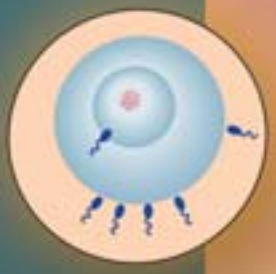

Selected Key Terms

The following terms and additional boldface terms in the chapter are defined in the Glossary

allele
amniocentesis
autosome
carrier
chromosome
congenital
dominant
gene
genetic
genotype
heredity
heterozygous
homozygous
karyotype
meiosis
mutagen
mutation
pedigree
phenotype
progeny
recessive
sex-linked
trait

Learning Outcomes

After careful study of this chapter, you should be able to:

1. Briefly describe the mechanism of gene function
2. Explain the difference between dominant and recessive genes
3. Compare *phenotype* and *genotype* and give examples of each.
4. Describe what is meant by a *carrier* of a genetic trait
5. Define *meiosis* and explain its function in reproduction
6. Explain how sex is det ermined in humans
7. Describe what is meant by the term *sex-linked* and list several sex-linked traits
8. List several factors that may influence the expression of a gene
9. Define *mutation*
10. Differentiate among congenital, genetic, and hereditary disorders and give several examples of each
11. List several factors that may produce genetic disorders
12. Define *karyotype* and explain how karyotypes are used in genetic counseling
13. Briefly describe several methods used to treat genetic disorders
14. Show how word parts are used to build words related to heredity (see Word Anatomy at the end of the chapter)

chapter 25

Heredity and Hereditary Diseases

We are often struck by the resemblance of a baby to one or both of its parents, yet rarely do we stop to consider *how* various traits are transmitted from parents to offspring. This subject—heredity—has fascinated humans for thousands of years. The *Old Testament* contains numerous references to heredity (although, of course, the word was unknown in biblical times). It was not until the 19th century, however, that methodical investigation into heredity was begun. At that time, an Austrian monk, Gregor Mendel, discovered through his experiments with garden peas that there was a precise pattern in the appearance of differences among parents and their **progeny** (PROJ-eh-ne), their offspring or descendents. Mendel's most important contribution to the understanding of heredity was the demonstration that there are independent units of heredity in the cells. Later, these independent units were given the name **genes**.

Genes and Chromosomes

Genes are actually segments of DNA (deoxyribonucleic acid) contained in the threadlike chromosomes within the nucleus of each cell. Genes govern the cell by controlling the manufacture of proteins, especially enzymes, which are necessary for all the chemical reactions that occur within the cell. Other proteins regulated by genes are those used for structural materials, hormones and growth factors.

When body cells divide by the process of mitosis, the DNA that makes up the chromosomes is duplicated and distributed to the daughter cells, so that each daughter cell gets exactly the same kind and number of chromosomes as were in the original cell. Each chromosome (aside from the Y chromosome, which determines sex) may carry thousands of genes, and each gene carries the code for a specific trait (characteristic). These traits constitute the physical, biochemical, and physiologic makeup of every cell in the body. (See Box 25-1 to learn about the Human Genome Project.)

In humans, every cell except the gametes (sex cells) contains 46 chromosomes. The chromosomes exist in pairs. One member of each pair was received at the time of fertilization from the offspring's father, and one was received from the mother. The paired chromosomes, except for the pair that determines sex, are alike in size and appearance. Thus, each body cell has one pair of sex chromosomes and 22 pairs (44 chromosomes) that are not involved in sex determination and are known as **autosomes** (AW-to-somes).

The paired autosomes carry genes for the same traits at exactly the same sites on each. The genes for each trait thus exist in pairs; each member of the gene pair that controls a given trait is known as an **allele** (al-LELE).

Checkpoint 25-1: What is a gene and what is a gene made of?

Dominant and Recessive Genes

Another of Mendel's discoveries was that genes can be either dominant or recessive. A **dominant** gene is one that expresses its effect in the cell regardless of whether its allele on the matching chromosome is the same as or different from the dominant gene. The gene need be received from only one parent to be expressed in the offspring. When the matching genes for a trait are different, the alleles are described as **heterozygous** (het-er-o-ZI-gus), or hybrid.

The effect of a **recessive** gene is not evident unless its paired allele on the matching chromosome is also recessive. Thus, a recessive trait appears only if the recessive genes for that trait are received from both parents. For ex-

Box 25-1 Hot Topics

The Human Genome Project: Reading the Book of Life

Packed tightly in nearly every one of your body cells (except the red blood cells) is a complete copy of your genome—the genetic instructions that direct all of your cellular activities. Written in the language of DNA, these instructions consist of genes parceled into 46 chromosomes that code for proteins. In 1990, a consortium of scientists from around the world set out to crack the genetic code and read the human genome, our "book of life." This monumental task, called the Human Genome Project, was completed in 2003 and succeeded in mapping the entire human genome – 3 billion DNA base pairs arranged into about 30,000 genes. Now, scientists can pinpoint the exact location and chemical code of every gene in the body.

The human genome was decoded using a technique called sequencing. Samples of human DNA were fragmented into smaller pieces and then inserted into bacteria. As the bacteria multiplied, they produced more and more copies of the human DNA fragments, which the scientists extracted. The DNA copies were loaded into a sequencing machine capable of "reading" the string of DNA nucleotides that composed each fragment. Then, using computers, the scientists put all of the sequences from the fragments back together to get the entire human genome.

Now, scientists hope to use all these pages of the book of life to revolutionize the treatment of human disease. The information obtained from the Human Genome Project may lead to improved disease diagnosis, new drug treatments, and even gene therapy.

ample, the gene for brown eyes is dominant over the gene for blue eyes, which is recessive. Blue eyes appear in the offspring only if genes for blue eyes are received from both parents. When both the genes for a trait are the same, that is, both dominant or both recessive, the alleles are said to be **homozygous** (ho-mo-ZI-gus), or pure-bred. A recessive trait only appears if a person's genes are homozygous for that trait.

