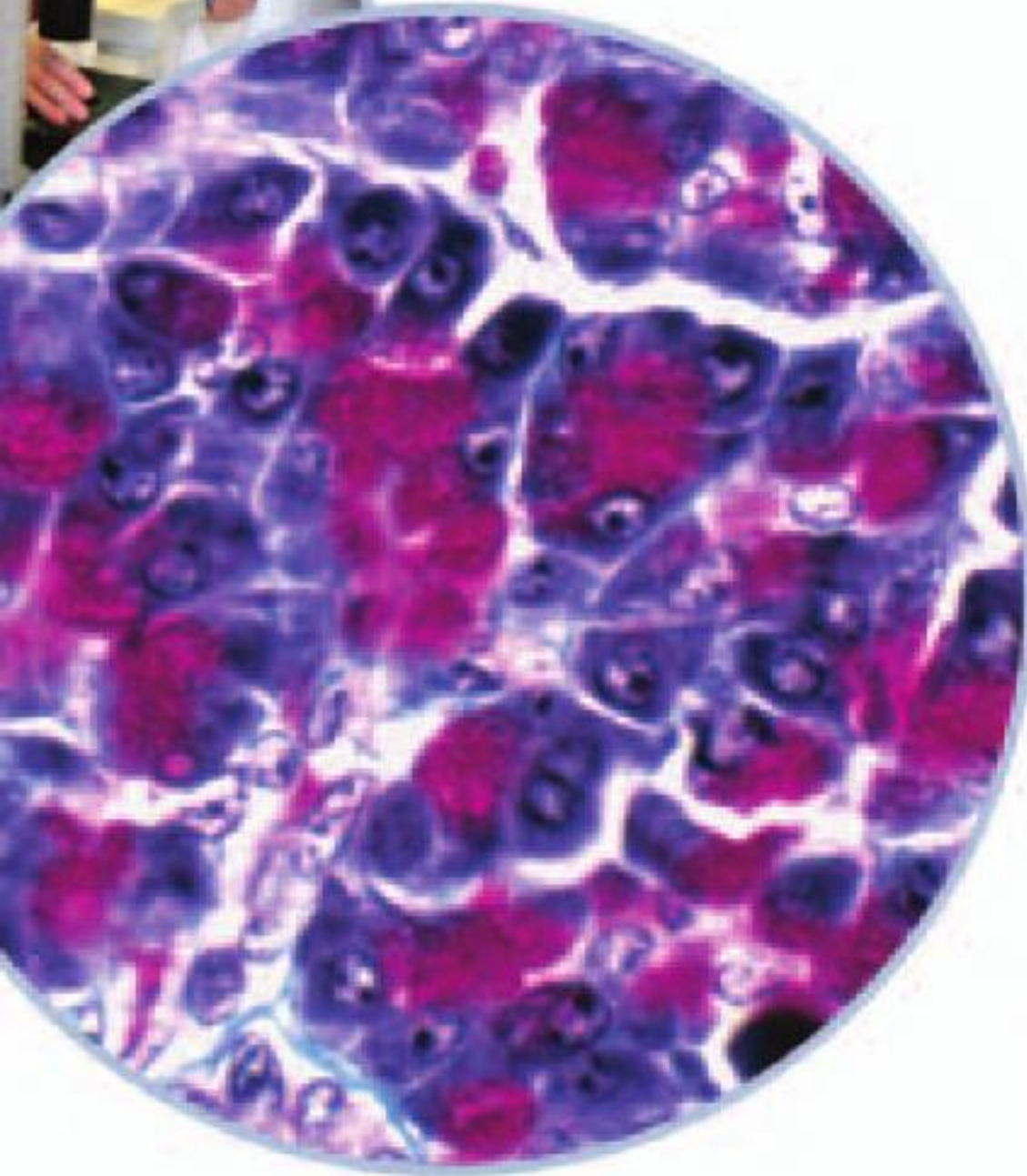


GENES & DISEASE

DIABETES



Toney Allman





Diabetes

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1

A DIAGNOSIS OF DIABETES

Amanda was 12 years old and always thirsty and always hungry. Even though she ate constantly, she lost 15 pounds in two months. It was the same with fluids. She just could not get enough. She remembers drinking not just glasses of water but gallons of water. She had to constantly go to the bathroom. Finally, her worried parents made a doctor's appointment for her, but before she could get there, she awoke one night dreadfully ill. She had sharp pains in her stomach and was so weak she could not stand. She collapsed on the bathroom floor, exhausted and unable to remain conscious. Her mother rushed her to the doctor, who sent her straight to the hospital. She remained in the hospital for about a week, recovering from her ordeal and learning the diagnosis that would change her life. Amanda had diabetes and that was what had caused all her symptoms.¹

Kassy was diagnosed with diabetes when she was only 6 years old. Her symptoms were not as obvious as Amanda's. She had stomachaches, but no one knew what was wrong with her. She had been drinking a lot of fluids, but the signal that alerted her parents was that she suddenly started wetting her bed at night. When her mother took her to the hospital emergency room, she fell asleep in the waiting room and wet her chair.²



Daniel, a resident of South Africa, was 14 years old when his diabetes was diagnosed. He remembers being so thirsty that he could drink 7 liters of cola a day and still yearn for more. He was not aware of any other symptoms, so the doctor's discovery of diabetes was a shock to him.³ Daniel's shock was not unusual. Adjusting to a serious disease is not easy for anyone, no matter what age. Even for those who have never heard the word *diabetes* before, shock, distress, and fear are common responses to this diagnosis.

