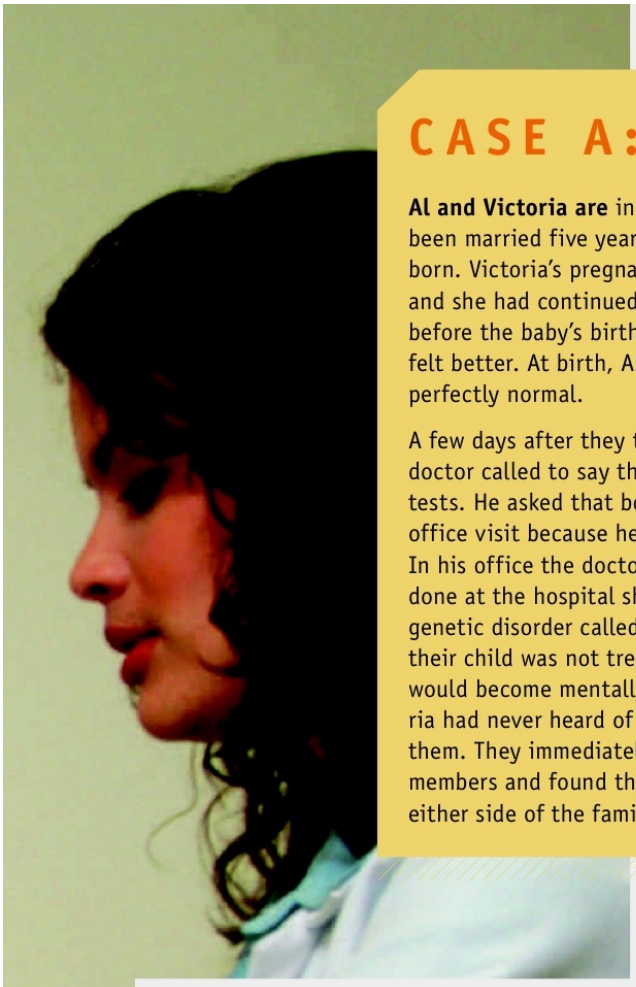

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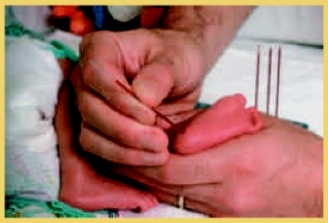
Genetic Testing Usually Involves Taking a Blood Sample

CASE A: Hospital Tests Babies

Al and Victoria are in their early 30s and had been married five years when their first child was born. Victoria's pregnancy was perfectly normal, and she had continued working until one week before the baby's birth. She said she had never felt better. At birth, Al and Victoria's son appeared perfectly normal.

A few days after they took the baby home, the doctor called to say that the baby needed more tests. He asked that both parents come to the office visit because he wanted to talk to them. In his office the doctor said that a blood test done at the hospital showed that the child had a genetic disorder called phenylketonuria (PKU). If their child was not treated using a special diet, he would become mentally retarded. Al and Victoria had never heard of PKU, and this news upset them. They immediately called around to family members and found that only a few relatives on either side of the family had ever heard of PKU, and none knew of any family member with this disorder. Al and Victoria wondered how a genetic disease that no one in their family had ever had could suddenly appear in their child. They made an appointment for another visit with the doctor and, in the meantime, began reading about PKU.



Dan McCoy/Getty Images

A heel stick is the most common method of obtaining a blood sample for testing in newborns.

Some questions come to mind when reading this case. Before we can address these questions, let's look at what genetic testing is, how it is used to diagnose genetic diseases, and the future prospects for this technology.

8.1 What Is Genetic Testing?

This chapter will discuss several methods used to determine whether someone has or is at risk for a genetic disease. Before exploring the rationale, methods, and issues involved, let's define the differences between the two major types: genetic testing and genetic screening. **Genetic testing** determines whether someone has a certain genotype—in other words, what is his or her genetic makeup? Genetic testing identifies individuals in the following groups:

1. those who may have or may carry a genetic disease
2. those who are at risk of having a child with a genetic disorder
3. those who may have a genetic susceptibility to drugs and environmental agents

Genetic screening is done on large populations rather than on individuals. The goals of genetic screening are more limited; it identifies people in the following groups:

1. those who may have or may carry a genetic disease
2. those who are at risk of having a child with a genetic disorder

Genetic testing is most often a matter of individual choice, whereas genetic screening is often mandated by law. Genetic testing can have a serious impact on the lives of individuals and their families, as in the following situations:

1. Identification of a person who has or is at risk for a genetic disorder often leads to the discovery of other affected or at-risk family members.

genetic testing testing for genetic conditions

genetic screening large-scale genetic testing

2. Testing for some disorders can identify a person who is healthy now but will develop serious or fatal genetic disorders in later life. When the condition is fatal—for example, Huntington disease, as in Alan's family (see Chapter 4)—this information often has serious personal, family, and social consequences.
3. The results of genetic testing may have a direct impact on siblings and the children or grandchildren of the person being tested.

Genetic counselors work with people who are about to have or have had genetic testing to explain the tests and the results and to help them make decisions based on the results.

What types of genetic testing are available?

Several forms of genetic testing are currently being used:

1. **Prenatal diagnosis**—to determine the genotype of a fetus, such as testing for sickle-cell anemia.
2. **Carrier testing**—to test members of a family with a history of a genetic disorder such as cystic fibrosis to identify heterozygotes and to determine their chances of having an affected child.

prenatal diagnosis diagnosis of conditions in a developing fetus

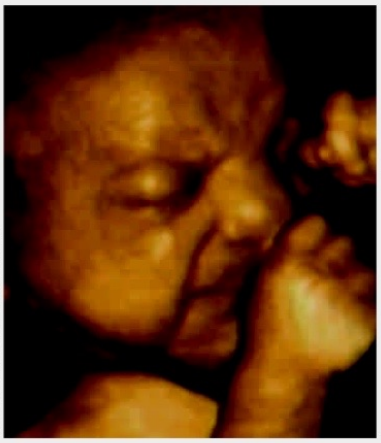
carrier testing a genetic test for carrier status of a recessive disorder

presymptomatic testing genetic testing before symptoms manifest themselves

ultrasonography, or ultrasound a prenatal test that uses sound waves to visualize an unborn fetus

amniocentesis a prenatal test that involves removal of amniotic fluid

chorionic villus sampling (CVS) a prenatal test that removes a small sample of villi



Dr. Benoit/Mona Lisa/PhotoTake

Figure 8.1
Three-dimensional ultrasounds show details of the fetus's facial features.

3. **Presymptomatic testing**—to identify individuals who will develop disorders in midlife, such as Huntington disease or adult polycystic kidney disease.

8.1 Essentials

- **Genetic testing determines what genotype a person has.**
- **Genetic testing can be done on fetuses, newborns, children, and adults.**

8.2 Why Is Prenatal Genetic Testing Done?

Prenatal genetic testing is used to detect genetic disorders and birth defects in a developing fetus. More than 200 single-gene disorders can be diagnosed by prenatal testing. Some of these are listed in Table 8.1.

In most cases, testing is done only when there is a family history or some other risk factor is identified (such as the age of the mother). Remember from Chapter 4 that families

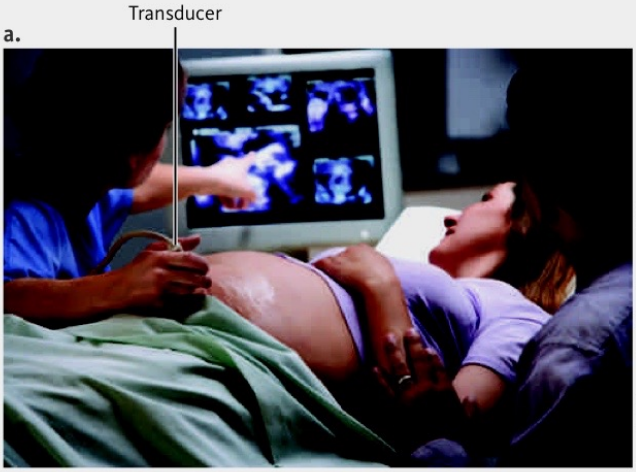
Table 8.1 **Some Genetic Disorders That Can Be Diagnosed by Genetic Testing**

Disorder	Incidence	Inheritance Pattern
Cystic fibrosis	1 in 2000 Caucasians	Autosomal recessive
Congenital adrenal hyperplasia	1 in 10,000	Autosomal recessive
Duchenne muscular dystrophy	1 in 3500 male births	X-linked recessive
Hemophilia A	1 in 8500 male births	X-linked recessive
Alpha and beta thalassemia	Varies	Autosomal recessive
Huntington disease	1 in 10,000	Autosomal dominant
Polycystic kidney disease	1 in 1000	Autosomal dominant
Sickle-cell anemia	1 in 400 African Americans	Autosomal recessive
Tay-Sachs disease	1 in 3600 Ashkenazi Jews and French Canadians; 1 in 360,000 in the general population	Autosomal recessive

who carry conditions inherited as autosomal recessive disorders such as sickle-cell anemia may not know that the mutant allele runs in their family until a child is born with the condition. The parents may be tested to determine whether they are heterozygous carriers of the disease before they conceive. If tests reveal that both parents are carriers, the fetus has a 25% chance of being affected with the condition.

