5·14–5·17 Biotechnology has the potential for improving human health (and criminal justice).

With the cloning of sheep, a new era in biotechnology began.

5·14 The treatment of diseases and production of medicines are improved with biotechnology.

You can't always get what you want. In the best of all worlds, biotechnology would *prevent* humans from ever getting debilitating diseases. Next best would be to *cure* diseases once and for all. But these noble goals are not always possible, so biotechnology often is directed at the more practical goal of *treating* diseases, usually by producing medicines more efficiently and more effectively than they can be produced with traditional methods. Biotechnology has had some notable successes in achieving this goal. The treatment of diabetes is one such success story.

Diabetes is a chronic disease in which the body cannot produce insulin, a chemical that allows cells to take up and break down sugar from the blood. Complications from diabetes can include vascular disease, kidney damage, and nerve damage. As recently as 1980, if you were one of the approximately 15 million Americans with diabetes, each day you would treat the disease by injecting yourself with insulin extracted from the pancreas of cattle or pigs that had been killed for meat. For most diabetics, the insulin injections kept the disease under control. But the traditional process of collecting insulin this way was difficult and costly.

Everything changed in 1982 when a 29-year-old entrepreneur, Bob Swanson, joined scientist Herbert Boyer to transform the potential of recombinant DNA technology. In doing so, they started the biotech revolution. Working with the scientist Stanley Cohen, Swanson and Boyer used restriction enzymes to snip out the human DNA sequence that codes for the production of insulin. They then inserted this sequence into the bacterium *E. coli,* creating a transgenic organism. After cloning the new, transgenic bacteria, the team was able to grow vats and vats of the bacterial cells, all of which churned out human insulin (**FIGURE 5-39**). The drug could be produced efficiently in huge quantities and made available for patients with diabetes. This was the first genetically engineered drug approved by the Food and Drug Administration and it continues to help millions of people every day.

Q Why do some bacteria produce human insulin?

Perhaps even more significant than providing a better source of insulin, Swanson, Boyer, and Cohen's application of biotechnology revealed a generalized process for genetic engineering. It instantly opened the door to a more effective method of producing many different medicines to treat diseases. Today, more than 1,500 companies work in the recombinant DNA technology industry, and their products generate more than $40 billion in revenues each year.

Several important achievements followed the development of insulin-producing bacteria. Here are just two examples.