Although most young people learn to adjust relatively soon, the tempo of their lives is changed forever. Diabetes is a lifelong condition and requires medical treatment and management. That most people succeed and live long, active lives is a tribute both to the courage and efforts of individuals and to the medical and scientific knowledge that makes these efforts possible.

TYPE 1 DIABETES

Diabetes is a complex and variable condition that can affect almost every organ in the body. To make matters even more complicated, it is not even one disease. Diabetes is actually several diseases with different causes, different ages of onset, and different treatment requirements. Amanda, Daniel, and Kassy have what is known as **type 1 diabetes**. According to the United States Centers for Disease Control (CDC), each year, more than 13,000 young people are diagnosed with type 1 diabetes. It usually begins in childhood, adolescence, or young adulthood. It has a rapid onset and can make the affected person very sick very quickly. Actress Halle Berry, for example, suddenly collapsed while working on a television sitcom one day in 1989 at the age of 21. She was rushed to the hospital in a diabetic coma. She had little

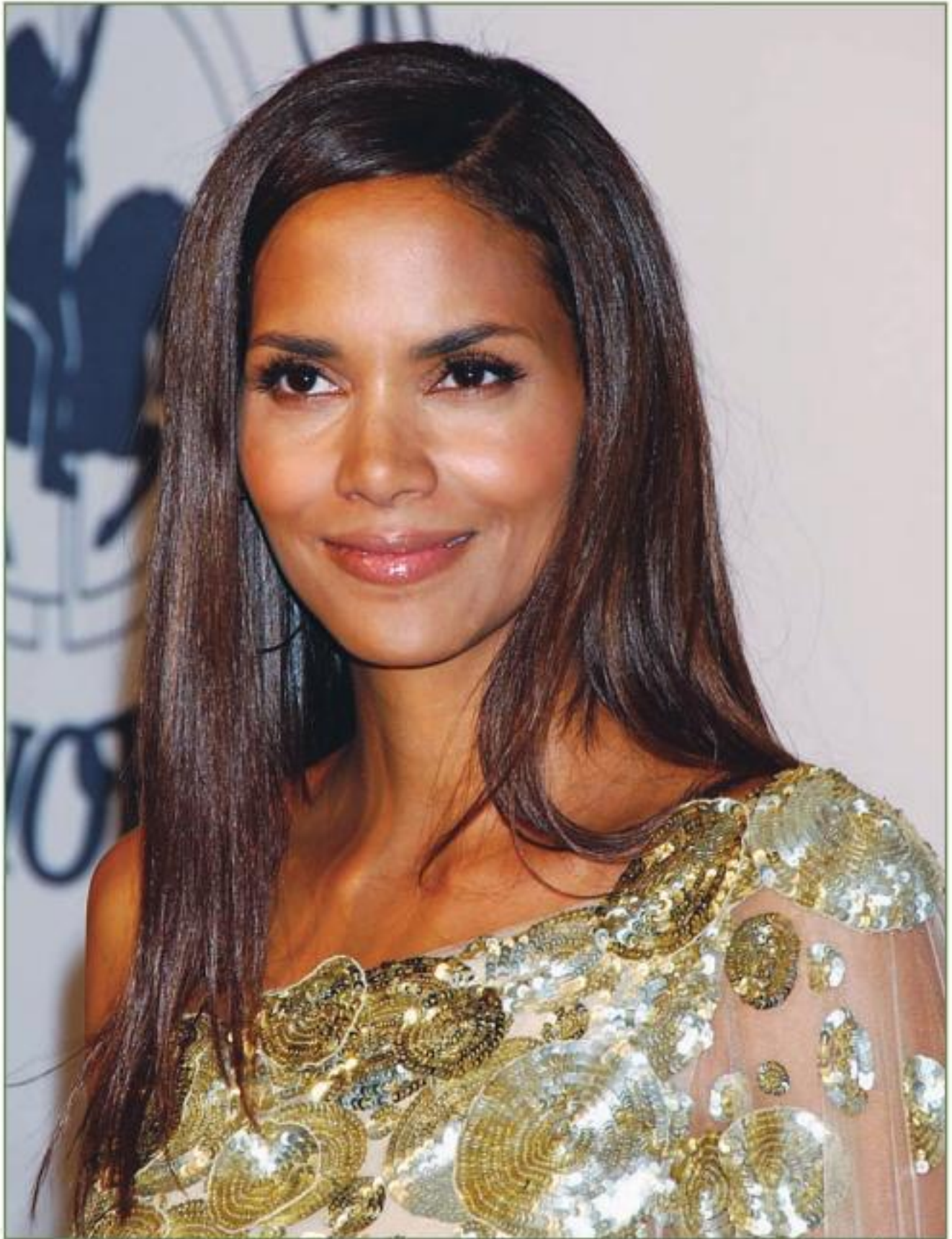


FIGURE 1.1 Actress Halle Berry, winner of the 2002 Oscar for Best Actress, has type 1 diabetes. She is an active volunteer for the Juvenile Diabetes Association.

warning that she was sick, except for feeling very tired and wanting to lie down that day.⁴

Berry's coma was a symptom of uncontrolled type 1 diabetes. Other symptoms are thirst, unusual hunger, weight loss, frequent urination, and tiredness. Sickness, stomach pain, blurred vision, weakness, and dizziness may also occur in type 1 diabetes. All these symptoms arise because the sick person's pancreas has stopped working effectively.