Any characteristic that can be observed or can be tested for is part of a person's **phenotype** (FE-no-tipe). Eye color, for example, can be seen when looking at a person. Blood type is not visible but can be determined by testing and is also a part of a person's phenotype. When someone has the recessive phenotype, his or her genetic make-up, or **genotype** (JEN-o-tipe), is obviously homozygous recessive. When a dominant phenotype appears, the person's genotype can be either homozygous dominant or heterozygous. Only genetic studies or family studies can reveal which it is.

A recessive gene is not expressed if it is present in the cell together with a dominant allele. However, the recessive gene can be passed on to offspring and may thus appear in future generations. An individual who shows no evidence of a trait but has a recessive gene for that trait is described as a **carrier** of the gene. Using genetic terminology, that person shows the dominant phenotype but has a heterozygous genotype for that trait.

Checkpoint 25-2: What is the difference between a dominant and a recessive gene?

Distribution of Chromosomes to Offspring

The reproductive cells (ova and spermatozoa) are produced by a special process of cell division called **meiosis** (mi-O-sis). This process divides the chromosome number in half, so that each reproductive cell has 23 chromosomes. Moreover, the division occurs in such a way that each cell receives one member of each chromosome pair that was present in the original cell. The separation occurs at random, meaning that either member of the original pair may be included in a given germ cell. Thus, the maternal and paternal sets of chromosomes get mixed up and redistributed at this time, leading to increased variety within the population. Children in a family resemble each other, but no two look exactly alike (unless they are identical twins), because they receive different combinations of maternal and paternal chromosomes.

Geneticists use a grid called a **Punnett square** to show all the combinations of genes that can result from a given parental cross (Fig. 25-1). In these calculations, a capital letter is used for the dominant gene and the recessive gene is represented by the lower case of the same letter. For example, if *B* is the gene for the dominant trait brown eyes, than *b* would be the recessive gene for blue eyes. In

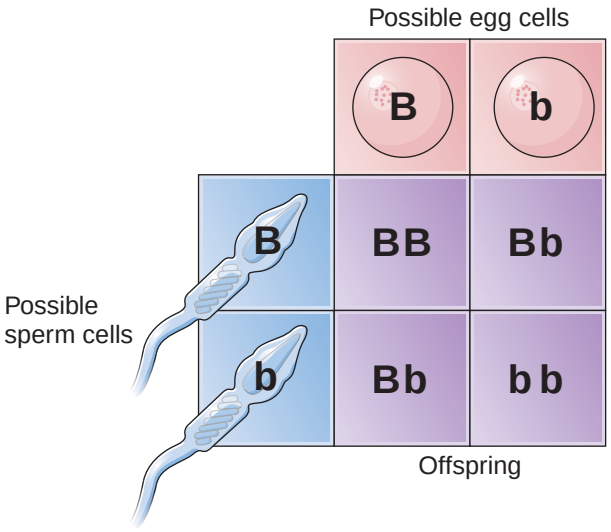

Figure 25-1 A Punnett square. Geneticists use this grid to show all the possible combinations of a given cross. *ZOOMING IN ✦ What percentage of children will show the recessive phenotype blond hair?*

the offspring, the genotype BB is homozygous dominant and the genotype Bb is heterozygous, both of which will show the dominant phenotype brown eyes. The homozygous recessive genotype bb will show the recessive phenotype blue eyes.

A Punnett square shows all the possible gene combinations of a given cross and the theoretical ratios of all the genotypes produced. Actual ratios may differ if the number of offspring is small. For example, the chances of having a male or female baby are 50-50 with each birth, but a family might have several girls before having a boy, and vice versa. The chances of seeing the theoretical ratios improve as the number of offspring increases.

Checkpoint 25-3: What is the process of cell division that forms the gametes?

Sex Determination

The two chromosomes that determine the offspring's sex, unlike the autosomes (the other 22 pairs of chromosomes), are not matched in size and appearance. The female X chromosome is larger than most other chromosomes and carries genes for other characteristics in addition to that for sex. The male Y chromosome is smaller than other chromosomes and mainly determines sex. A female has two X chromosomes in each body cell; a male has one X and one Y.

By the process of meiosis, each male sperm cell receives either an X or a Y chromosome, whereas every egg cell receives only an X chromosome (Fig. 25-2). If a sperm cell with an X chromosome fertilizes an ovum, the resulting infant will be female; if a sperm with a Y chromosome fertilizes an ovum, the resulting infant will be male (see Fig. 25-2).

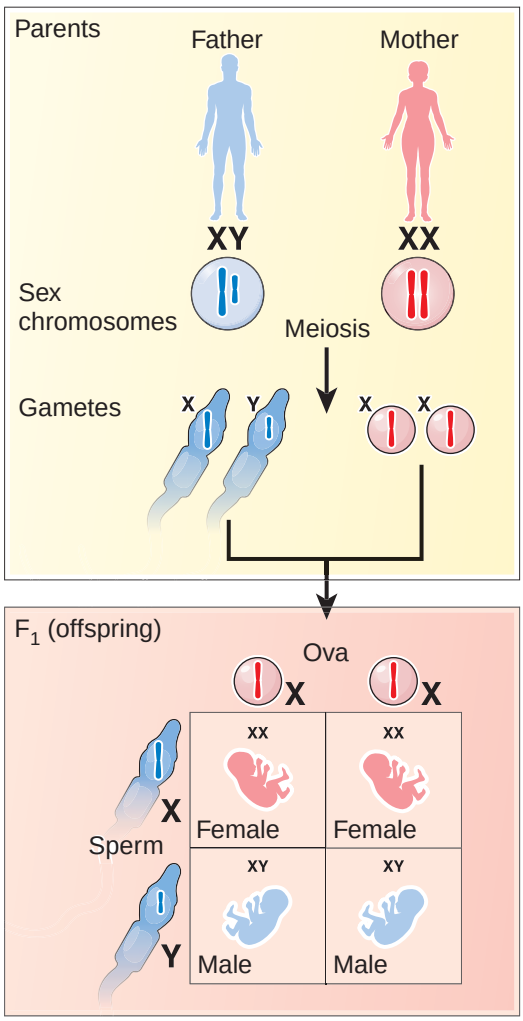

Figure 25-2 **Sex determination.** If an X chromosome from a male unites with an X chromosome from a female, the child is female (XX); if a Y chromosome from a male unites with an X chromosome from a female, the child is male (XY).