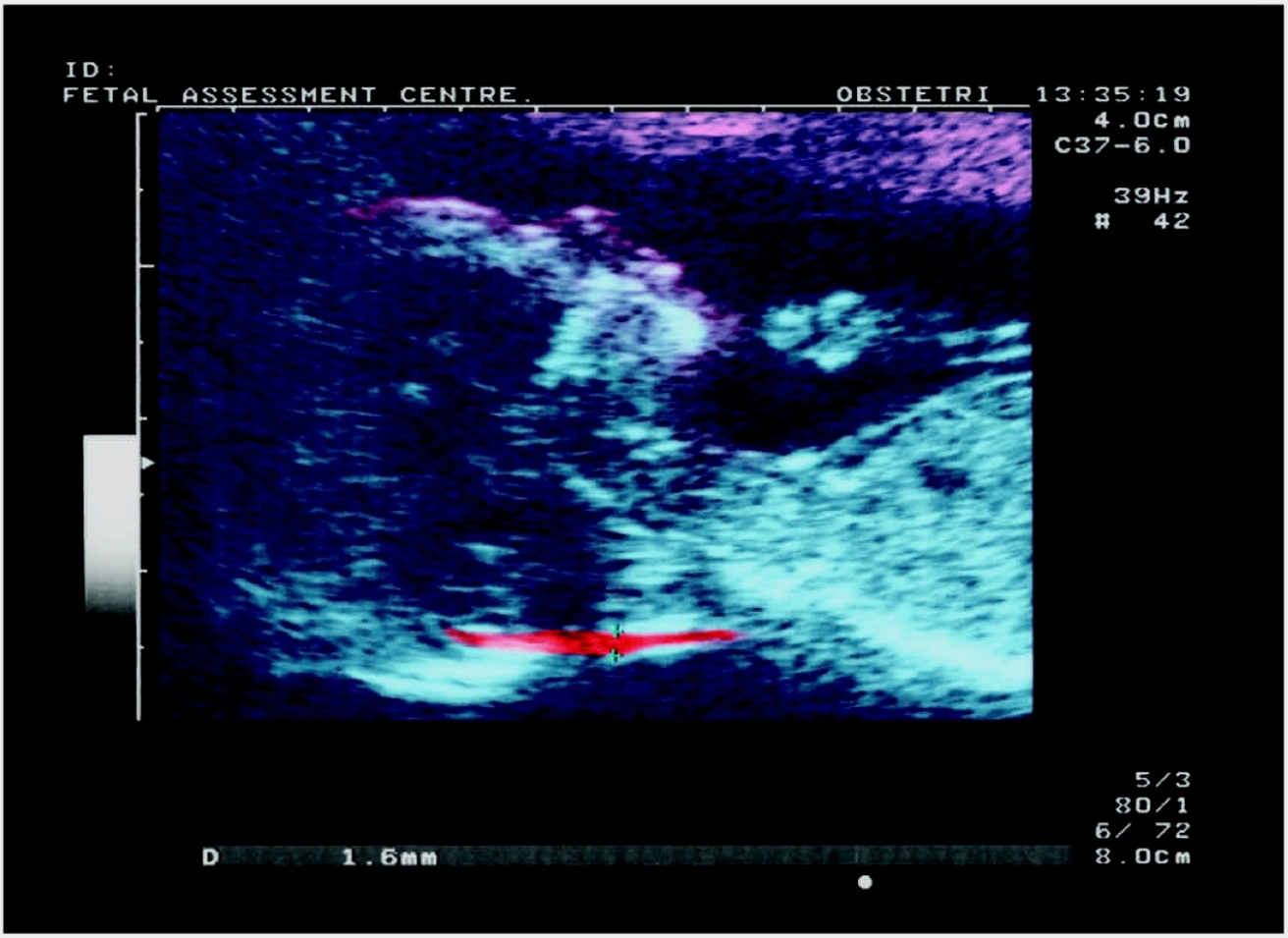
In Chapter 3 we discussed a technique known as **ultrasound** (see Figure 8.1), a method that can provide some information about the health of the fetus. But for conditions caused by chromosomal aberrations, such as Down syndrome (trisomy 21), chromosome analysis is the most direct way to identify an affected fetus. Because the risk of Down syndrome increases dramatically with the age of the mother (see Chapter 3), chromosomal analysis of fetal cells is recommended for all pregnancies in which the mother is age 35 or older. Prenatal testing for any genetic disease requires a sample of cells from the fetus, which can be obtained by using **amniocentesis** or **chorionic villus sampling (CVS)**, as discussed in Chapter 3.

a.



Jose Luis Peaez, Inc./Blend Images LLC

b.



Science Photo Library/Photo Researchers

Figure 8.2 **Ultrasonography** (a) Ultrasonography (ultrasound) is a noninvasive testing procedure based on sonar technology originally developed for the military to find submarines underwater. A transducer is placed on the abdomen over the uterus. The transducer emits pulses of high-frequency sound; the reflected sound waves are converted into images and displayed on a screen. Many women routinely have ultrasounds during pregnancy to monitor the development of the fetus, determine its sex, and check for problems. (b) Ultrasound can also be used to diagnose some genetic disorders, including Down syndrome. In the ultrasound below, extra skin at the fold of the neck is outlined in red. This condition is associated with a Down syndrome fetus.

How is ultrasound done? The procedure for ultrasound is shown in Figure 8.2a, page 167. Ultrasound is one of the prenatal tests used to diagnose genetic disorders. It can be used to identify trisomy 13, trisomy 18, and, to a lesser extent, trisomy 21 (Down syndrome) because each of these disorders has unique physical traits that can be seen via ultrasound. For example, in Down syndrome, affected children often have a thick fold of skin in the neck region. This can be seen in ultrasound, and amniocentesis can confirm the diagnosis. An ultrasound image of a fetus with a neck fold (outlined in red) is shown in Figure 8.2b.

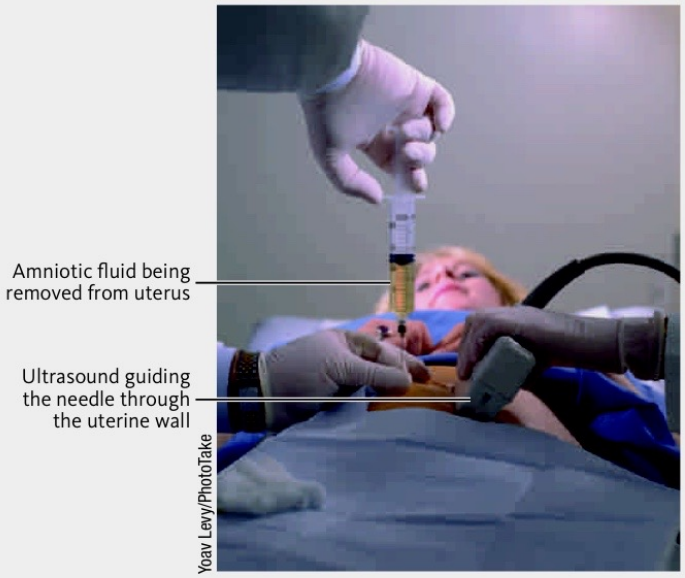
How is amniocentesis done? The procedure for amniocentesis is shown in Figure 8.3 and was briefly described in Chapter 3. More than 100 disorders can now be diagnosed by amniocentesis. The cells retrieved by this method can be analyzed to detect biochemical disorders, chromosomal abnormalities, and the sex of the fetus.