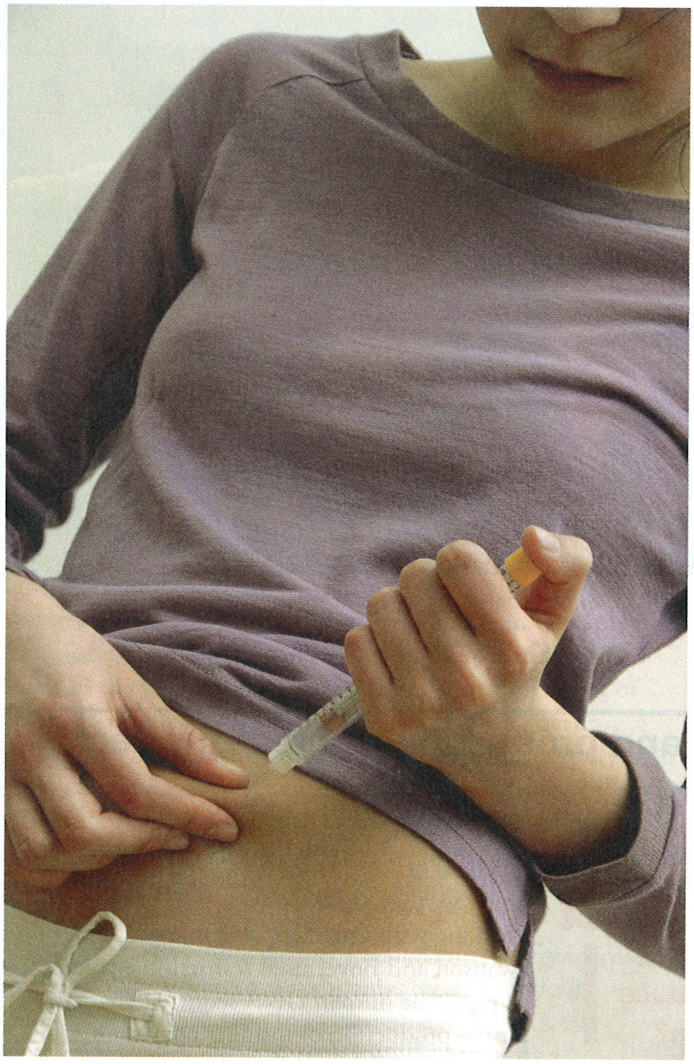

FIGURE 5-39 Life-saving insulin. Human insulin is engineered through recombinant DNA technology.

1. Human growth hormone (HGH). Produced by the pituitary gland, human growth hormone has dramatic effects throughout the body. It stimulates protein synthesis, increases the utilization of body fat for energy to fuel metabolism, and stimulates the growth of virtually every part of the body (**FIGURE 5-40**). Insufficient growth hormone production, usually due to pituitary malfunctioning, leads to dwarfism.

When treated with supplemental HGH, individuals with dwarfism experience additional growth. Until 1994, however, HGH treatment was prohibitively expensive because the growth hormone could only be produced by extracting and purifying it from the pituitary glands of human cadavers.

FIGURE 5-40 Bulking up with a little (illegal) help. Sylvester Stallone—age 61 in this photo—used human growth hormone (along with strength training) to develop larger muscles for a film role.

Through the creation of transgenic bacteria, using a technique similar to that used in the creation of insulin-producing bacteria, HGH can now be produced in virtually unlimited supplies and made available to more people who need it.

The availability of HGH, which can increase strength and endurance, may be irresistibly tempting to some people (who don't need it for medical reasons)—even at $7,500 for a month's supply. Recent sporting scandals suggest that the illegal use of HGH occurs frequently among elite swimmers, cyclists, and other athletes.

2. Erythropoietin. Produced primarily by the kidneys, erythropoietin (also known as EPO) is a hormone that regulates the production of red blood cells. Numerous clinical conditions (nutritional deficiencies and lung disease, among others) and treatments (such as chemotherapy) can lead to anemia, a lower than normal number of red blood cells, which reduces an individual's ability to transport oxygen to tissues and cells. This lack of sufficient oxygen, in turn, can cause a variety of symptoms, including weakness, fatigue, and shortness of breath.

First cloned in 1985, recombinant human erythropoietin (rhu-EPO) is now produced in large amounts in hamster ovaries. It is used to treat many forms of anemia. Worldwide sales of EPO are in the billions of dollars.

Q What is "blood doping"? How does it improve some athletes' performance?

EPO has been at the center of several "blood doping" scandals in professional cycling. This hormone increases the oxygen-carrying capacity of the blood, so some otherwise healthy athletes have used EPO to improve

their athletic performance. It can be very dangerous, though. By increasing the number of red blood cells, the blood can become much thicker and this can increase the risk of heart attack.

Beyond these and other medicines currently produced by transgenic organisms, plans are under way to create a variety of other useful products—including potatoes that produce antibodies enabling a more effective response to illnesses—for treating disease. In the next section we examine the strategies for preventing genetic diseases, and the much less successful attempts to cure diseases through biotechnology.

TAKE-HOME MESSAGE 5·14

Biotechnology has led to some notable successes in treating diseases, usually by producing medicines more efficiently and effectively than they can be produced with traditional methods.

5·15 Gene therapy: biotechnology can help diagnose and prevent diseases, but has had limited success in curing them.