Sex-Linked Traits

Any trait that is carried on a sex chromosome is said to be **sex-linked.** Because the Y chromosome carries few traits aside from sex determination, most sex-linked traits are carried on the X chromosome and are best described as *X-linked.* Examples are hemophilia, certain forms of baldness, and red-green color blindness.

Sex-linked traits appear almost exclusively in males. The reason for this is that most of these traits are recessive, and if a recessive gene is located on the X chromosome in a male it cannot be masked by a matching dominant gene. (Remember that the Y chromosome with which the X chromosome pairs is very small and carries few genes.) Thus, a male who has only one recessive gene for a trait will exhibit that characteristic, whereas a female must have two recessive genes to show the trait. The female must inherit a recessive gene for that trait from each parent and be homozygous recessive in order for the trait to appear.

Checkpoint 25-4: What sex chromosome combination determines a female? A male?

Checkpoint 25-5: What term is used to describe a trait carried on a sex chromosome?

Hereditary Traits

Some observable hereditary traits are skin, eye, and hair color and facial features. Also influenced by genetics are less clearly defined traits, such as weight, body build, lifespan, and susceptibility to disease.

Some human traits, including the traits involved in many genetic diseases, are determined by a single pair of genes; most, however, are the result of two or more gene pairs acting together in what is termed **multifactorial inheritance.** This type of inheritance accounts for the wide range of variations within populations in such characteristics as coloration, height, and weight, all of which are determined by more than one pair of genes.

Gene Expression

The effect of a gene on a person's phenotype may be influenced by a variety of factors, including the individual's sex and the presence of other genes. For example, the genes for certain types of baldness and certain types of color blindness may be inherited by either males or females, but the traits appear mostly in males under the effects of male sex hormone.

Environment also plays a part in gene expression. One inherits a potential for a given size, for example, but one's actual size is additionally influenced by such factors as nutrition, development, and general state of health. The same is true of life span and susceptibility to diseases.

Genetic Mutation

As a rule, chromosomes replicate exactly during cell division. Occasionally, however, for reasons not yet totally understood, the genes or chromosomes change. This change may involve a single gene or whole chromosomes. Alternatively, it may consist of chromosomal breakage, in which there is loss or rearrangement of gene fragments. Often these changes occur during cell division (mitosis or meiosis) as chromosomes come together, re-assort and get distributed to two new cells. Such changes are termed genetic **mutations**. Mutations may occur spontaneously or may be induced by some agent, such as ionizing radiation or chemicals, described as a **mutagen** (MU-tah-jen) or mutagenic agent.

If a mutation occurs in an ovum or a sperm cell, the altered trait will be inherited by the offspring. The vast majority of harmful mutations never are expressed because the affected fetus dies and is spontaneously aborted. Most remaining mutations are so inconsequential that they have no visible effect. Beneficial mutations,

Box 25-2 Clinical Perspectives

Mitochondrial Disease: When the Powerhouses Shut Down

Mitochondria are the powerhouse organelles of cells, converting the energy in nutrients into the ATP needed for cell activities. Because they may have evolved as separate organisms early in the history of life on earth, they exist almost as special entities within the cell. They have their own DNA and multiply at their own pace, independent of the cell's pattern. When mitochondria do not function properly, disease can result.

Some mitochondrial diseases are caused by genetic mutations in mitochondrial DNA, while others are caused by mutations in nuclear DNA that codes for certain mitochondrial proteins. Both types of mutations disrupt ATP synthesis. Mitochondrial diseases are believed to affect several thousand children in the United States, causing serious damage to metabolically active cells in the brain, heart, liver, muscles, kidneys, and endocrine organs. The disorders are difficult to diagnose because they cause a variety of symptoms that have been confused with epilepsy, cerebral palsy, and multiple sclerosis.

If a mitochondrial defect is programmed in the nuclear DNA, it could be inherited from either parent. If, however, it is carried in the mitochondrion itself, it would be passed only from a mother to her offspring. This is because the mitochondria in the zygote come only from the ovum; sperm cells, which are much smaller, do not carry any mitochondria.

on the other hand, tend to survive and increase as a population evolves. (See Box 25-2 for information about genetic mutations and mitochondrial diseases.)

Checkpoint 25-6: What is a mutation?

Genetic Diseases

Any disorders that involve the genes may be said to be genetic, but they are not always hereditary, that is, passed from parent to offspring in the reproductive cells. Noninherited genetic disorders may begin during maturation of the sex cells or even during development of the embryo.

Advances in genetic research have made it possible to identify the causes of many hereditary disorders and to develop genetic screening methods. In people who are "at risk" for having a child with a genetic disorder, as well as fetuses and newborns with a suspected abnormality, tests can often confirm or rule out the presence of a genetic defect.

Congenital Versus Hereditary Diseases

Before we discuss hereditary diseases, we need to distinguish them from other congenital diseases. To illustrate, let us assume that two infants are born within seconds in adjoining delivery rooms of the same hospital. It is noted that one infant has a clubfoot, a condition called **talipes** (TAL-ih-pes); the second infant has a rudimentary extra finger attached to the fifth finger of each hand, a condition called **polydactyly** (pol-e-DAK-til-e). Are both conditions hereditary? Both congenital? Is either hereditary? We can answer these questions by defining the key terms, congenital and hereditary. **Congenital** means present at the time of birth; **hereditary** means genetically transmitted or transmissible. Thus, one condition may be both congenital and hereditary; another, congenital yet not hereditary.

Hereditary conditions are usually evident at birth or soon thereafter. However, certain inherited disorders, such as adult polycystic kidney disease and Huntington disease, a nervous disorder, do not manifest themselves until about midlife (40 to 50 years of age). People with these genetic defects may pass them on to their children before they are aware of them unless genetic testing reveals their presence. In the case of our earlier examples, the clubfoot is congenital, but not hereditary, having resulted from severe distortion of the developing extremities during intrauterine growth; the extra fingers are hereditary, a familial trait that appears in another relative, a grandparent perhaps, or a parent, and that is evident at the time of birth.