When is amniocentesis used? Amniocentesis carries a small risk of maternal infection and a slight increase in the probability of a spontaneous abortion. To offset these risks, amniocentesis is normally used only under certain conditions:

1. When the mother is age 35 or older. Because the risk of having a child with chromosomal abnormalities increases dramatically after age 35, amniocentesis is recommended for pregnant women who are age 35 or older. Most amniocentesis procedures are performed because of advanced maternal age.
2. When the family has a previous child with a chromosomal abnormality. The recurrence risk in such cases is 1 to 2%.
3. When a parent has a chromosomal abnormality. This can cause an abnormal karyotype in the child, and amniocentesis should be considered.
4. When the mother is a carrier of an X-linked disorder.

chorionic villi finger-like projections of the fetal chorion that work their way into the wall of the uterus

Figure 8.3 **Amniocentesis** As discussed in Chapter 3, amniocentesis is one way fetal cells can be collected for prenatal testing. First, the fetus and the placenta are located by ultrasound and a needle is inserted through the abdominal wall, avoiding the fetus and the placenta. Approximately 10–30 ml of amniotic fluid is removed. Amniotic fluid is mostly fetal urine containing cells shed from the fetus's skin. The cells are isolated from the fluid by centrifugation, grown in the laboratory, and used to construct a karyotype (see Chapter 3). Amniocentesis is usually not performed until the 16th week of pregnancy.



How is chorionic villus sampling (CVS) done? Chorionic villus sampling (CVS) is another method of prenatal diagnosis. After implanation and formation of the chorion by the fetus, cords of cells from the chorion grow into the uterine wall, forming finger-like structures called **chorionic villi**. Eventually, the fetal chorionic villi and maternal tissue combine to form the placenta (Figure 8.4). Cells from the villi are removed by suction during CVS (Figure 8.5). Enough material is usually obtained to allow karyotype preparation, biochemical testing, or extraction of DNA for molecular analysis.

Because tissue is taken directly from the fetus itself, CVS has several advantages over amniocentesis:

1. CVS is performed earlier in the pregnancy (8 to 10 weeks) than amniocentesis (16 weeks). This allows the patient to find out test results earlier.
2. Because placental cells are already dividing, karyotypes are available within a few hours or a few days. With

Figure 8.4 **An Early Embryo Surrounded by Its Tissues** The chorionic villi are embryonic tissues that can be sampled for genetic testing.

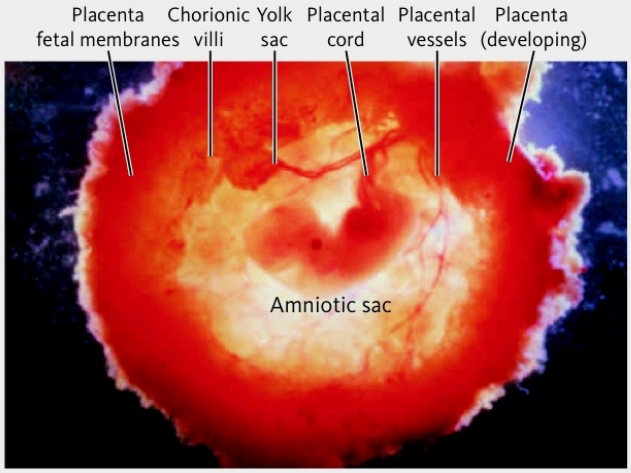
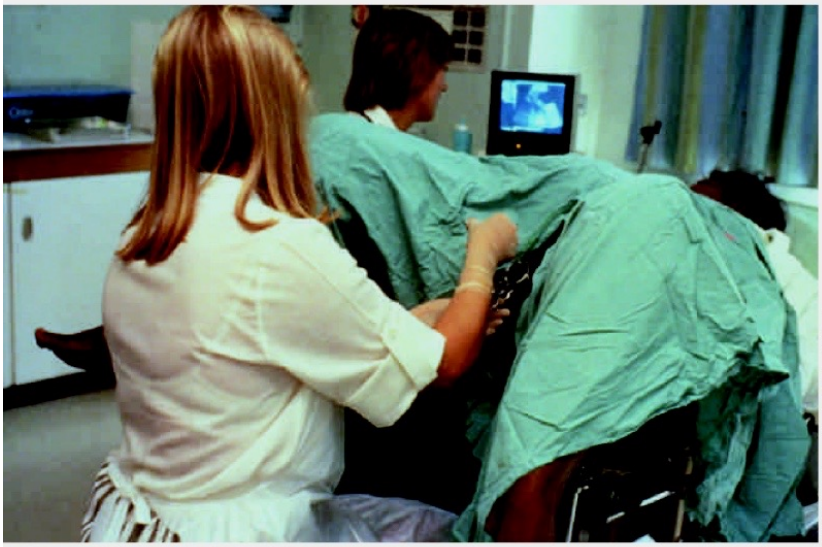


Figure 8.5 **Chorionic Villus Sampling** As discussed in Chapter 3, during this procedure, a flexible catheter is inserted through the vagina or abdomen into the uterus, guided by ultrasound images. A sample of the chorionic villi (fetal tissue that forms part of the placenta) is removed by suction. The cells of the villi are used for karyotype preparation, biochemical testing, or DNA extraction for genotype analysis.



NMSB/Custom Medical Stock Photo

amniocentesis, fetal cells must be stimulated to divide and grown in the laboratory for several days before a karyotype can be prepared.

When is CVS used? In the past, CVS was used less frequently than amniocentesis because of its increased risk of spontaneous abortion. However, if the procedure is performed at a major medical center, the risks are similar to those associated with amniocentesis. CVS offers early diagnosis of genetic diseases, and if termination of pregnancy is elected, maternal risks are lower at an earlier stage of pregnancy. The conditions under which CVS is used are similar to those for amniocentesis (Table 8.2), but because it can be used earlier in pregnancy, some couples choose CVS if they know they are at risk of having a child with a genetic condition.

Are there less invasive methods for prenatal genetic testing? Realizing that amniocentesis and CVS carry a 0.2 to 0.3% risk of miscarriage, researchers are working to develop new, less-invasive ways of prenatal testing. As discussed in Chapter 3, one of these less-invasive methods involves recovering fetal cells or fetal DNA from the mother's blood, which minimizes risk to both the mother and the fetus because all that is necessary is a sample of blood from the pregnant woman.

Several types of fetal cells enter the maternal circulation, including:

1. placental cells
2. white blood cells
3. immature red blood cells with nuclei

These cells probably begin to enter the mother's bloodstream in detectable amounts between the 6th and 12th weeks of pregnancy.

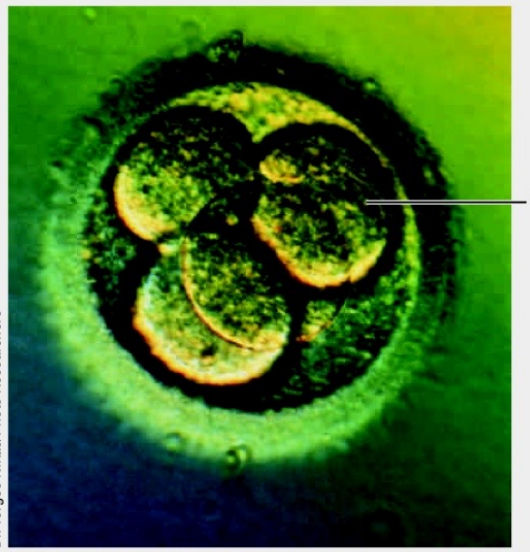
A problem with using fetal cells from the mother's circulation is that only 1 in every 100,000 cells in the mother's blood is a fetal cell. Collecting enough fetal cells from a blood sample is one of the challenges facing those working to develop this technique. Fetal cells collected this way have been used to diagnose some genetic disorders, including sickle-cell anemia, and chromosomal abnormalities, but the method needs further development before being widely adopted.

The amniotic fluid surrounding the fetus also contains fetal DNA (called free fetal DNA or ffDNA) produced when fetal cells break down. The DNA is released as chromosomes become fragmented. The ffDNA can cross the placenta and enter the mother's bloodstream. Recent breakthroughs in the use of ffDNA to detect genetic disorders in the fetus are discussed in Chapter 17.

Table 8.2 **Comparison of Prenatal Diagnosis Tests**

	Ultrasound	Amniocentesis	CVS
When do we test?	Week 18	Week 16	Week 11
When do you get the results?	Immediately	Week 18	Week 12
What does it test for?	Structural problems such as limb growth, size of head, and heart abnormalities	Chromosomal abnormalities, biochemical disorders, fetal genotype	Chromosomal abnormalities, biochemical disorders, fetal genotype
With whom do physicians use this procedure?	Most pregnant women	Women age 35 and older	Women at high risk for having a child with a genetic disorder
Chance of miscarriage?	None	0.2–0.3%	0.2–0.3%

Figure 8.6 **An Early Embryo Composed of Several Blastomeres**



Dr. Yorgos Nikas/Photo Researchers

Can embryos be tested before they are implanted in the mother? In Chapter 1, we discussed the use of preimplantation genetic diagnosis (PGD) for sex selection. This test can also be used to diagnose genetic disorders in the earliest stages of embryonic development. Here we will focus on the use of PGD to detect genetic disorders.

