Chapter 3
Genetic and Genomic Influences in Maternal, Newborn, and Child Health

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We are now 12 weeks' pregnant and have been on cloud nine until today, when we learned our baby might have Down syndrome. We really never considered that possibility—what do we do now? Our physician suggested we could have chorionic villus sampling (CVS) or amniocentesis to find out for sure, but there is a small chance of miscarrying our baby. She also mentioned a newer blood test that is extremely accurate but still not perfect. Our world is upside down. Do we want to know? What would be the benefit, unless we were going to end our pregnancy? We don't know anyone with Down syndrome, or anyone who has raised a child with Down syndrome, or what that would be like. Our happiness has really turned into turmoil.

—Jessica, age 30

Learning Outcomes

3.1 Understand foundational concepts of genetics and genomics, including how DNA influences health and illness.

3.2 Explain mechanisms by which alterations in DNA cause disease.

3.3 Distinguish between single-gene (Mendelian) and multifactorial diseases and health conditions.

3.4 Identify characteristics of common inheritance patterns of single-gene conditions.

3.5 Describe the uses, implications, and limitations of various prenatal and postnatal types of genetic tests that are offered to childbearing families and children, distinguishing between screening and diagnostic tests.

3.6 Explain ways that nurses can advocate for and support clients and families undergoing genetic testing.

3.7 Describe the role of the nurses in assessing and communicating genetic risk, including eliciting a family history, creating a genetic pedigree, and incorporating genetics into physical assessment.

3.8 Identify children or families who might benefit from genetic information and services or referral to a genetic professional, and explain the nurse's role in supporting the family undergoing genetic counseling.

3.9 Discuss ethical, legal, and social implications of genomic health care.

Pregnancy and childbirth usually take their normal course and a healthy baby is born without problems. Three to five percent of pregnancies, however, result in the birth of a child with some sort of birth defect or genetic disorder. Genetic problems may become evident during pregnancy, at birth, or during the newborn period, or may not appear for some time. The Human Genome Project, which was completed in 2003, brought rapid progress in genome science and an understanding that essentially all diseases and health conditions have a genetic component. It is predicted that health care will increasingly be

personalized, based on each individual's genetic information. **Genomics**, the study of all human genes including their interactions with each other and with environmental factors, is now considered to be a central science for nursing practice. All registered nurses should be able to identify, refer, support, and care for children and families affected by conditions or diseases with a genetic component. This chapter presents information nurses must understand to provide competent care in the genome era of health care.

Genetic Basics

A basic knowledge of the cell, cell division, DNA, chromosomes, and genes is essential to deliver the genetic standard of care to children, adolescents, and their families.

Cells and DNA

The **cell** is the basic unit of life and the working unit of all living systems. Life starts when a sperm and ovum combine to form a single cell, which develops to form a human body made up of trillions of cells. These cells share common features such as a nucleus that contains the DNA and **organelles** such as mitochondria. Cells are specialized in appearance and function, according to their location. For example, pancreatic cells function much differently than nerve cells.

All human cells, except red blood cells, contain a complete set of DNA molecules, which are long sequences of nucleotides. A nucleotide is a base with an attached sugar and phosphate group. Four different bases, designated A, C, T, and G, make up DNA. The order, or sequence, of these bases provides exact instructions for protein building. The entire DNA in a human cell is referred to as the **human genome**. Most of the DNA is organized into **chromosomes**, which are contained in the cell nucleus. A small amount of DNA is found in the mitochondria and will be discussed later in this section. Each person's genome is unique, with the exception of monozygotic twins, who are derived from the same fertilized ovum and therefore share identical DNA.

The nucleus of each cell (except gametes) contains about 6 feet of DNA that is tightly wound and packaged into 23 pairs of chromosomes, making a complete set of 46 chromosomes. The set includes 22 pairs of **autosomes**, which are by tradition numbered according to size, with chromosome 1 being the largest. There are two copies of each autosome, one inherited from the mother and the other from the father. Copies of a chromosome pair are called **homologous chromosomes**. The 23rd chromosome pair, the **sex chromosomes**, determines an individual's sex. A female has two copies of the X chromosome (one copy inherited from each parent), and a male has one X chromosome (inherited from his mother) and one Y chromosome (inherited from his father). The structure and number of chromosomes can be shown by preparing a **karyotype**, or picture of an individual's chromosomes. Figure 3–1 depicts a normal male and female karyotype. A karyotype is usually obtained from specially treated and stained peripheral blood lymphocytes, but a fetal karyotype can be obtained by sampling amniotic fluid or placental tissue.