Causes of Congenital Disorders Although causes of congenital deformities and birth defects often are not known, in some cases, they are known and can be avoided. For example, certain infections and toxins may be transmitted from the mother's blood by way of the placenta to the fetal circulation. Some of these cause serious developmental disorders in affected babies.

German measles (rubella) is a contagious viral infection that is ordinarily a mild disease, but if maternal infection occurs during the first 3 or 4 months of pregnancy, the fetus has a 40% chance of developing defects of the eye (cataracts), ear (deafness), brain, and heart. Infection can be prevented by appropriate immunizations.

Ionizing radiation and various toxins may damage the genes, and the disorders they produce are sometimes transmissible. Environmental agents, such as mercury and some chemicals used in industry (*e.g.,* certain phenols and PCB), as well as some drugs, notably LSD, are known to disrupt genetic organization. (See Box 25-3 for information about preventing genetic damage.)

Box 25-3 • Health Maintenance

Preventing Genetic Damage

It is sometimes difficult to determine whether a genetic defect is the result of a spontaneous random mutation or is related to exposure of a germ cell to an environmental toxin. Male and female sex cells are present at birth but do not become active until the reproductive years. This leaves a long time span during which toxic exposure can occur. Most of what we know about chemicals that cause mutations has been learned from environmental accidents. For example, mercury compounds have found their way into the food chain, causing neural damage to the children of parents who consumed foods containing mercury. Lead, which is toxic when ingested, as from air or water pollution, has been implicated in sperm cell abnormalities and in reduced sperm counts. Radiation accidents have been linked to increased susceptibility to certain cancers in children born after these accidents.

Meiosis is the step most prone to genetic errors. This process can be studied in males with specimens obtained from testicular biopsy. Also, samples of sperm cells, which are produced continuously in males,can be obtained easily and studied for visible defects. Advancing age in both the mother and the father is known to increase errors in meiosis. Males between 20 and 45 years of age carry the least risk of transmitting a genetic error. For females, the least risk is between ages 15 to 35 years. Because new sperm cells are produced on a 64-day cycle, men are advised to avoid conception for a few months after exposure to x-rays, cancer chemotherapy, or other chemicals capable of causing mutations.

Intake of alcohol and cigarette smoking by a pregnant woman often cause growth retardation and low birthweight in her infant. Smaller than normal infants do not do as well as average weight babies. Some congenital brain and heart defects have been associated with a condition called **fetal alcohol syndrome**. Total abstinence from alcohol and cigarettes is strongly recommended during pregnancy.

Spina bifida (SPI-nah BIF-ih-dah) is incomplete closure of the spine, through which the spinal cord and its membranes may project (Fig. 25-3). The defect usually occurs in the lumbar region. If the meninges protrude (herniate), the defect is termed a meningocele (meh-NIN-go-sele); if both the spinal cord and meninges protrude, it is a myelomeningocele (mi-eh-lo-meh-NIN-go-sele). In the latter case, the spinal cord ends at the point of the defect, which affects function below that point. Folic acid, a B vitamin, reduces the risk of spina bifida and other CNS defects in the fetus. Women of childbearing age should eat foods high in folic acid (green leafy vegetables, fruits, and legumes) and should take folic acid supplements even before pregnancy, as the nervous system develops early. In the U.S., folic acid is added to grain products, such as bread, pasta, rice and cereals.

Checkpoint 25-7: Can a disorder be congenital but not hereditary? Explain.

Examples of Genetic Diseases

The best known example of a genetic disorder that is not hereditary is the most common form of **Down syndrome,** also known as **trisomy 21** because it results from an extra chromosome number 21 in each cell. This abnormality arises during formation of a sex cell. The disorder is usually recognizable at birth by the child's distinctive facial features (Fig. 25-4). Children with Down syndrome have poor muscle tone. They have lowered immunity and are also prone to heart disease, leukemia and Alzheimer disease. Their intellectual function is impaired. However, the amount of skill they can gain depends on the severity

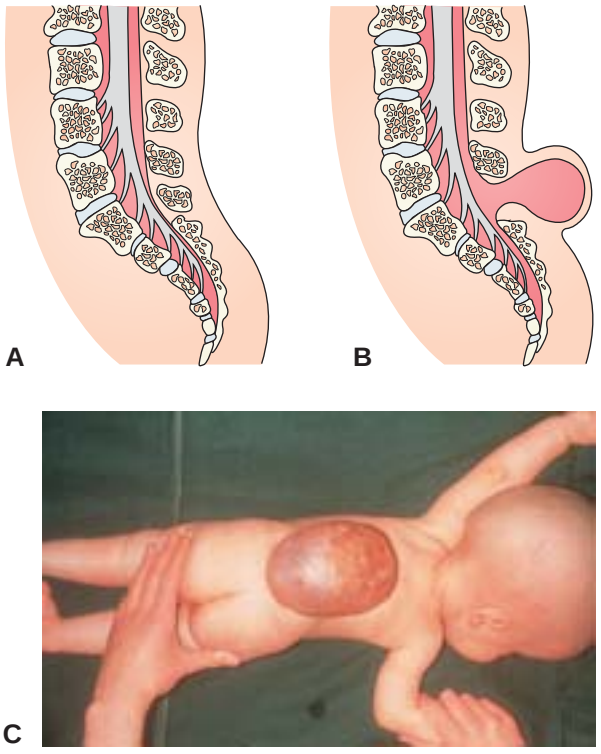

Figure 25-3 Spina bifida, incomplete closure of the spinal cord. (A) Normal spinal cord (B) Spina bifida with protrusion of the meninges (meningocele) (C) Protrusion of the spinal cord and meninges (myelomeningocele). (Reprinted with permission from Pillitteri A. Maternal and Child Health Nursing. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Figure 25-4 Child with Down syndrome (trisomy 21). The typical facial features are visible in this photo. (Reprinted with permission from Pillitteri A. Maternal and Child Health Nursing. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

of the disease and their family and school environments. Down syndrome is usually not inherited, although there is a hereditary form of the disorder. In most cases, both parents are normal, as are the child's siblings. The likelihood of having a baby with Down syndrome increases dramatically in women past the age of 35 years and may result from defects in either the male or female germ cells owing to age.