In vitro fertilization (IVF) always precedes analysis by PGD. For IVF, eggs are collected, fertilized, and allowed to develop in a culture dish for several days. On about the third day after fertilization, the embryo consists of six to eight cells. Each of these cells is called a **blastomere** (Figure 8.6).

For PGD, one of the blastomeres is removed (Figure 8.7). DNA is extracted from this cell and analyzed to determine whether the embryo has a genetic disorder. Blastomere testing can be used for many common autosomal recessive disorders, such as **Tay-Sachs disease**, dominant disorders, and most X-linked disorders, including muscular dystrophy and hemophilia. Embryos that do not have a genetic disorder are implanted in the mother's uterus for development.

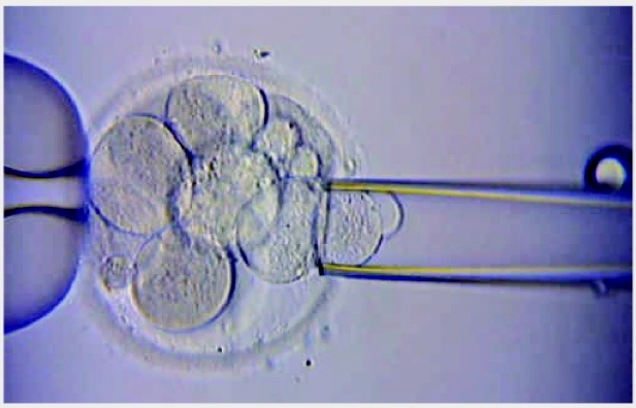
8.2 Essentials

- **Prenatal testing is usually done to detect genetic disorders in the fetus when there is a risk of such conditions.**
- **Preimplantation genetic diagnosis can detect genetic abnormalities *before* the embryo is implanted into the mother.**

blastomere one of the early embryonic cells

Tay-Sachs disease a recessive genetic trait that is almost always fatal

Figure 8.7 **A Blastomere Is Removed from an Embryo for Genetic Testing**



Denny Sakkas PhD., Yale Fertility Center of the Yale University School of Medicine

8.3 How Are Fetal Cells Analyzed?

The fluids and cells obtained by amniocentesis, CVS, and PGD can be analyzed (Figure 8.8) using several different methods, including karyotyping (see Chapter 3), biochemical analysis, and recombinant DNA techniques (see Chapter 7).

Direct DNA analysis is the most specific and sensitive method currently available. The accuracy, sensitivity, and ease with which recombinant DNA technology can be used to identify a genetic disease and susceptibilities carried by an individual have raised a number of legal and ethical issues that have yet to be resolved; these will be discussed later in this chapter.

8.3 Essentials

- **Prenatal testing can determine the genotype of a fetus by examining cells retrieved using several different procedures.**

Figure 8.8 **A Technician Prepares a Karyotype in a Cytogenetics Laboratory**

Hop Americain/Photo Researchers

8.4 How Can Prenatal Tests Diagnose Phenylketonuria?

Like all babies born in the United States, Al and Victoria's baby was tested for phenylketonuria at birth. However, if there is a family history of PKU, the test is often done prenatally. PKU is a metabolic disorder found in people across all ethnic and racial groups. It is inherited as an autosomal recessive trait; therefore, both parents must be heterozygous carriers for their child to inherit the disorder. The gene that causes PKU is called ***PAH*** and is located on chromosome 12 (Figure 8.9). People with this condition cannot convert an important amino acid, **phenylalanine**, into another amino acid, tyrosine.

The enzyme that converts phenylalanine into tyrosine is called phenylalanine hydroxylase (PAH). In PKU, a mutation in the *PAH* gene inactivates the enzyme. Therefore, phenylalanine cannot be broken down and builds up in the body's tissues, causing damage to the brain and other organs.

PKU is a genetic disorder, but it is also an environmental disease. If phenylalanine is removed from the diet, the child will develop normally, and there is no mental retardation. This is a successful treatment for the condition. Because the brain is fully mature by the early teen years, many people with PKU switch to a normal diet at this time.

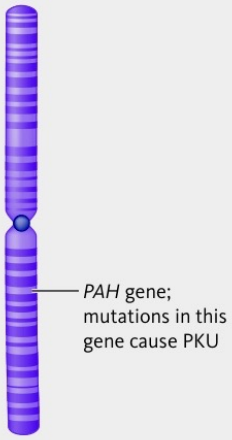
However, if a woman with PKU gets pregnant, she must follow the PKU diet very carefully; otherwise, the child may be seriously affected because the excess amount of phenylalanine in the mother's blood would pass into the fetus, causing serious mental retardation, even if the fetus has a normal or a heterozygous genotype.

Can we test everyone for conditions such as PKU? Genetic testing on a large scale (genetic screening) is not always possible. For some disorders, such as the sickle-cell anemia that Martha Johnson's twins had (see Chapter 5), a single mutation is always responsible, so testing is efficient and uncovers all cases. However, several hundred different mutations have been identified in the *PAH* gene, and testing for all of these mutations is impractical. However, most states screen newborns for PKU using a simple blood test that measures phenylalanine levels.This test is simple and not based on DNA analysis; therefore, it is not testing for mutations in the *PAH* gene. Figure 8.10 shows a photo of a *Guthrie card* containing blood samples taken from a child soon after birth. The blood is transferred to the card and analyzed for PKU levels. The card is kept as part of the child's medical record.

8.4 Essentials

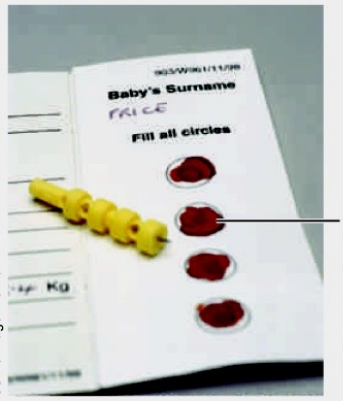
- **PKU is one of the few genetic conditions that has a treatment.**

Figure 8.9 **Chromosome 12, Showing the Location of the PAH Gene at 12q24.1**
A mutant allele of this gene is responsible for phenylketonuria.



Chromosome 12

Figure 8.10 **Guthrie Card**
Blood samples from newborns are placed on a card before being tested for PKU.



SSPL/Image Works

PAH a gene associated with PKU

phenylalanine an essential amino acid

8.5 Can Adults Be Tested for Genetic Conditions?

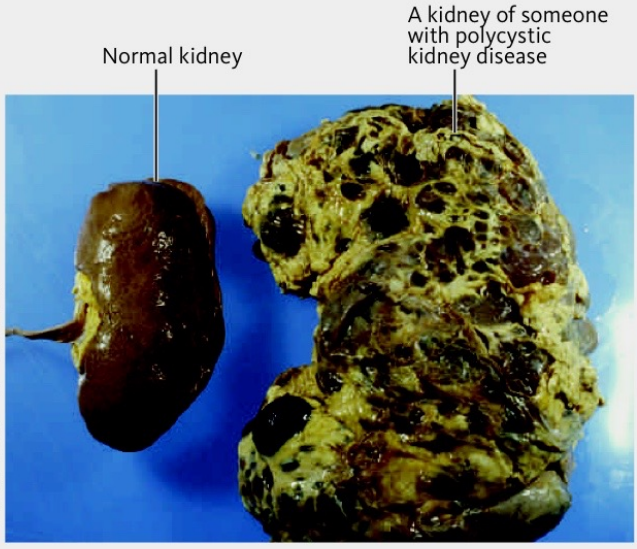
Some conditions—such as Huntington disease, which runs in Alan's family (see Chapter 4)—show up much later in life but can be detected by testing long before symptoms appear; these are called presymptomatic tests. A genetic predisposition to breast cancer (discussed in Chapter 12) also falls into this category. This test can detect a predisposition to breast cancer before the disease develops. Adult-onset disorders, including Huntington disease, amyotrophic lateral sclerosis (ALS), adult polycystic kidney disease (ADPKD), and others, all begin later in life. As an example, the symptoms of ADPKD, which affects about 1 in 1000 individuals, usually appear between ages 35 and 50. This disease is characterized by the formation of cysts in one or both kidneys; these cysts grow and gradually destroy the kidney. Figure 8.11 shows a normal kidney (left) and one with ADPKD (right).