WHAT'S HAPPENING INSIDE THE BODY

The **pancreas** is an organ located behind the stomach. This fish-shaped organ has two main functions. First, it helps the body to digest food by producing enzymes. The enzymes are chemicals that help the intestine to break down food. Most importantly, the pancreas also manufactures **insulin** so that the body can use the food that is eaten. Insulin is a **hormone**, a chemical made by one part of the body that controls the function of another part of the body. Insulin is critical to life. It is the key that enables the body to use the food that is its fuel.

When food is eaten and digested, the nutrients are turned into a special kind of sugar called **glucose**. Glucose is the food and energy for all the **cells** that make up bodies. Human bodies are made of trillions of microscopic cells. Each cell is a tiny factory enclosed in a membrane, somewhat like a balloon. Cells in the lungs breathe; cells in the heart beat; cells in the eyes gather light. Every cell does the work of some part of the body, and every cell requires glucose as energy in order to do its job.

The Insulin Glucose System

Glucose is carried throughout the body by the bloodstream. It is delivered to the cells of the body by the blood, but it

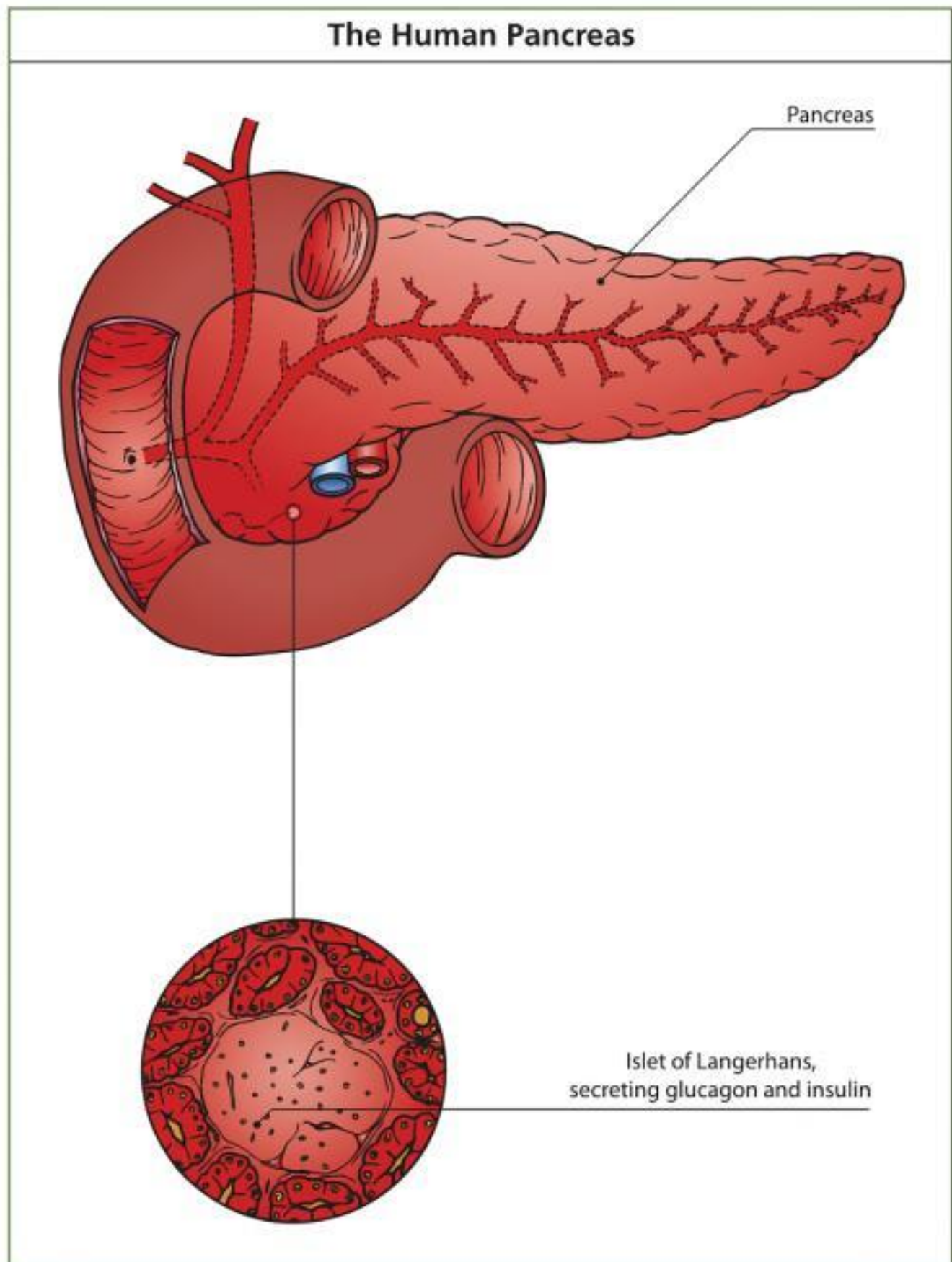


FIGURE 1.2 This image shows the structure of the human pancreas, including the islets of Langerhans.

cannot enter the cells without the help of insulin. Every time food is eaten, glucose enters the blood. The pancreas responds to the presence of glucose by making and sending out insulin. The insulin travels to the cells. Substances called **insulin receptors**, which are on the surfaces of cells, bind together with the insulin, and this unlocks the cell's door to admit the glucose. The cells use the glucose for the energy they need to do their work. Without glucose, cells would starve and die. Without insulin, however, cells cannot get glucose. Without insulin, the body's cells would, in effect, starve to death.