Most genetic diseases are **familial** or **hereditary**; that is, they are passed on from parent to child in the egg or sperm. In the case of a disorder carried by a dominant gene, only one parent needs to carry the abnormal gene to give rise to the disease. Any child who receives the defective gene will have the disease. Any children who do not show the disease do not have the defective gene nor are they carriers. One example is **Huntington disease**, a progressive degenerative disorder associated with rapid, involuntary muscle activity and mental deterioration. The disease does not appear until about age 40 and leads to death within 15 years. There is no cure for Huntington disease, but people with the defective gene can be identified by genetic testing. Another example is **Marfan syndrome**, a connective tissue disease. People with Marfan syndrome are tall, thin, and have heart defects.

If the disease trait is carried by a recessive gene, as is the case in most inheritable disorders, a defective gene must come from each parent. Some recessively inherited diseases are described next.

In **phenylketonuria** (fen-il-ke-to-NU-re-ah) (**PKU**), the lack of a certain enzyme prevents the proper metabolism of **phenylalanine** (fen-il-AL-ah-nin), one of the common amino acids. As a result, phenylalanine accumulates in the infant's blood and appears in the urine. If the condition remains untreated, it leads to mental retardation before the age of 2 years. Newborn infants are routinely screened for PKU.

Sickle cell disease is described in Chapter 13, where it is stated that the disease is found almost exclusively among black patients. By contrast, **cystic fibrosis** is most common in white populations; in fact, it is the most frequently inherited disease among this group. Cystic fibrosis is characterized by excessively thickened secretions in the bronchi, the intestine, and the pancreatic ducts, resulting in obstruction of these vital organs. It is associated with frequent respiratory infections, intestinal losses, particularly of fats and fat-soluble vitamins, as well as massive salt loss. Treatment includes oral administration of pancreatic enzymes and special pulmonary exercises. Cystic fibrosis was once fatal by the time of adolescence, but now, with appropriate care, life expectancies are extending into the third decade. The gene responsible for the disease has been identified, raising hope of better diagnosis, treatment, and perhaps even correction of the defective gene that causes the disorder.

In **Tay-Sachs disease**, a certain type of fat is deposited in neurons of the CNS and retina because cellular lysosomes lack an enzyme that breaks it down. The disease occurs mainly in eastern European (Ashkenazi) Jews and generally leads to death by age four. There is no cure for Tay-Sachs, but a blood test can identify genetic carriers of the disease.

Another group of heritable muscle disorders is known collectively as the **progressive muscular atrophies.** Atrophy (AT-ro-fe) means wasting due to decrease in the size of a normally developed part. The absence of normal muscle movement in the infant proceeds within a few months to extreme weakness of the respiratory muscles, until ultimately the infant is unable to breathe adequately. Most afflicted babies die within several months. The name *floppy baby syndrome,* as the disease is commonly called, provides a vivid description of its effects.

Albinism is another recessively inherited disorder that affects the cells (melanocytes) that produce the pigment melanin. The skin and hair color are strikingly white and do not darken with age. The skin is abnormally sensitive to sunlight and may appear wrinkled. People with albinism are especially susceptible to skin cancer and to some severe visual disturbances, such as myopia (nearsightedness) and abnormal sensitivity to light (photophobia).

Other inherited disorders include **osteogenesis** (oste-o-JEN-eh-sis) **imperfecta**, or brittle bones, in which multiple fractures may occur during and shortly after fetal life, and a disorder of skin, muscles, and bones called

neurofibromatosis (nu-ro-fi-bro-mah-TO-sis). In the latter condition, multiple masses, often on stalks (pedunculated), grow along nerves all over the body.

More than 20 different cancers have been linked to specific gene mutations. These include cancers of the breast, ovary, and colon as well as some forms of leukemia. Note, however, that hereditary forms of cancer account for only about 1% of all cancers and that the development of cancer is complex, involving not only specific genes but also gene interactions and environmental factors.

Genetic components have been suggested in some other diseases as well, including certain forms of heart disease, diabetes mellitus, types of cleft lip and cleft palate, and perhaps Parkinson and Alzheimer disease.

Checkpoint 25-8: What causes phenylketonuria?

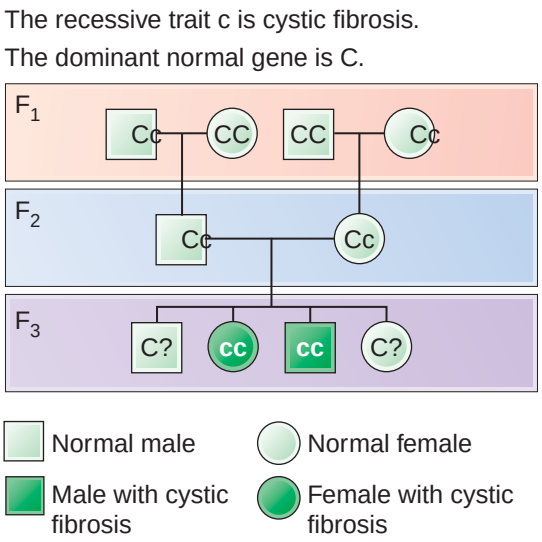

Figure 25-5 A pedigree (family history) showing three generations (F_1-F_3). The pedigree is a tool used in genetic studies and genetic counseling. In this example, one parent in each F_1 cross and both parents in the F_2 cross are normal but carry the recessive gene (c) for cystic fibrosis. For the normal children in F_3, only one gene (the dominant normal gene) is known. Note that the F_3 generation does not show strict predicted genetic ratios. Theoretically, only one in four children should be homozygous recessive (have two recessive genes). *ZOOMING IN ✦ What are the possible genotypes of the two normal children in the F_3 generation?*

Treatment and Prevention of Genetic Diseases

The number of genetic diseases is so great (more than 4000) that many pages of this book would be needed simply to list them all. Moreover, the list continues to grow as sophisticated research techniques and advances in biology make it clear that various diseases of previously unknown origin are genetic—some hereditary, others not. Can we identify which are inherited genetic disorders and which are due to environmental factors? Can we prevent the occurrence of any of them?