Treatment options for ADPKD include kidney dialysis or transplantation of a normal kidney, but many affected individuals die prematurely before a transplant becomes available. Because ADPKD is a dominant trait, anyone who is heterozygous for the mutant gene will be affected. Genetic testing can determine which family members carry a mutant allele and will develop this disorder. Testing for these and other disorders that appear in adults can be done at any age before (or after) the condition appears. The decision on whether to be tested for these traits is a personal choice.

8.5 Essentials

- **Adults can be tested for many genetic conditions. A person may want to find out if he or she is a carrier of a condition before marriage.**

Figure 8.11 (left) A normal kidney. (right) An enlarged kidney from someone with polycystic kidney disease.



Arthur Glauberman/Science Photo Library —(represented by Photo Researchers)

8.6 What Is a Genetic Screening Program?

Some genetic screening programs, such as those for newborns, are mandated by law in the United States. All states and the District of Columbia require newborns to be tested for a range of genetic disorders, although the number and types of disorders screened for vary significantly from state to state. These programs began in the 1960s with screening for PKU and gradually expanded to all states and a wide range of genetic disorders. Al and Victoria's baby was tested under the screening program in their state.

Many states screen for only three to eight disorders (Figure 8.12). However, using new technology, labs can now screen for 30 to 50 metabolic disorders from a single blood sample. The number of tests currently mandated in each state is shown in the map. Parents should be aware of which disorders are included in their state's screening program.

Are there screening programs to detect adult carriers of genetic disorders? As discussed in Chapter 4, a person can carry a gene for a recessive genetic condition but remain disease free. These individuals are heterozygous for the disorder and are called *carriers*. Carriers of certain recessive disorders, such as PKU and sickle-cell anemia, are found in higher frequencies in certain ethnic groups.

Population screening for carriers of genetic disorders is possible only under certain circumstances, including the following:

1. The disease must occur mainly in defined populations. For example, in the United States, sickle-cell carriers are most often found among African Americans. However, PKU, the condition present in Al and Victoria's baby, occurs across all racial and ethnic groups and would not qualify for carrier testing.
2. Tests for carriers must be available, fast, and fairly inexpensive.
3. Screening for these disorders must give at-risk couples several options for having only unaffected children.

At this point, there are no mandated programs for carrier screening; however, one disorder that meets these three conditions is Tay-Sachs disease, a fatal autosomal recessive trait that affects 1 in 360,000 individuals (Figure 8.13). This disease is associated with a disorder in the lysosomes in the body's cells (see "Biology Review: Cells and Cell Structure"). It can lead to mental retardation, blindness, and death by age 3 or 4.

In Jews of Eastern European ancestry (Ashkenazi Jews), the frequency of this disorder is almost 100 times higher than in the general population (Figure 8.14). In the 1970s,

Figure 8.12 **Genetic Screening Programs in the United States** The key shows how many tests are mandated by law in each state.

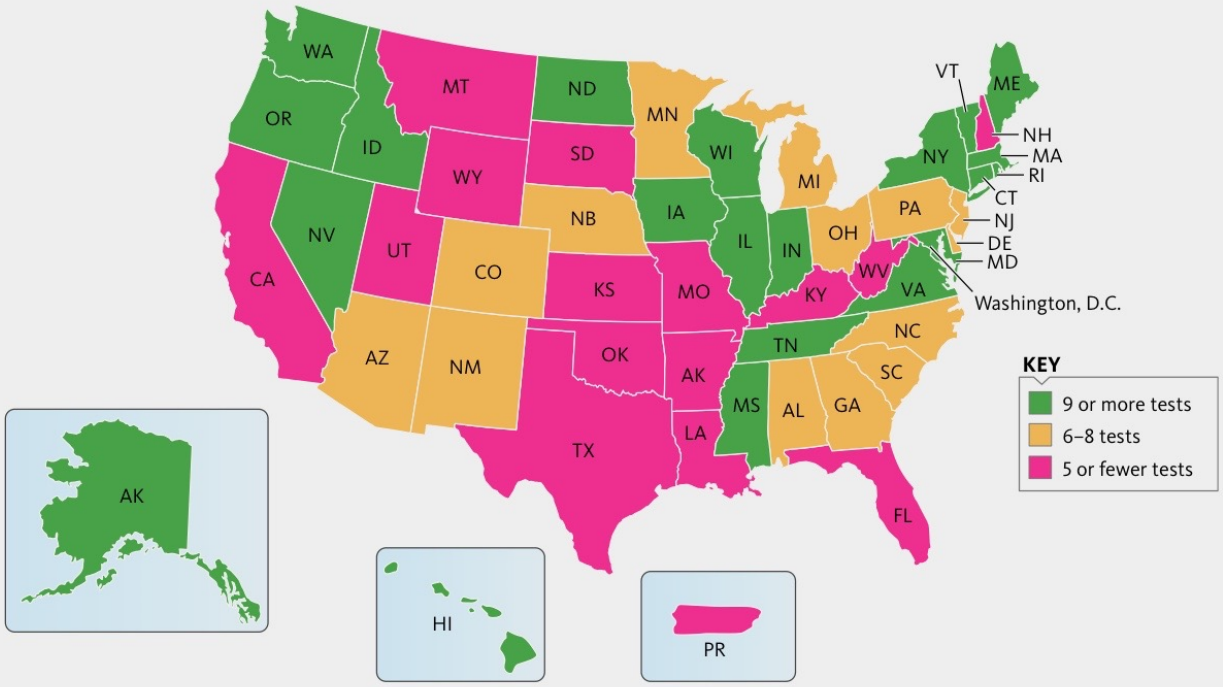
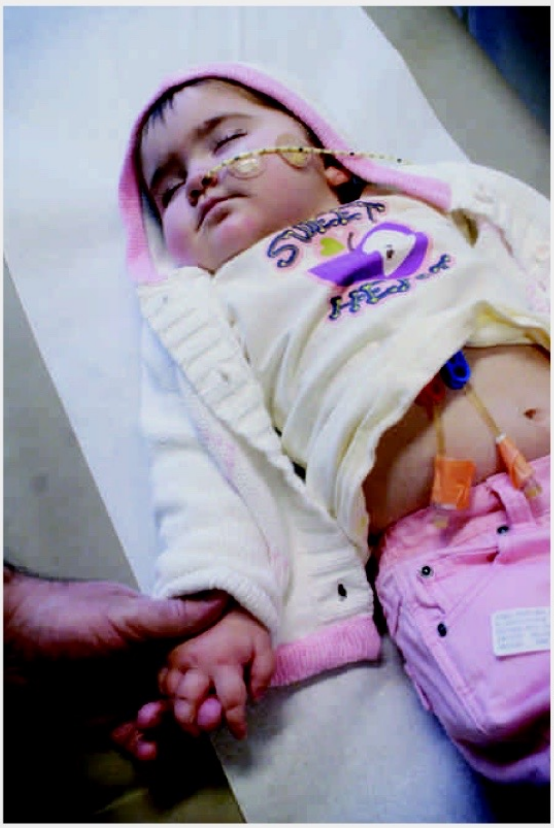


Figure 8.13 **A Child with Tay-Sachs Disease** In this fatal genetic disorder, degeneration of cells in the nervous system leads to death by age 2 or 3.



Seungjae Seo/The Minnesota Daily

Figure 8.14 **Members of Orthodox Jewish Communities Have Embraced Genetic Testing for Tay-Sachs Disease**

© blickwinkel/Alamy

BY THE NUMBERS

1 in 4500
Frequency of births with PKU among people of Irish or Scotch descent

© Mark Antman/The Image Works

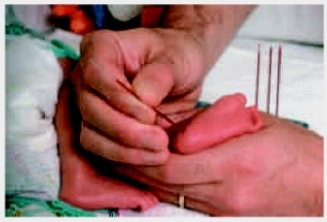
1 in 13,000 to 1 in 19,000
Frequency of births with PKU in the United States

1 in 300 to 1 in 500
Number of miscarriages after amniocentesis

1 in 300 to 1 in 500
Number of miscarriages after CVS

CASE A: QUESTIONS

Now that we understand how prenatal testing is done and why, let's look at some of the issues raised in Al and Victoria's case.


Dan McCoy/Getty Images

A heel stick is the most common method of obtaining a blood sample for testing in newborns.

1. Why was Al and Victoria's baby tested for PKU?
2. Neither Al's family nor Victoria's family has a history of PKU. Should Al and Victoria's baby have been tested at all? Explain.
3. Should Al and Victoria have the right to refuse this testing for their child? Why or why not?
4. Based on what you know about the law, do Al and Victoria have a right to sue the hospital? Why?
5. PKU is a treatable genetic disorder. Affected children must follow a strict diet that prevents many of the condition's symptoms. Does this information change your opinion about testing the baby?
6. Testing of newborns for PKU is done in every state; some states offer more extensive testing for newborns. Al and Victoria live in one of these states. Should they have been notified of the testing? Why or why not?