This insulin and glucose system works perfectly in most bodies to keep the cells healthy. The more food that is eaten and digested, the more insulin is made by the pancreas. If no food is eaten, the pancreas turns off insulin production

DIABETES AND THE HALL OF FAMER

Jackie Robinson was the first African American to play major league baseball. He began in 1947 with the Brooklyn Dodgers. Despite being a major star, he faced terrible prejudice and bigotry, which he handled calmly and gracefully. He became a civil rights leader and a hero to many millions. Racism, however, was not the only challenge Robinson had to face. In 1957, shortly after he retired from baseball, he was diagnosed with type 2 diabetes. The disease eventually disabled him and shortened his life during a time when treatments were not as successful as they are today. Robinson's hair turned white, his legs were numb and crippled, he had high blood pressure, and he was almost completely blind before a heart attack killed him in 1972 at the age of only 53.

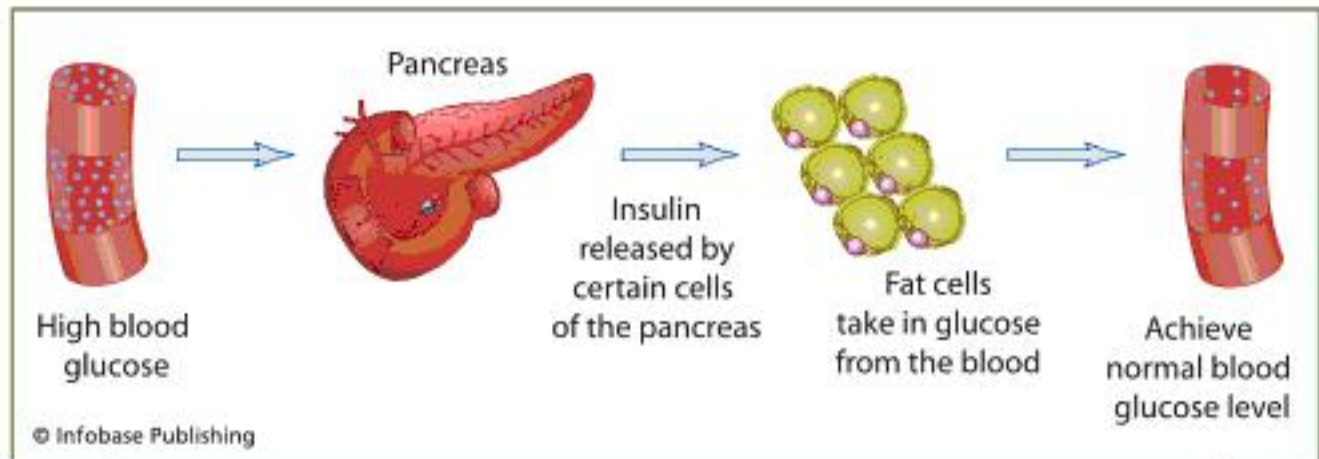


FIGURE 1.3 After a meal, the level of glucose in blood usually rises. In response, beta cells in the pancreas release insulin. Insulin stimulates body cells, such as fat cells and muscle cells, to take up the glucose to be used for energy or storage. As a result, glucose levels in the blood return to normal.

because glucose in the blood is low. A healthy pancreas never allows too much or too little glucose to exist in the blood. Just enough insulin is produced so that the glucose in the blood can be used by the cells. If extra glucose is available (for instance, if a person ate a huge meal), the pancreas directs fat cells and the liver to store it for future use. That way, if a person is doing a lot of work and has not eaten enough, glucose is available to give the muscles the extra energy they need. Insulin keeps the blood glucose level in balance all the time. It ensures that cells never lack energy.

Beta Cells

Insulin is made in special areas of the pancreas called islets of Langerhans. These areas are named after Paul Langerhans, the German scientist who discovered them. Two of the most important kinds of cells in the islets of Langerhans are alpha cells and **beta cells**. Both help the body to control and use its blood sugar. Alpha cells make a hormone called

glucagon. This hormone raises blood sugar if it gets too low. Beta cells produce insulin. Insulin lowers blood sugar by directing cells to use it or store it.

People with type 1 diabetes have a pancreas that cannot make enough insulin because beta cells have been destroyed. If 80% of beta cells die, type 1 diabetes develops, and the pancreas produces either very little or no insulin. Body cells cannot get enough glucose to stay healthy or even survive. Glucose in the blood rises higher and higher without ever entering the cells. This is what makes a person with type 1 diabetes so sick. A person with untreated diabetes is, in a sense, “starving in the midst of plenty,” because the cells are starving no matter how much food the person eats.

High blood sugar causes serious problems, too. Almost every organ in the body is damaged by high levels of glucose in the blood. Kidneys work very hard to filter out the extra sugar in the blood. This makes people have to urinate often and can damage the kidneys, too, as they work overtime to try to clean the blood. Muscles with too little glucose are worn out and tired. In a desperate effort to feed the cells, fat and muscle cells are broken down for the energy they contain. As the body breaks down, the person loses weight. If the diabetes is not treated, every organ in the body will die. A person with type 1 diabetes must get insulin in some way if he or she is to survive.