Genetic Counseling

It is possible to prevent genetic disorders in many cases and even to treat some of them. The most effective method of preventing genetic disease is through genetic counseling, a specialized field of health care. Genetic counseling centers use a team approach of medical, nursing, laboratory, and social service professionals to advise and care for clients. People who might consider genetic counseling include prospective parents over 35, those who have a family history of genetic disorders, and those who are considering some form of fertility treatment.

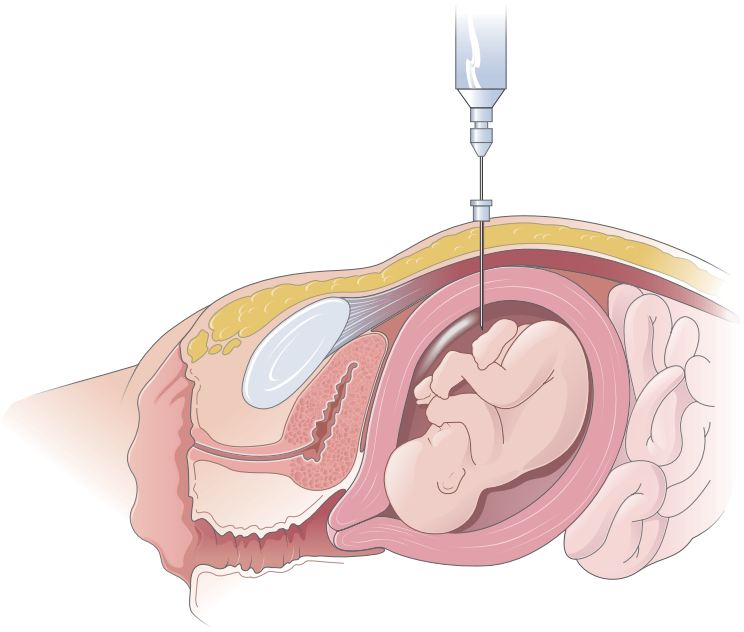

Figure 25-6 Amniocentesis. A sample of amniotic fluid is removed from the amniotic sac. Cells and fluid are tested for fetal abnormalities. (Reprinted with permission from Cohen BJ. Medical Terminology. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2004.)

The Family History An accurate and complete family history of both prospective parents is necessary for

genetic counseling. This history should include information about relatives with respect to age, onset of a specific disease, health status, and cause of death. The families' ethnic origins may be relevant because some genetic diseases predominate in certain ethnic groups. Hospital and physician records are studied, as are photographs of family members. The ages of the prospective parents are considered as factors, as is parental or ancestral relationship (*e.g.*, marriage between first cousins). The complete, detailed family history, or tree, is called a **pedigree.** Pedigrees are used to determine the pattern of inheritance of a genetic disease within a family (Fig. 25-5). They may also indicate whether a given family member is a carrier of the disease. Note that in some cases, there is not enough family data to determine the genotype of all members with regard to a given trait. Also, small numbers of offspring may not show the strict genetic ratios expected from a given cross.

Laboratory Studies One technique that enables the geneticist to study an unborn fetus is **amniocentesis** (am-ne-o-sen-TE-sis). During this procedure, a small amount of the amniotic fluid that surrounds the fetus is withdrawn (Fig. 25-6). Fetal skin cells in the amniotic fluid are removed, grown (cultured), and separated for study. The chromosomes are examined, and the amniotic fluid is analyzed for biochemical abnormalities. With these methods, almost 200 genetic diseases can be detected before birth.

Another method for obtaining fetal cells for study involves sampling of the chorionic villi through the cervix. The chorionic villi are hairlike projections of the membrane that surrounds the embryo in early pregnancy. The method is called **chorionic villus sampling** (CVS). Samples may be taken between 8 and 10 weeks of pregnancy, and the cells obtained may be analyzed immediately. In contrast, amniocentesis cannot be done before the 14th to 16th week of pregnancy, and test results are not available for about 2 weeks.

Abnormalities in the chromosome number and some abnormalities within the chromosomes can be detected by **karyotype** (KAR-e-o-tipe) analysis. A karyotype is produced by growing cells obtained by amniocentesis or CVS in a special medium and arresting cell division at the metaphase stage. A technician uses special stains to reveal certain changes in fine structure within the chromosomes. The chromosomes, visible under the microscope, are then photographed, and the photographs are cut out and arranged in groups according to their size and form (Fig. 25-7). Errors involving abnormalities in the number or structure of the chromosomes can thereby be detected.