The sickle-cell anemia screening program generated unanticipated problems. In 1981, the Air Force policy that denied sickle-cell carriers admission to the Academy was reversed under threat of a lawsuit. In other cases, carriers were reportedly turned down for insurance and employment, even though carriers have no inherent health problems.

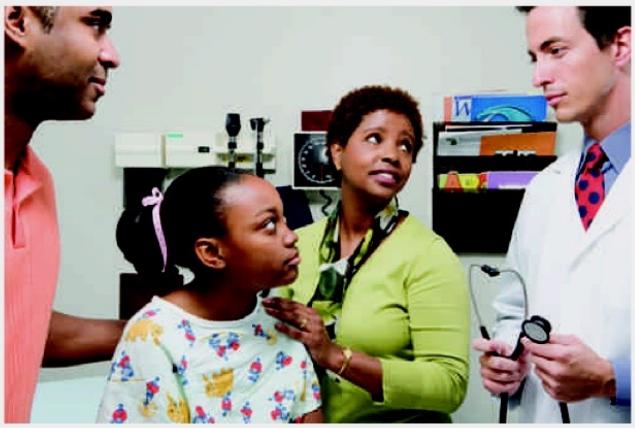
Some sickle-cell screening programs were criticized for not maintaining confidentiality of records and not providing counseling to those identified as heterozygotes (carriers). In the late 1970s and early 1980s, many of these screening programs were cut back or reorganized, and only a few states currently offer, but don't mandate, testing for adults, although all 50 states and the District of Columbia screen newborns for sickle-cell anemia.

voluntary carrier screening programs were initiated in Ashkenazi populations in the United States. More than 300,000 individuals were tested in the first 10 years of screening, and 268 couples were identified in which both members were carriers and had not yet had a child. This test is not DNA based; rather, it tests for the level of an enzyme in the blood. These simple blood tests have been effectively used for years.

In the Ashkenazi community, Tay-Sachs screening programs are coupled with counseling sessions that provide information about the risks of having an affected child, the availability of prenatal testing, and reproductive options. These programs are voluntary, although some states require that couples be informed about Tay-Sachs testing. Before the screening programs began, each year between 50 and 100 children were born with Tay-Sachs disease in the United States. This number decreased to fewer than 10 such births each year after screening programs were implemented.

Another population screening program began when the U.S. Congress passed the National Sickle-Cell Anemia Control Act in 1972. This law was designed to establish a screening program to identify carriers of sickle-cell anemia (Figure 8.15). Each state received funds to set up a screening program. Some states established compulsory programs requiring that all African American children be tested before attending school; others required testing before obtaining a marriage license. Testing was also done on professional football players and applicants to the U.S. Air Force Academy, because carriers were not allowed to enter the academy.

Figure 8.15 These parents are concerned about their child, who may have sickle-cell anemia.



Masterfile

8.6 Essentials

- **Genetic screening tests many individuals in a population.**

8.7 Which Genetic Conditions Can Be Treated?

Many of the genetic disorders we have discussed can be treated to alleviate symptoms, but none of them has a cure. Table 8.3 lists some conditions and their treatments, if available.

Table 8.3 **Treatments for Genetic Disorders**

Name of Condition	Is Treatment Available?	Treatment
PKU	Yes	Diet low in phenylalanine
Sickle-cell anemia	Yes	Bone marrow transplants, blood transfusions
Hemophilia	Yes	Recombinant DNA Factor VIII
Cystic fibrosis	Yes	Inhalers, antibiotics
Polycystic kidney disease	Yes	Kidney transplant, dialysis
Tay-Sachs disease	No	
Huntington disease	No	
Muscular dystrophy	No	
Trisomies (Down syndrome, trisomy 18, etc.)	No	

CASE B: Company Gives Big Party

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A company celebration.

A wonderful party was in full swing. Representative Prescott Smith had been to many parties since being elected to Congress from his state, but this one was the best. The party was hosted by MegaGene, a large pharmaceutical company. MegaGene had just developed a test to detect the mutant allele for a disease that was rare and serious but had no treatment or cure.

Finally, at the end of the evening, MegaGene came to the point. Company representatives suggested that Mr. Smith sponsor a bill the company had drafted to require that every baby born in the United States be tested for this gene.

1. **Why was MegaGene throwing this party? Give three reasons.**
2. **Why did the company draft the law? Give two reasons.**
3. **What should Congressman Smith do if asked to sponsor such a bill?**
4. **Today all babies born in hospitals are tested for several to dozens of genetic diseases by law (which condition is dependent on the state). Should parents be allowed to refuse this testing? Why or why not?**
5. **What do you think will happen, years from now, when we have tests for all the human genes?**

8.7 Essentials

- **A few genetic conditions can be treated but not cured.**

8.8 What Are the Legal and Ethical Issues Associated with Genetic Testing?

The use of genetic testing and screening has a number of accompanying ethical and legal problems. Because these methods examine and record a person's genetic makeup, privacy is extremely important. Both federal and state laws require that medical records be kept private and their contents not be revealed to anyone without the patient's explicit consent.

Information from these tests can affect a patient's health insurance, job security, and even personal life. For example, as discussed in Chapter 4, if an insurance company discovers that a family carries the gene for Huntington disease, it may not insure them. In another example, would a person be willing to marry someone who carries the gene for Huntington disease or the gene for polycystic kidney disease?

These questions are dealt with either personally, on a one-to-one basis, in the courts, or in the legislature. In some cases, laws have been passed prohibiting discrimination against someone because of his or her genetic makeup. During the 1970s, many people were discriminated against based on their carrier status for sickle-cell anemia, and many screening laws were repealed.

On another level, companies that work to create a test for a specific disease gene spend millions of dollars on research and development. For this reason, they are looking to sell this test to as many potential customers as possible. If, as MegaGene wanted, the company's test were used in a screening program of newborns, this would be one way to recover the money spent on research and development.

Table 8.4 addresses some of the ethical and legal questions in testing and screening.

8.8 Essentials

- **Genetic testing must be done under circumstances that ensure that the results will remain private.**

Table 8.4 **Legal and Ethical Questions about Genetic Testing**

Question	How Are These Questions Decided?	Related Case or Legal Issue
How should genetic test results be used?	Laws control the use of information, but insurance companies ask potential insurees to sign a release for their medical records.	The Kennedy-Kassebaum law stops insurance companies from discriminating against patients with genetic conditions.
Should we test for conditions that have no cure or treatment?	The individual makes the decision for this testing (except as mandated by screening laws) after meeting with a genetic counselor or a physician.	Newborns and children have no right to refuse testing; however, adults can refuse, and the law has upheld this right.
Should the government decide who should be tested?	Since the 1970s, the U.S. government has mandated testing for all newborns born in a hospital. Babies born at home may be missed. The numbers of tests is increasing.	Parents have sued to be excluded from the testing and have won on religious and moral grounds. But most parents don't even know the testing occurs.
Should insurance companies or employers be allowed to require genetic testing of their potential customers or employees?	This has happened only in a few cases. The argument is usually that it is for the customer's or employee's own good.	In *EEOC v. Burlington N. Santa Fe Railway Co.* (see Spotlight on Law, Chapter 5), the company wanted to test all employees for a gene that predisposes them to carpal tunnel syndrome. The court decided that the testing violated the Americans with Disabilities Act, and the company immediately stopped the testing.

Spotlight on Society

Iceland and Its Genetic Code

This spotlight will examine the nationwide genetic testing being done in Iceland. In 1996 an Icelandic scientist, Kari Stefansson, started a company called deCODE Genetics to find disease genes in the human genome. It seemed logical that if he could identify a large population of closely related people, any genetic differences related to disease would stand out.

Iceland has a relatively small, homogenous population of approximately 290,000. Few people have immigrated there, and even fewer have left. Iceland keeps meticulous records of families as well as comprehensive health records that date back to the early 1900s. Figure 8.16 shows some children from Iceland, all with similar phenotypes.

Figure 8.16 Members of this crowd in Iceland have very similar phenotypes, reflecting their genotypic similarities.

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Stefansson thought that if he could get DNA samples from everyone in Iceland, as well as their health and genealogy records, he could identify disease genes more easily. In the beginning, he asked for volunteers to supply samples for his DNA database. However, to speed up the process of gene hunting, he approached the Icelandic government with an idea. He proposed that the government ask each citizen of Iceland to come forward and give a sample of his or her DNA for this database. After a great deal of debate, a law was written, and on December 17, 1998, the Health Sector Database Act was voted into law by the Icelandic parliament.