When type 1 diabetes is diagnosed, doctors prescribe insulin injections. These shots provide the insulin that the pancreas is no longer producing. For the rest of their lives, people with diabetes carefully balance the insulin they inject, the food they eat, and the exercise they get so that they can keep their bodies healthy. Once this is achieved, most can live long, active lives.

TYPE 2 DIABETES

Not everyone with diabetes needs insulin shots. As a matter of fact, according to the CDC, 90% to 95% of people with diabetes do not. These people have a different kind of diabetes, known as **type 2 diabetes**. Type 2 diabetes is also a disease of high blood glucose, but it differs from type 1 in several important ways. People diagnosed with type 1 are usually underweight, for example, while those with type 2 tend to be overweight and physically inactive. Also, type 2 most often appears in people older than 40 years (although it increasingly is found in younger people). It tends to come on much more slowly than type 1, and does not make people so sick so fast. When it does strike, though, it can be just as serious.

Danielle Kazista was a 39-year-old mother of two. For about a year, she just felt “out of sorts.” Month after month, she caught different minor illnesses. She had stomach upsets and headaches frequently. She was always tired and wanted to sleep a lot. Then one day, while she was on a vacation cruise, she fainted after eating a particularly rich, sugary meal. Once she got home, she felt even more run down. She had cramps and diarrhea. She slept almost all the time, just waking up to go to the bathroom. Finally, her doctor tested her blood and urine. He discovered that she had type 2 diabetes. The glucose in her blood was very high. Her urine showed that her kidneys were working so hard to filter out the glucose in her blood that they were not keeping up. Kazista was frightened and could not believe what she was hearing. She left the doctor’s office in despair and cried all the way home.⁵

Singer Patti LaBelle found out about her type 2 diabetes in an even more dramatic way. In 1994, when she was 50 years old, LaBelle was feeling overworked and exhausted.



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by overweight; high-fat, sugary diets and lack of exercise in young people. The only way to stop the dramatic rise in type 2 diabetes in the young is to change this lifestyle. Usually, complications occur after decades of living with diabetes, and that means when people are elderly. Diabetes is becoming a national and even global epidemic, however, and experts believe if diabetes continues to be diagnosed at younger ages, the age at which complications occur will likewise drop in the future.

Diabetes, whether type 1 or type 2, is a serious, lifelong disease. Fortunately, good treatments are available today, and most people can achieve good health. Living with

THE THIRD MAJOR KIND OF DIABETES

Scientists and doctors today recognize a third major type of diabetes. It is called gestational diabetes. This kind of diabetes develops only when a woman is pregnant, and disappears after she has given birth. Gestational diabetes brings on high blood sugar in a woman who has never had the problem before. About 135,000 pregnant women develop gestational diabetes every year. Just as with type 1 and type 2, no one is sure what causes gestational diabetes, but scientists have identified some risk factors. Women who have type 2 diabetes in their families, are overweight before getting pregnant, or are older than 25 appear to have a greater chance of getting diabetes during pregnancy than others. It is also more common in Native Americans, African Americans, and Pacific Island peoples. Even though gestational diabetes usually goes away once the baby is born, doctors are concerned about it. If it is not treated, it can be dangerous for the baby, and it signals a risk for the mother to develop type 2 diabetes later in life.

diabetes, however, is complicated and life-changing. This volume focuses on the genetic basis of diabetes—what scientists currently know and what they hope to learn in the near future about the relationship between diabetes and our genes. The discussion begins in Chapter 2 with how diabetes was discovered and how it is currently treated. Chapter 3 explores how genes and DNA work. Genetic engineering of human insulin, which has transformed treatment, is described in Chapter 4. The following two chapters look at the genetic basis of type 1 and type 2 diabetes, and Chapter 7 explores gene therapy for diabetes, a promising new area of research. Chapter 8 examines stem cell research and how it may someday lead to a cure for diabetes. That cure has been a long time coming. People have suffered with diabetes for thousands of years, and for most of that time, science had few answers.

2

TREATING DIABETES

Today, young people like Daniel, Kassy, and Amanda are leading normal, healthy lives. Halle Berry and Patti LaBelle are active entertainers, and Danielle Kazista is a grandmother of six who is successfully controlling her diabetes. Medical science enables most people with diabetes to lower their blood sugars and be healthy. The treatment of diabetes, however, can be difficult, especially over the long term. Modern science continues to search for better treatment methods.

Normalizing blood sugar is the major goal of all diabetes treatment. Nowadays, good control of blood sugar keeps people with diabetes healthy, but this was not always the case. Throughout most of human history, doctors had no way to alter blood sugar levels. Diabetes has been around since ancient times, and until the twentieth century, it was an invariably fatal disease.

ANCIENT KNOWLEDGE OF DIABETES

More than 3,500 years ago, Egyptian physicians described a disease marked by excessive urination. Ancient Hindu physicians often diagnosed diabetes because ants and flies were attracted to the urine of those affected. They





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chemicals in their lab. Then they had DNA sequences that a bacterium's RNA could read.

Next, they cut the plasmids with restriction enzymes and inserted the human DNA sequence. The plasmids were

FRANKENSTEIN'S BACTERIA?