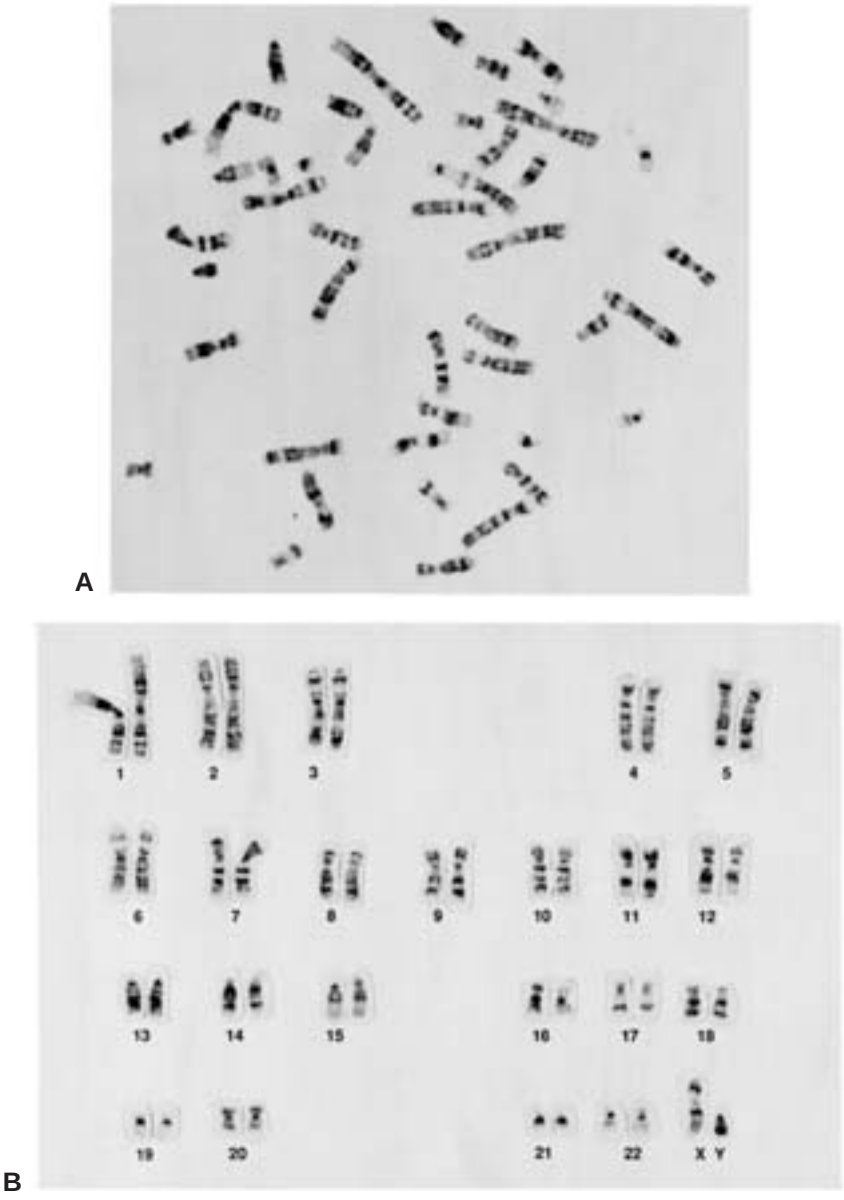

Figure 25-7 **Chromosomes.** (A) Metaphase spread of normal male chromosomes. The chromosomes have doubled and are ready to divide. The bands are produced by staining. (B) Karyotype. The chromosomes are arranged in matching pairs according to size and other characteristics. (Courtesy of Wenda S. Long, Thomas Jefferson University, Philadelphia) *ZOOMING IN ✦ How many autosomes are shown in B?*

Counseling Prospective Parents Armed with all the available pertinent facts, and with knowledge of genetic inheritance patterns, the counselor is equipped to inform the prospective parents of the possibility of their having genetically abnormal offspring. The couple may then use this information to make decisions about family planning. Depending on the individuals and their situation, a couple might elect to have no children, have an adoptive family, use a donor gamete, terminate a pregnancy, or accept the risk.

Checkpoint 25-9: What is a pedigree and how is a pedigree used in genetic counseling?

Checkpoint 25-10: What is a karyotype?

Progress in Medical Treatment

The mental and physical ravages of many genetic diseases are largely preventable, provided the diseases are diagnosed and treated early in the individual's life. Some of these diseases respond well to dietary control. One such disease, called **maple syrup urine disease**, responds to very large doses of thiamin along with control of the intake of certain amino acids. The disastrous effects of Wilson disease, in which abnormal accumulations of copper in the tissue cause tremor, rigidity, uncontrollable stagger, and finally extensive liver damage, can be prevented by a combination of dietary and drug therapy.

Phenylketonuria is perhaps the best-known example of dietary management of inherited disease. If the disorder is undiagnosed and untreated, 98% of affected patients will be severely mentally retarded by 10 years of age. In contrast, if the condition is diagnosed and treated before the baby reaches the age of 6 months, and treatment is maintained until the age of 10 years, mental deficiency will be prevented, or at least minimized. A simple blood test for PKU is now done routinely in hospitals throughout the United States. Infants are usually screened immediately after birth, but they should be retested 24 to 48 hours after taking in protein.

Klinefelter (KLINE-fel-ter) **syndrome**, which occurs in about 1 in 600 males, is a common cause of underdevelopment of the gonads with resulting infertility. Victims of this disorder have abnormal sex chromosome patterns, usually an extra X chromosome. Instead of the typical male XY pattern, the cells contain an XXY combination owing to failure of the sex chromosomes to separate during cell division. Treatment of this disorder includes the use of hormones and psychotherapy.

In the future, we can anticipate greatly improved methods of screening, diagnosis, and treatment of genetic diseases. There have been reports of fetuses being treated with vitamins or hormones after prenatal diagnosis of a genetic disorder. Ahead lies the possibility of treating or correcting genetic disorders through genetic engineering—introducing genetically altered cells to produce missing factors, such as enzymes or hormones, or even correcting faulty genes in the victim's cells. Researchers have already made some attempts to supplement failed genes with healthy ones.

For the present, it is important to educate the public about the availability of screening methods for both parents and offspring. People should also be made aware of the damaging effects of radiation, drugs, and other toxic substances on the genes. Because so many congenital disorders are associated with environmental factors, public education and better health habits will probably yield greater overall benefits than genetic manipulations.

Word Anatomy

Medical terms are built from standardized word parts (prefixes, roots, and suffixes). Learning the meanings of these parts can help you remember words and interpret unfamiliar terms.

WORD PART	MEANING	EXAMPLE
Genes and Chromosomes		
chrom/o	color	*Chromosomes* color darkly with stains.
aut/o-	self	*Autosomes* are all the chromosomes aside from the two that determine sex.
heter/o	other, different	*Heterozygous* paired genes (alleles) are different from each other.
homo-	same	*Homozygous* paired genes (alleles) are the same.
phen/o	to show	Traits that can be observed or tested for make a up a person's *phenotype*.
Hereditary Traits		
multi-	many	*Multifactorial* traits are determined by multiple pairs of genes.
Genetic Diseases		
dactyl/o	digit (finger or toe)	In *polydactyly* there is an extra finger on each hand.
con-	with	A *congenital* defect is present at the time of birth.
-cele	swelling	In spina bifida, the meninges can protrude through the spine as a *meningocele*.

WORD PART	MEANING	EXAMPLE
Treatment and Prevention of Genetic Diseases		
-centesis	tapping, perforation	*Amniocentesis* is a tap of the amniotic fluid.
kary/o	nucleus	A *karyotype* is an analysis of the chromosomes contained in the nucleus of a cell.