Would you want to know? Once, this was just a hypothetical question: if you carried a gene that meant you were likely to develop a particular disease later in your life, would you want to know about it? Or another question: would you want to know if there's a good chance that your future children will be born with a genetic disease? Now, for better or for worse, these are becoming real-life questions that we all must address. And there is more at stake than simply peace of mind. As biotechnology develops the tools to identify some of the genetic time-bombs that many of us carry, it also carries the danger that such information may become the basis for greater discrimination than we have ever known.

Intervening to prevent diseases through biotechnology focuses on answering certain questions posed at three different points in time.

1. Is a given set of parents likely to produce a baby with a genetic disease? Many genetic diseases occur only if an individual inherits two copies of the disease-causing gene, one from each parent. This is true for Tay-Sachs disease, cystic fibrosis, and sickle-cell anemia, among others. Individuals with only a single copy of the disease-causing gene never fully show the disease, but they may pass on the disease gene to their children. Consequently, two healthy parents (that is, having no disease symptoms) may produce a child with the disease. In these cases, it can be beneficial for the parents to be screened to determine whether they carry a disease-causing copy of the gene. Such screening, combined with genetic counseling and testing of embryos following fertilization, can reduce the incidence of the disease dramatically. Since screening began in 1969, the incidence of Tay-Sachs disease, for example, has fallen by more than 75% (**FIGURE 5-41**).

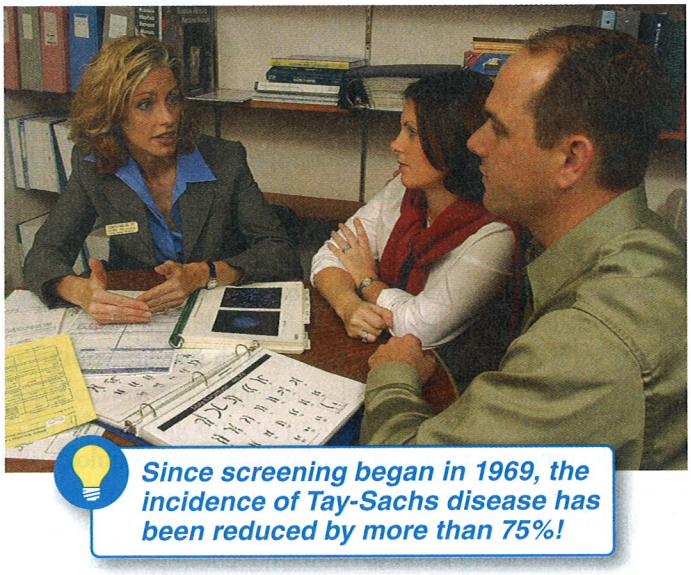

FIGURE 5-41 Genetic screening can determine the presence of the Tay-Sachs gene.

2. Will a baby be born with a genetic disease? Once fertilization has occurred, it is possible to test an embryo or developing fetus for numerous genetic problems. Prenatal genetic screening can detect cystic fibrosis, sickle-cell anemia, Down syndrome, and a rapidly growing list of other disorders.

To screen the fetus, doctors must examine some of the fetal cells and/or the amniotic fluid (which surrounds the fetus in the uterus and carries many chemicals produced by the developing embryo). Cells and fluid are usually collected by amniocentesis or chorionic villus sampling (CVS), techniques that we explore in detail in Chapter 6.

3. Is an individual likely to develop a genetic disease later in life? DNA technology can also be used to detect disease-causing genes in individuals who are currently healthy but are at increased risk of developing an illness later. Early detection of many diseases, such as breast cancer, prostate cancer, and skin cancer, greatly enhances the ability to treat the disease and reduce the risk of more severe illness or death.

These potential benefits of genetic technology come with significant potential costs. People who have a gene that puts them at increased risk of developing a particular disease, for example, might be discriminated against, even though they are not currently sick and may never suffer from the particular disease. Although a federal Genetic Information Nondiscrimination Act was signed into law in 2008, the law does not cover life insurance, disability insurance, and long-term care insurance. Insurance companies have already denied such coverage on discovering that an individual carries a gene that puts him or her at increased risk of disease. Additionally, parents who discover that their developing fetus will develop a painful, debilitating, or fatal disease soon after birth are confronted with the difficult question of how to proceed.