Recombinant DNA was a suspect and frightening technology when it was first introduced. The public, many politicians, and some scientists worried that "playing God" with bacterial genes could result in a monstrous disease. Throughout the world, governments stepped in and placed restrictions and regulations on any laboratory that was recombining human DNA. These restrictions did not affect Genentech because researchers there were making copies of DNA rather than using DNA itself. It was a loophole that made it easier for them to develop human insulin. Biogen, an English biotechnology company founded around the same time as Genentech, also was trying to make human insulin. Its scientists, however, were using human DNA. They had to function under containment regulations that ensured no killer virus or bacterium could escape into society. They were required to work in a biological warfare laboratory where they could be sealed off from the world. Researchers had to wear special clothing, sterilize everything that went into and out of the lab, and shower before they left each day. These restrictions slowed them down so much that they lost the race to clone human insulin to Genentech. Today, this simple recombinant DNA technology is considered so safe that college students can experiment with the techniques. It is routinely used to make human insulin, but in the 1970s, many people were wary of recombinant DNA.



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that carries only the coding for insulin and is cleaned of introns. This DNA sequence is pasted into the bacteria or yeasts, which then produce the proteins for insulin.

Almost all the insulin in use in the United States is synthetic insulin. It is usually called Humulin™, which is the name given to it by Eli Lilly, the company that supported Genentech financially when Boyer, Cohen, and Swanson were first struggling to produce human insulin. (It was also the company that produced and sold the animal insulin used for decades before biotechnology became a reality.) Humulin™ comes in several different forms now, too. One form, called Humalog™, is referred to as the mealtime insulin. It goes to work within minutes of injection so that a person with diabetes can inject and then eat right away. It acts almost as fast as insulin produced by the pancreas. Slow-acting Humulin™ is released steadily into the body over several hours. It takes longer to reach the bloodstream and is powerful for a longer time than the fast-acting Humalog™. With a combination of the two, a person with diabetes can test blood sugars and then make a decision to inject whichever insulin is needed. This helps prevent hypoglycemic episodes (which could result from fast-acting insulin) and also allows a sudden decision to eat a meal, which could cause hyperglycemia without an extra dose of insulin.

Genetic engineering for human insulin is a true success story and has improved the treatment of diabetes around the world. It is still just a treatment, however, and it did not lead to an understanding of what causes diabetes. Even the identification of the gene that codes for insulin production does not explain why people get diabetes. The next goal of genetic scientists is to identify the genes related to diabetes and to find the mutations or variations in the genes that actually contribute to or cause diabetes.



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scientist suggests that diabetes genes are like a loaded gun. Something in the environment has to pull the trigger before type 1 can develop. Around the world, different scientific teams search for both environmental and genetic factors that may increase the chances of getting type 1 diabetes.

IMMUNE SYSTEM GENES

So far, genetic scientists have found about 18 regions on the human genome that seem to increase the risk for developing type 1 diabetes. These regions have multiple genes, most of which have not yet been identified.

Each human chromosome is one long strand of DNA. The chromosome pairs have been numbered by genetic



is called a double-blind study. Neither the subjects nor the researcher knows who is getting the insulin and who is getting the placebo. When the study is over, Finnish scientists hope to know if giving insulin before type 1 develops can prevent it from occurring. This idea is based on some animal studies that suggest that extra insulin can calm the immune system and slow or prevent attacks in the future.

Other Finnish studies have examined flu epidemics and early childhood diet to see if they increase the risk for type 1 diabetes. One study examined the effect of flu vaccines on the risk for type 1, but it found no difference among children who were vaccinated and those who were not. Unraveling the cause of Finland's growing population of diabetes in its youth is proving very difficult.



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too. Some DQ genes protect against diabetes, but others seem to increase the risk, since they show up more often in people with type 1 diabetes than in healthy people. So far, it is very difficult for scientists to tell which kind of genes are more important—the DR genes or the DQ genes. The variations that increase risk are too often linked and inherited together. All scientists can say is that inheriting these gene variations increases susceptibility to type 1 diabetes.

ANTIBODIES AGAINST BETA CELLS

One symptom that is linked with HLA genes is the development of **autoantibodies**. These are antibodies made by the immune system against the beta cells of the pancreas. They indicate that the immune system has mistakenly recognized beta cells as foreign invaders and attacked them. The antibodies are ready and waiting to attack any other beta cells that might “invade” in the future. Scientists can identify these antibodies in people’s blood. Interestingly, these antibodies can be found in people who have not developed type 1 diabetes. They have been found in family members of people with type 1 diabetes, and they have been found in people who later developed type 1 diabetes. (Beta cells can be attacked and destroyed without causing diabetes. Type 1 diabetes does not develop until 80% of the beta cells have been destroyed.)

In 2006, P.J. Bingley and E.A. Gale at the University of Bristol in England did a study of people who had autoantibodies to beta cells. There were 549 people in the study, from 20 different countries, and all of them had a parent or sibling with type 1 diabetes. The people were of all different ages, both children and adults. The scientific team



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be what triggers type 1 diabetes, the researchers will also interview each mother about her pregnancy. They will ask for all the details of her pregnancy, including what she ate and if she ever got sick.