Summary

I. Genes and chromosomes

1. Genes
   a. Hereditary units
   b. Segments of DNA
   c. Control manufacture of proteins (e.g. enzymes, hormones)
2. Chromosomes
   a. Threadlike bodies in nucleus; 46 in humans
   b. Composed of genes
   c. 22 pairs autosomes (non-sex chromosomes)
   d. 1 pair sex chromosomes

A. Dominant and recessive genes

1. Dominant gene—always expressed
   a. May be heterozygous (two genes different)
   b. May be homozygous dominant (two genes the same)
2. Recessive gene—expressed only if homozygous recessive (received from both parents)
   a. Carrier—person with recessive gene that is not apparent but can be passed to offspring
   b. Phenotype—characteristic that can be seen or tested for
   c. Genotype—genetic make-up

B. Distribution of chromosomes to offspring

1. Meiosis
   a. Cell division that forms sex cells with 23 chromosomes
   b. Each cell receives one of each chromosome pair
   c. Punnett square shows results of crosses

C. Sex determination

1. X chromosome larger and carries other traits
2. Y smaller and carries mainly gene for sex determination
3. Female cells have XX; male cells have XY

D. Sex-linked traits

1. Traits carried on sex chromosome (usually X)
2. Sex-linked traits appear mostly in males
   a. Passed from mother to son on X chromosome
   b. If recessive, not masked by dominant gene on Y
   c. Examples—hemophilia, baldness, red-green color blindness

II. Hereditary traits

1. Genes determine physical, biochemical, and physiologic characteristics of every cell
2. Some traits determined by single gene pairs
3. Most determined by multifactorial inheritance
   a. Involves multiple gene pairs
   b. Produces a range of variations in a population
   c. Examples—height, weight, coloration, susceptibility to disease

A. Gene expression

1. Factors
   a. Sex
   b. Presence of other genes
   c. Environment

B. Genetic mutation

1. Change in genes or chromosomes
2. May be passed to offspring if occurs in germ cells
3. Mutagenic agents
   a. Factors causing mutation
   b. Examples—ionizing radiation, chemicals

III. Genetic diseases—disorders involving genes

A. Congenital versus hereditary diseases

1. Congenital disorders
   a. Present at birth
   b. May or may not be hereditary
   c. Causes: infections, toxins, ionizing radiation, alcohol, smoking
   d. Examples—defects caused by rubella, fetal alcohol syndrome, spina bifida
2. Hereditary (familial) disorders
   a. Passed from parent to offspring in sex cells

B. Examples of genetic diseases

1. Down syndrome—results from extra chromosome 21 (trisomy 21)
2. Dominant inheritance—Huntington disease, Marfan syndrome
3. Recessive inheritance—PKU (phenylketonuria), cystic fibrosis, sickle cell anemia, Tay-Sachs disease, progressive muscular atrophies, albinism, osteogenesis imperfecta, neurofibromatosis

IV. Treatment and prevention of genetic diseases

A. Genetic counseling

1. Pedigree—family history
2. Laboratory studies
   a. Amniocentesis—withdrawal of amniotic fluid for study at 14 to 16 weeks of pregnancy
   b. Chorionic villus sampling—done at 8 to 10 weeks of pregnancy
   c. Karyotype—analysis of chromosomes
3. Counseling the prospective parents

B. Progress in medical treatment

1. Dietary control—maple syrup urine disease, Wilson disease, PKU
2. Hormone therapy—Klinefelter disease
3. Fetal therapy
4. Correction of faulty genes—experimental

Questions for Study and Review

Building Understanding

Fill in the blanks

1. The basic unit of heredity is a(n) _____.
2. Chromosomes not involved in sex determination are known as _____.
3. Any trait that is carried on a sex chromosome is said to be _____.
4. Change in a gene or chromosome is called _____.
5. Incomplete closure of the spine results in a disorder called _____.

Matching

Match each numbered item with the most closely related lettered item.

___ 6. A gene that is always expressed if present
___ 7. A gene that is not always expressed if present
___ 8. Term for paired genes for a trait that are the same
___ 9. Term for paired genes for a trait that are different

a. dominant
b. recessive
c. homozygous
d. heterozygous

Multiple choice

___ 10. The genetic code is composed of
a. deoxyribonucleic acid
b. ribonucleic acid
c. protein
d. nuclear membrane

___ 11. Genes govern the cell by controlling the manufacture of
a. carbohydrates
b. lipids
c. proteins
d. electrolytes

___ 12. Paired genes for a given trait are known as
a. chromosomes
b. ribosomes
c. nucleotides
d. alleles

___ 13. A condition characterized by extra fingers or toes is called
a. talipes
b. polydactyly
c. osteogenesis imperfecta
d. neurofibromatosis

___ 14. A complete detailed family history can be obtained by doing
a. chorionic villus sampling
b. amniocentesis
c. a karyotype
d. a pedigree

Understanding Concepts

15. How many chromosomes are there in a human body cell? In a human gamete?
16. Dana has one dominant allele for brown eyes (B) and one recessive allele for blue eyes. What is Dana's genotype? What is her phenotype?
17. Describe the process of meiosis and explain how it results in genetic variation.
18. Explain the great variation in the color of skin and hair in humans.
19. Describe how a mutagenic agent can produce genetic variation.
20. What is the difference between a congenital disease and a hereditary disease? List some congenital and hereditary diseases.
21. What is PKU and how should this disease be treated.
22. Compare and contrast amniocentesis and chorionic villus sampling. List some diseases that can be diagnosed using these techniques.
23. What is the most common inheritable disease among black people? Among white people? What are the symptoms of these two diseases?

Conceptual Thinking

24. If mitosis were used to produce gametes, what consequences would this have on the offspring's genotype, phenotype, and chromosome number?
25. Jason and Nicole are expecting their first child and are wondering what their child's eye color might be. Jason has blue eyes (a recessive trait) and Nicole has brown eyes (a dominant trait). Both of Jason's parents have blue eyes. One of Nicole's parents has brown eyes, the other has blue eyes. What are Jason's and Nicole's genotype and phenotype? What are the possible genotypes and phenotypes of their children?