection of "winning" and "losing" companies in our economic system similar to the way natural selection works in biological systems? How is it different?

2. Ninety-five percent of worldwide HIV/AIDS cases occur in developing countries, where most of the population cannot afford combination drug therapy. Does the United States have an obligation to provide people in the developing world with low-cost, effective anti-AIDS therapy? In countries where the needs of daily survival often overshadow the requirement to take the drugs in the proper dosage, drug-resistant strains of HIV may be more likely to develop. What do you think will best help to reduce the toll of HIV/AIDS in these regions?