For a one-time fee of $950,000 paid to the Icelandic government, deCODE was given complete access to family histories, medical records, and genetic information for the entire population of Iceland. According to the law, deCODE will construct a database (at a cost of $10–20 million) of DNA samples from members of the population. Differences in DNA sequence would be used to search for disease-associated genes. In exchange, deCODE will receive and retain all profits derived from its operating license.

To ensure privacy of medical records, the law forbids deCODE from sharing medical information with anyone. In exchange, Icelanders have been promised free access to genetic tests and medications developed from this project. deCODE has signed drug development contracts with several pharmaceutical companies, including Merck, Roche Diagnostics, and Hoffmann–La Roche.

Some of deCODE's accomplishments include the discovery of a number of disease genes, including those linked to schizophrenia and heart disease, and clinical trials on drugs developed to treat these disorders are underway. In addition, deCODE has recently started a service called deCODEme. Using a DNA sample collected by swabbing the inside of the cheek, this online service offers a genome scan to identify genomic variations associated with risks for a number of genetic disorders. Results from the genome scan can also be used to trace an individual's genetic ancestry, compare genome data with other individuals, and make predictions about someone's physical attributes, based on the analysis of the genome scan.

Iceland has had a serious financial setback recently and is trying to recover. As a result, deCODE genetics has also met with some financial difficulties (Figure 8.17). The CEO of deCODE has suggested the personal testing wing of the company (deCODEme) will carry it through the next few years.

QUESTIONS

1. One of the interesting parts of Iceland's Health Sector Database Act is that it presumes consent of all the members of the population. What problems do you see with this?
2. Should Icelanders have the right to opt out of the testing? Explain.

Figure 8.17 The Icelandic headquarters of deCODE, where much of its work takes place.

Icelandic Photo Agency/Alamy Limited

Figure 8.18 **A Page from an Icelandic Phone Book** Notice the similarities in names, and the number of people with the same name.