The goal of TEDDY is to try to find changes in the immune system that occur in the first years of life. If the scientists can link these changes both to genes and to environmental factors, they may actually discover the true causes of type 1 diabetes. But as one TEDDY scientist says, “The bottom line is that it’s not going to be a simple answer.”¹⁸



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slow metabolic rate? Since 1984, Eric Ravussin, an NIDDK scientist, has been trying to answer that question. Although he has not yet found the gene or genes responsible, he believes that the answer is a “thrifty gene.” The idea of a thrifty gene was first proposed in 1962 by geneticist James V. Neel, who hypothesized that those individuals with the thrifty gene were very efficient at taking in and using food. For most of humanity’s time on earth, conditions mostly cycled between feast and famine. A gene variant that conserved blood sugar and slowed metabolism may have been a lifesaver. It probably protected people from starvation.

For hundreds of generations, people like the Pima Indians were farmers and hunter-gatherers. They had to survive under difficult conditions. Some seasons or years, they were very successful in getting enough food, but sometimes crops failed and animals were hard to find. Those who survived this feast or famine cycle were the ones able to use food most efficiently. Their cells naturally became insulin resistant in order to cope with the diet. People with slow metabolic rates were able to continue functioning through the lean times. Their thrifty genes let them easily store fat during times of plenty so that they could live off this fat when no food was available. Since they were successful at surviving, they were more likely to have children than people who starved to death. They passed the thrifty gene on to their children.

Until the end of World War II, Pima Indians lived a traditional tribal lifestyle. Their diets contained only about 15% fat. They ate mostly lean proteins, grains, and vegetables. Even though they no longer lived a feast or famine lifestyle, the thrifty gene did them no harm. After World War II, however, Pima Indians on the Gila River began to eat a more American diet. There was always plenty to eat, and much of the food was high in calories and fats. Today, Pima



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because so many are apparently involved. Scientists have found genetic variations that occur with insulin resistance and type 2 diabetes on many chromosomes, but the interaction is so complicated that they are far from identifying the actual genetic causes of type 2 diabetes. So far, they have found about 20 different areas of the genetic map that seem to increase the risk of insulin resistance and type 2 diabetes. They continue to search for genetic variations and to try to understand what they do in the body, but it is slow going.

One gene variant discovery was reported in 2006. It was found by a large study group, the Diabetes Prevention Program. The gene, named TCF7L2, apparently is involved in producing insulin. People with a common variant of this gene had decreased insulin secretion, which is associated with an increased incidence of diabetes. From

DANGER FOR MANY PEOPLES

Native, or indigenous, people throughout the world face a devastating epidemic of type 2 diabetes when they eat a Western diet. Scientist Paul Zimmet calls the problem the “coca-colonization” of cultures. In Australia, where Zimmet lives, about 20% of the indigenous people have diabetes. In Nauru, a Pacific Island community, almost 50% of the people have diabetes. In Canada, 30% of the native peoples have diabetes. On Australia’s Torres Strait Island, 30% of the people have diabetes. Even in China, as it opens up to Western culture, the rate of type 2 diabetes is skyrocketing. The rate of type 2 diabetes for indigenous peoples is disastrous and may mean the extinction of some cultures within 100 years if something does not change. Zimmet says it is the biggest epidemic the world has ever seen.



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age people to work to lose weight, eat a healthy diet, and get enough exercise. Long before insulin resistance or diabetes developed, the risk could be diagnosed. ChemGenex scientists believe that a PSARL gene test could delay or prevent type 2 diabetes. The test is neither easy nor inexpensive yet. Even though scientists have sequenced the whole human genome, they are not used to having to identify a variation in just one gene. ChemGenex, however, predicts it will have such a test by about 2009. If they do, it will be the first genetic test for type 2 diabetes, and it may help prevent the disease in vulnerable people.

GENE MARKERS AND INTERVENTION

A team of scientists in Italy tried to prevent type 1 diabetes by identifying genetic markers of risk, too. They concentrated on HLA genes that seem to cause immune system attacks. Between 1999 and 2002, the team tested newborn babies and selected those with the HLA variations that increase risk for type 1 diabetes. Then, they set up an experiment to see if early use of cow's milk causes the development of the autoantibodies that often lead to diabetes. The study was named PREVEFIN. The scientists checked the babies for two years. Those who were bottle fed were given extra vitamin D. Vitamin D is believed to have a protective effect for beta cells. Also, these babies were fed a formula made from a special cow's milk that did not contain casein. Casein is the protein that scientists suspect may cause antibodies to develop in vulnerable children. It is the foreign food protein typically encountered first by infants. After two years, the PREVEFIN scientists tested the children for the antibodies that are always found before type 1 diabetes begins. Breastfed babies had no antibodies to beta cells, and babies that drank the special cow's milk did not develop beta cell



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However, the Pittsburgh scientists also discovered a major problem. They tested the drugs that stop the immune system from attacking transplanted cells in normal, healthy rats. These rats all developed severe diabetes and died. Stewart looked at these results and worried that the same thing was happening in people who had to use the powerful drugs for islet cell transplants. Immune system drugs could be hurting islet cells. This could explain why islet cell transplants do not last. It could explain why most transplant patients needed to go back to insulin shots after only two years. If immune system drugs damage beta cells, a true cure for type 1 diabetes may have to involve gene therapy for the immune system.