When it comes to curing a disease by using biotechnology, there is good news and bad news. The good news is that, in the 1990s, a handful of humans with a usually fatal genetic disease called severe combined immunodeficiency disease (SCID) were completely cured through the application of biotechnology. The bad news is that it has not been possible to apply these promising techniques to other diseases.

It's not for a lack of trying. There have been more than 500 other clinical trials for **gene therapies** designed to treat or cure a variety of diseases by inserting a functional gene into an individual's cells to replace a defective version of the gene. But no clear successes. Not one.

Let's examine the case of SCID, which has served as a model for gene therapy. SCID is a condition in which a baby is born with an immune system unable to properly produce a type of white blood cell. This leaves the infant vulnerable to most infections and usually leads to death within the first year of life (**FIGURE 5-42**). In gene therapy for SCID, researchers removed from an affected baby's bone marrow some **stem cells,** cells that have the ability to develop into any type of cell in the body. In bone marrow, they normally produce white blood cells, but in individuals with SCID, a malfunctioning gene disrupts normal white blood cell production.

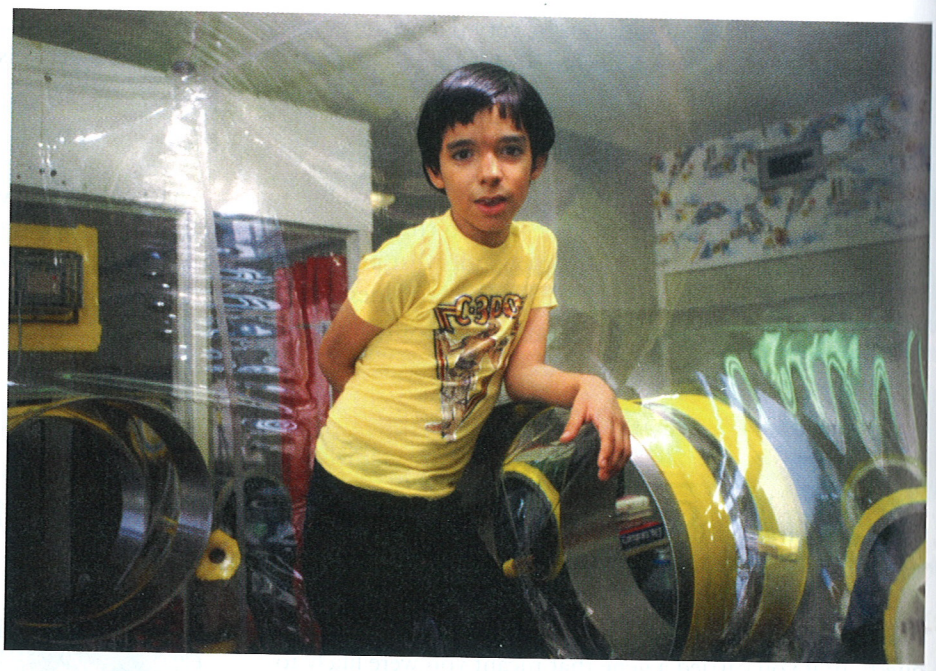

FIGURE 5-42 Protected by a bubble. This child with severe combined immunodeficiency lived 12 years in a protective bubble at Baylor Medical Center.

Next, in a test tube, the bone marrow stem cells were infected with a transgenic virus carrying the functioning gene. Ideally, the virus inserted the good gene into the DNA of the stem cells, which were then injected back into the baby's bone marrow. There, the cells could produce normal white blood cells, permanently curing the disease. Although this strategy worked to cure several cases of SCID, treatment has been suspended indefinitely following the recent deaths of two patients from illness related to their treatment.