REYKJAVÍK OG NÁGRENNI 163

Edda E

Edda Kjartansdóttir Áftanmýri 56 108 Rey 553 4864
Edda Kjartansdóttir Hraunbær 84 110 Rey . 567 4250, 892 4280
Edda Kjartansdóttir Lækjasmiðjustraut 9
170 Sel 561 1487, 863 8487
- Netfang . . . . . ekj@simnet.is
Edda M Kjartansdóttir Smáratorgsmi 3 220 Hfj. 555 0355
Edda Elísabet Kjerúlf Fjóltasels 2 109 Rey. 557 2238
Edda Klemensdóttir bitrstj 893 1703
Edda Klingbeil Áttatúnum 4 111 Rey. 587 9285
Edda Konráðsdóttir Vogatungu 31a 200 Kóp 564 4446
Edda Pérey Kristfinnsdóttir Vesturbergsm 182
112 Rey 557 1856
Edda Kristinsdóttir Boðagranda 2a 107 Rey. 551 8034
Edda Kristinsdóttir Grettisgötu 49 101 Rey 897 8345
Edda S Kristinsdóttir Bláskógum 22 201 Kóp. 867 1451
Edda Kristjánsdóttir Blöndubakki 64
109 Rey 557 2771, 864 5304
Edda Kristjánsdóttir Markland 12 108 Rey 588 9094
Edda Kristjánsdóttir munnlækningahjúkrunarfr
Heiðarseli 97 109 Rey 553 0078, 867 8704
Edda Kristjánsdóttir ritari Hagamel 17
107 Rey 552 2517, 691 7230
Edda Kristjánsdóttir verslunarstj
Blikahrrum 2 112 Rey 567 6292, 663 5292
Edda Birna Kristjánsdóttir Eikarvel 7 107 Rey. 846 5277
Edda Björk Kristjánsdóttir
Hálsaseli 6 210 Gbæ. 555 4985, 869 4985
Edda Rúna Kristjánsdóttir bóksafnsfr Greniteig 40
107 Rey 562 4331
Edda Fanný Ágústsdóttir Krokones Gramatyzla 19
200 Kóp 865 5439
Edda I Larsen húsm Grensásvegi 58 108 Rey 553 5084
Edda Stefanía Levy Sléttahrauni 61 112 Rey. 587 3975, 862 3975
Edda Lingaas Fiskarnesi 37 101 Rey 552 0804, 893 0676
Edda Birna Logadóttir Lyngbrekku 11 200 Kóp 848 5946
Edda Lára Lúðvígsdóttir Furugerði 6 108 Rey. 696 8089
Edda Lúðvíksdóttir skrifstofust
Klapparstíg 13B 104 Rey 553 6160, 663 4552
Edda Lýðsdóttir Lautasmári 16 200 Hfj. 565 3068, 698 8323
Edda Magnúsdóttir Austurbrún 4 104 Rey. 868 7211
Edda Magnúsdóttir Laugarnesvegi 89
105 Rey 581 2795, 824 2795
Edda Magnúsdóttir Marargötu 7 101 Rey . 552 8214, 845 3497
Edda Magnúsdóttir Ólafsgeisla 117 113 Rey 588 8027
Edda Magnúsdóttir Skjólbraut 16 200 Kóp. 866 0981
Edda Magnúsdóttir frá Suðurbraut 1
200 Kóp 554 1888, 691 7163
Edda Magnúsdóttir matvælafr Álfheimum 32 104 Rey . 588 5420
Edda Magnúsdóttir nemi Álfaseli 70
230 Hfj. 555 1615, 820 1890
Edda Ingibjörg Margeirsdóttir
Lerkihlíð 5 105 Rey 553 1902, 847 7533
Edda Márusdóttir Hörðaland 10 108 Rey. . 553 7908, 893 7908
Edda Selma Márusdóttir sjúkraliði
Lyngbrekku 1a 200 Kóp 557 6095, 699 6094
Edda Yr Meier Kleppsvegi 116 104 Rey 552 3480
Edda Marianne Michelsen
Markarflöt 26 109 Rey 557 8505, 692 2775
Edda Miðkvn Silfurmýra 28 108 Rey. 522 2000
- Sjá Edda Urðgata ehf
Edda Möller Linnetsstíg 2 220 Hfj 565 1478
Edda R Níels Arnarási 12d 210 Gbæ 565 8630
Edda Nikulásdóttir Viðimel 36 107 Rey . 552 6657, 849 7377
Edda Njálsdóttir Barðaströnd 3 170 Sel . . 561 2243, 899 2293
Edda Sigurdis Oddsdóttir
Skeiðarvogi 75 104 Rey 588 0113, 892 4503, 893 0113
Edda Ólgeirsdóttir Hamraborg 16 200 Kóp 552 8167, 691 1167
Edda Olsen Hjallabraut 32 109 Rey 517 8292
Edda Ottadóttir Seljabraut 42 109 Rey. . . 557 4953, 863 4653
Edda Óttarsdóttir Nordurgötu 33 101 Rey. 551 3208
Edda Ólafsdóttir Asparási 4 210 Gbæ . . . 565 5335, 899 8442
Edda Ólafsdóttir Njálsgötu 76 101 Rey 551 4875
Edda Ólafsdóttir lífeindafræðingur Kópavogsbraut 99
200 Kóp 564 2707
Edda Borg Ólafsdóttir hönnuður
Geitlandi 9 109 Rey 587 1997, 896 4662
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- Vefföng . . . . . www.eddaborg.com
- Vefföng . . . . . www.klest.it.is
Edda G Ólafsdóttir ritari
Lindarsmári 22b 210 Gbæ. 557 7445, 690 3838
Edda Ósk Ólafsdóttir tölvunarfr
Skipholti 50c 105 Rey. 551 8645, 856 6494
EDDA SIGRÚN ÓLAFSDÓTTIR hérðsdómslögm
Klapparstíg 1 101 Rey 561 5763, 896 5763
- Fax 562 5763
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Edda Óskarsdóttir Gunnarsbraut 30 220 Hfj. 555 3423
- Netfang . . . . . eddaosk@simnet.is
Edda Óskarsdóttir Kópavogsbraut 1a
200 Kóp 560 4123, 690 8010
Edda Óskarsdóttir Lindasmára 30 200 Kóp 554 4590, 863 6372
Edda Óskarsdóttir myndlistarm
Víðilundi 18 220 Hfj. 555 1599, 898 3599
Edda Óskarsdóttir sérkennari
Bústaðavegi 29 105 Rey 561 4541, 696 3625
Edda Ósk Óskarsdóttir Breiðuvík 12 200 Kóp 691 8766
Edda Sóley Óskarsdóttir Begstíg 8
105 Rey 581 4398, 698 4398
Edda Tegeder Óskarsdóttir Nýbýlavegi 92 105 Rey. . . . 697 4284
Edda Mary Ottarsdóttir Eskihlíð 8a
105 Rey 551 7003, 697 4755
Edda Guðrún Pálsdóttir 869 5590
Edda Pétursdóttir kennari
Kaplaskjólsvegi 61 107 Rey 552 3523, 822 3523
Edda Maggý Rafnsdóttir Lautasmára 65 112 Rey 587 4999
Edda Ragnarsdóttir 551 3713
Edda Ragnarsdóttir húsfreyj Þjórsárgötu 1 101 Rey. . 551 3323
Edda Björk Ragnarsdóttir Hæðarsmára 14 108 Rey. 848 6321
Edda Björk Ragnarsdóttir
Merkisteigi 1 270 Mos 554 7984, 893 8817
Edda Rún Ragnarsdóttir Hraunbergi 15
105 Rey 517 8402, 699 8402
Edda Rún Ragnarsdóttir tannlæknakona
Rauðási 19 110 Rey 557 8088, 692 0889
Edda Kristín Reynis Fífuhvammi 5 201 Kóp . . . 564 5878, 895 8501
EDDA G RICHARDSDÓTTIR læknir/sérfræðingur
Hlíðasmári 14 200 Kóp. 564 2844, 897 0351
- Teiknistofan Garðatorgi 7 . . . . . 564 4828
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Edda H Waage Ásvallagötu 24 101 Rey 552 1606, 865 6768
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Edda Dan Róbertsdóttir kerfisfr
Hamraborg 63 200 Hfj. 555 4114, 698 4115
Edda Runólfsdóttir sjúkraliði Valsheiði 6 111 Rey . . . 557 7083
Edda Valborg Scheving Ásvallab 4 111 Rey 586 2703, 867 3082
Edda S Sigfúsdóttir Hléskógum 24
109 Rey 557 1800, 864 3660
Edda Björg Sigmarsdóttir snyrtir Urðarbaksa 2
109 Rey 587 1122
Edda Sigurbergsdóttir
Ásvegi 15 104 Rey 553 0902, 821 3636, 821 3600
Edda Sigríður Sigurbjarnadóttir bókbindari
Arnlaun 1 201 Kóp 869 3096
Edda Sigurðardóttir Hverafold 23
112 Rey 567 2360, 848 3031
Edda Sigurðardóttir Hverafold 4 112 Rey . 567 5521, 895 6521
Edda Sigurðardóttir Langagerði 32 108 Rey 581 3912
Edda Sigurðardóttir Skipholti 8 105 Rey . 551 8892, 699 6364
Edda Sigurðardóttir Ölduslóða 10 220 Hfj 867 8263
Edda Sigurðardóttir lífeindafræðingur Reynimel 92
107 Rey 552 7798
Edda Björg Sigurðardóttir
Sogamýri 16 210 Gbæ. 565 7244, 661 7244
Edda Björk Sigurðardóttir Bæjargili 35 210 Gbæ . . . 899 6165
Edda Björk Sigurðardóttir Mariubaugi 75 113 Rey . . 588 3518
Edda Hrund Sigurðardóttir Skógarhlíð 10 200 Kóp . 534 5482
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200 Kóp 554 6566
Edda Saga Sigurðardóttir Skeiðarvogi 2 221 Hfj. 695 0981
Edda Sif Sigurðardóttir Kjóahraun 16 220 Hfj. 565 2472
Edda Sif Sigurðardóttir Sundmeði 9
110 Rey 557 9880, 697 3935
Edda Janette Sigurðsson Hamraskóla 270 Mos. 566 7601
Edda Sigurgeirsdóttir Kambasel 12
109 Rey 895 0984, 695 0984
Edda Sigurjónsdóttir Dalseli 34 109 Rey. . 557 4222, 691 4222
EDDA SIGURJÓNSDÓTTIR bókmyndari og söluma
Kleppsvegi 140 104 Rey . 561 7541, 861 7515, 820 7547
Edda Guðrún Sigvaldadóttir félagsfr Framnesvegi 14
101 Rey 869 1660
Edda Símonardóttir Hofteigi 1 210 Gbæ 478 2330
Edda Ásgerður Skúladóttir Grundarhúsum 38 112 Rey 698 8028
Edda Björk Skúladóttir Furuvöll 19
271 Hfj. 554 7173, 897 7173
Edda Lóa Skúladóttir Hryggjarseli 28 109 Rey. 557 5718
Edda Ósk Smáradóttir grunnskólakennari Ykurási 1
110 Rey 899 1884
Edda Snorradóttir Frostafold 41 112 Rey. . 565 0136, 661 7134
Edda Snorradóttir Keldugranda 4
107 Rey 551 0965, 821 2591
Edda Snorradóttir Nóatúni 4 251 Kóp . . . 557 1188, 691 0385
Edda Snorradóttir kennari Tunguvegi 6
220 Hfj. 565 4933, 892 4933
Edda Snæhólm Hagamel 28 107 Rey 552 0254
Edda Snæhólm Hlíðgrði 18 Bess 225 Álft. 565 1399
Edda S Stefánsdóttir Lerkebakka 2 109 Rey. 587 4284
Edda Hrönn Steingrímsdóttir
Lindasmára 89 201 Kóp 564 4654, 696 4220, 698 6683
Edda Sturlaugsdóttir Furugerði 7 108 Rey 568 5096
Edda Hrund Svanhildardóttir Reykhúsatröð 21
101 Rey 659 7978
Edda Svavarsdóttir Bjarmahlíð 4 221 Hfj. 565 4787
Edda Svavarsdóttir Ferjubakka 6 109 Rey 557 8938
Edda Svavarsdóttir Laugarnesvegi 87 105 Rey 557 6479
Edda Sveinbjörnsdóttir
Grenitorgsreit 166 113 Rey. 561 3305, 699 0050
Edda Sveinbjörnsdóttir Lautasmára 3 201 Kóp 564 5576
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Edda Sverrisdóttir kvikmyndagerðarm
Bergstaðastræti 38a 101 Rey 554 5475, 898 5475
Edda Guðrún Sverrisdóttir Hraunsalavís 30 203 Rey . . . 863 9096
Edda Matthíasdóttir Swan
Austurtúni 6 225 Álft 565 0233, 867 7735
Edda Björk Sævarsdóttir hárgreiðsluma
Markarflöt 12 200 Kóp. 564 3604, 899 0886
Edda Sif Sævarsdóttir Kirkjubergi 18
105 Rey 551 7212, 898 9723
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Edda Sölvadóttir Skaftahlíð 36 105 Rey. 553 3557
Edda Ósk P Thorarensen
Álfaseli 15 200 Kóp 517 6266, 694 6266, 698 6266
Edda Thorlacius Lækjasmári 4 108 Rey 553 2482, 820 1934
Edda Thors Hlíðargerði 12 108 Rey 568 1231, 861 1231
Edda Traustadóttir Kirkjuteigi 15 105 Rey 691 4088
Edda Traustadóttir hjúkrunarfræðingur
Bústaðavegi 25 105 Rey 553 7462, 661 5759
Edda Tryggvadóttir fulltrúi Hlaðbæsi 20 210 Gbæ . . 564 3921
Edda Sólveig Úlfarsdóttir bankastarfsm
Brúnási 3 210 Gbæ 557 5769, 864 2344, 699 0503
Edda Valgarðsdóttir Ásbrekku 5
225 Álft 587 8747, 694 8747
Edda Valsdóttir lækkabastjóri
Álfaseli 4 200 Kóp 554 1206, 894 1267
Edda Valtýsdóttir iðnrekstr
Skúlagötu 2 101 Rey 552 6767, 868 8748
Edda Vésteinsdóttir líffræðingur Ida
101 Rey 561 5545, 868 5884
Edda Björk Viðarsdóttir Laufengi 152
112 Rey 567 9906, 692 7705
Edda Vigfúsdóttir Grettisgötu 3 200 Kóp. . . . 554 5825, 899 8081
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3. Why should deCODE have a monopoly on the data and the ability to profit from such information? Give both pro and con arguments.
4. Will deCODE or other companies own part or all of an individual's genome? Explain.
5. deCODE has promised Icelanders free medications. Will it be liable for any unforeseen side effects? Explain.
6. Figure 8.18 shows a page from an Icelandic phone book. Notice how many of the first and last names are the same. What does this tell you about the genetics of the people of Iceland?
7. If deCODE genetics has to go out of business, what do you think might happen to all the samples taken from the citizens of Iceland?