GENE THERAPY FOR THE IMMUNE SYSTEM

A NOD mouse experiment by University of Pittsburgh scientist Khaleel Rehman Khaja might provide an answer. Khaja added a gene named IL-4 to a virus. IL-4 codes for proteins that make regulatory T cells. These are cells that regulate the immune system by suppressing its activity when needed. Khaja injected the virus into the beta cells of NOD mice. The IL-4 genes seemed to act like an immune system switch and prevented the mice from developing high blood glucose levels or hyperglycemia. The mice stayed healthy, and T cells did not attack their beta cells. Khaja believes a technique like this could also prevent people at high risk for type 1 from developing diabetes.

In 2006, Matthias von Herrath, an expert on type 1 diabetes, cured NOD mice of their diabetes by getting their immune systems to tolerate rather than attack beta cells. His approach combined two treatment approaches. He treated the mice with a kind of “anti-antibody” that calms down the immune system, and also added a vaccine that induces regu-



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yet able to proliferate and differentiate, they are the very stuff of life. Without them, human beings would not develop. They are the process by which life begins.

TOTIPOTENT STEM CELLS

A zygote is really a super stem cell. The zygote splits into two cells, each with all the genetic information of the parent cell. The two cells divide again, becoming four and then eight. During these first few cell divisions, the cells are **totipotent** stem cells. Each cell is capable of giving rise to every cell needed to grow an embryo, a fetus, and then a newborn baby. At the next cell divisions, when there are 16 cells, totipotency is gone. The cells have already begun to slightly differentiate. By the fourth day of growth, the new life is a ball about 120 cells large. It is called a **blastocyst**. The outer layers of the blastocyst attach to the wall of the mother's uterus and eventually become the placenta and umbilical cord for the growing embryo. These are the baby's lifelines through which it receives food and oxygen from the mother's body.

PLURIPOTENT STEM CELLS

The inner cells of the blastocyst are **pluripotent** stem cells. These cells cannot differentiate into all the cells needed to grow a new life, such as the placenta, but they are capable of giving rise to any cell in the body. If the outer cells successfully implant in the uterus, the pluripotent stem cells of the blastocyst continue to multiply and then group together, form layers, and begin specializing into all the organs, tissues, and body parts of a growing embryo. By the time eight weeks have passed, the embryo is a fetus, and the pluripotent stem cells have disappeared. They have specialized into



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cells. Stem cell scientists around the world are experimenting with adult stem cells to see if they can be persuaded to wake up, turn on, and heal injuries or grow new body cells. There have been some exciting successes with animals, but for diabetes, as well as many other severe diseases, adult stem cells do not seem to be the answer for most scientists. Embryonic stem cells, with their flexibility, pluripotency, and ability to differentiate into any body cell, seem to hold the most promise for cures.

ES CELLS IN THE LAB

Scientists can remove embryonic stem cells from the blastocysts of animals or people and grow them in their laboratories. In the case of humans, the ES cells are retrieved from the unwanted and often discarded zygotes stored at in vitro fertilization clinics. These are zygotes formed in lab petri dishes for couples who have trouble conceiving. In vitro clinics usually prepare several fertilized eggs that are not implanted in the mother's uterus. They are extras, in case the first efforts at pregnancy do not work. With the couple's permission, these are the zygotes used by stem cell scientists.

The zygotes are grown to the blastocyst stage in a special nutrient bath in petri dishes. Then the ES cells are moved to new petri dishes, where they are bathed in a chemical "soup" that encourages them to divide and grow. Scientists are able to grow millions of ES cells this way and to keep them alive indefinitely. The cells can be encouraged to differentiate into different body cells with other nutrient chemicals. These **stem cell lines** are the raw material with which scientists believe they will someday cure many diseases, including diabetes.



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with the new nucleus, would be encouraged to divide and grow into a blastocyst. (This can be done without fertilization by a sperm; a chemical or electrical stimulation is used to start the growth.) Once the blastocyst is grown, its stem cells would be removed and grown into a stem cell line in the lab. The stem cells could now be differentiated into beta cells or any cells, each an exact genetic match to the patient who gave the skin cell. The beta cells would now be available as a treatment that would not be attacked by the body's immune system. The treatment could be repeated every year or so, keeping the patient healthy and normal for life.

THE MORAL DILEMMA OF STEM CELLS

Scientists can imagine unlimited future stem cell treatments, and many have already been successful with animal tests. They predict that stem cells will revolutionize medicine and make diabetes a disease of the past. When, or even if, this will happen, however, is not certain. Many thoughtful people are opposed to human embryonic stem cell research. Embryonic stem cell research means destroying an embryo, and people who are opposed believe this means killing some lives in order to save others.

Many are also opposed to the use of therapeutic cloning techniques. The process of therapeutic cloning is the same that has been used to clone animals. Theoretically, humans could be cloned if the egg were placed in a uterus to grow instead of being grown to the blastocyst stage and used in the lab. Almost no one believes such reproductive cloning is either safe or moral. Stem cell scientists say cloning a human being is too dangerous. Too often in animals the attempts lead to death for the baby and the mother. They argue that therapeutic cloning has a much different goal than reproductive cloning, but the opponents are not convinced. Stem



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Type 2 diabetes A disease characterized by high amounts of glucose in the blood caused by the body's failure to produce enough insulin or to use the insulin it does produce. Type 2 diabetes is characterized by insulin resistance.

Unspecialized Without the ability to perform a specific body function; a property of stem cells. However, unspecialized stem cells can give rise to specialized cells.

Zygote A fertilized egg.

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