Q Why has gene therapy had such a poor record of success in curing diseases?

Difficulties with gene therapy have been encountered in several different areas, usually related to the organism used to transfer the normal-functioning gene into the cells of a person with a genetic disease. They include:

1. Difficulty getting the working gene into the specific cells where it is needed.
2. Difficulty getting the working gene into enough cells and at the right rate to produce a physiological effect.

3. Difficulty arising from the transfer organism getting into unintended cells.
4. Difficulty regulating gene expression.

Beyond these technical problems, for most diseases the malfunctioning gene has not been identified or the disease is caused by more than one malfunctioning gene. And finally, it is important to keep in mind that gene therapy targets cells in the body other than sperm and eggs. Consequently, while a disease might, in theory, be cured in an individual, he or she can still pass on the disease-causing gene(s) to offspring. It's not clear what the future holds for gene therapy, but a great deal of research is still in progress.

TAKE-HOME MESSAGE 5·15

Biotechnology tools have been developed to identify whether a set of parents is likely to produce a baby with a genetic disease, whether a baby is likely to be born with a genetic disease, and whether an individual carries disease-causing genes that may have their effect later in life. These tools can help reduce suffering and the incidence of diseases, but come with significant potential costs. Gene therapy has had a poor record of success in curing human diseases, primarily because of technical difficulties in transferring normal-functioning genes into the cells of a person with a genetic disease.

5·16 Cloning—ranging from genes to organs to individuals—offers both promise and perils.

Cloning. Perhaps no scientific word more readily conjures horrifying images of the intersection of curiosity and scientific achievement. But is fear the appropriate emotion to feel about this burgeoning technology? Perhaps not.

For starters, let's clarify what the word means. "Cloning" actually refers to a variety of different techniques. To be sure, cloning can refer to the creation of new individuals that have exactly the same genome as the donor individual—a process called "whole organism cloning." That is, a clone is like an identical twin, except that it may differ in age by years or even decades. It is also possible to clone tissues (such as skin) and entire organs from an individual's cells. And, as we saw in Section 5-11, it is possible to clone genes.

Cloning took center stage in the public imagination in 1997, when Ian Wilmut, a British scientist, and his colleagues first reported that they had cloned a sheep—which they named Dolly. Their research was based on ideas that went back to 1938, when Hans Spemann first proposed the experiment of removing the nucleus from an unfertilized egg and replacing it with the nucleus from the cell of a different individual. Although the process used by Wilmut and his research group was difficult and inefficient, it was surprisingly simple in concept (**FIGURE 5-43**). They removed a cell from the mammary gland of a grown sheep, put its nucleus into another sheep's egg from which the nucleus had been removed, induced the egg to divide, and transplanted it into the uterus of a surrogate mother sheep. Out of 272 tries, they achieved just one success. But that was enough to show that the cloning of an adult animal was possible.

Shortly after news of Dolly's birth, teams set about cloning a variety of other species, including mice, cows, pigs, and cats (**FIGURE 5-44**). Not all of this work was driven by simple curiosity. For farmers, cloning could have real value. It can take a long time to produce animals with desirable traits from an agricultural perspective—such as increased milk production in cows. And with each successive generation of breeding, it can be difficult to maintain these traits in the population. But through the process of transgenic techniques and whole animal cloning, large numbers of valuable animals with such traits can be produced and maintained.

Q *Are there any medical justifications for cloning?*

Medical researchers, too, see much to gain from cloning. In particular, transgenic animals containing human genes—such as the hamsters producing rhu-EPO, discussed earlier—can be very valuable. But can a human be cloned? At this point, it is almost certain that the cloning of a human will be possible. Many people wonder, though, whether such an endeavor should be pursued. There is near unanimity among scientists that human cloning to produce children should not be attempted. Some of the reasons cited relate to problems of safety for the mother and the child, legal and philosophical issues relating to the inability of