Cell Division

Mitosis and meiosis are the two types of cell division in humans. **Mitosis** takes place in somatic or tissue cells of the body, allowing the formation of new cells. Cell division by mitosis results in two cells called *daughter cells* that are genetically identical to the original cell and to each other. Mitosis is responsible for rapid human growth in early life and also replaces cells lost daily from skin surfaces and the lining of gastrointestinal and respiratory tracts.

Meiosis is also known as *reduction cell division*. Meiosis occurs only in the reproductive cells of the testes and ovaries and results in the formation of sperm and ova, (**gametes**). Meiosis is similar to mitosis in that it is a form of cell division; however, through a series of complex mechanisms, the amount of genetic material is reduced to half. Each gamete contains a single copy of each of the 22 autosomes, plus a single sex chromosome. This is critical to ensure that when two gametes combine during fertilization, the correct total number of chromosomes (46) is present in the offspring's cells. The other purpose of meiosis is to make new combinations of genetic material through processes of crossing over and independent assortment. New combinations are necessary to promote diversity in the human population. **Crossing over** results in an exchange or shuffling of

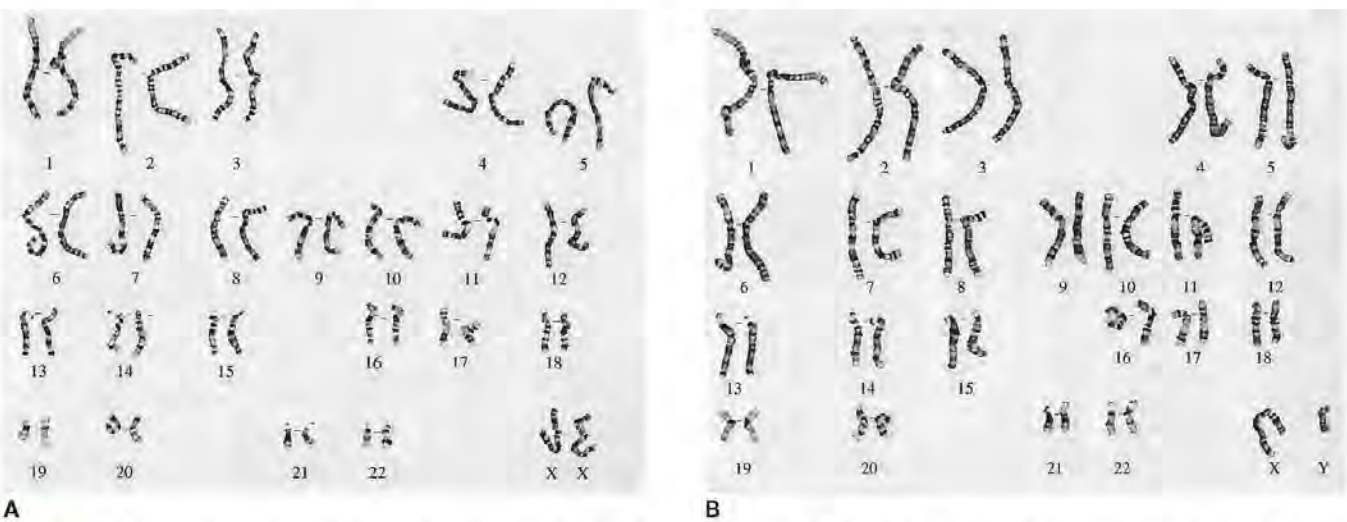

Figure 3–1 **A karyotype is a picture of an individual's chromosomes. It depicts the number and structure of the 22 pairs of autosomes and the sex chromosomes.** *A*, **Female.** *B*, **Male.**

SOURCE: Courtesy of the Greenwood Genetic Center, Greenwood, SC.

material between homologous chromosomes, so that sperm and ova contain a patchwork of genetic material from an individual's maternal and paternal chromosomes. **Independent assortment** means that chromosome pairs segregate randomly into one or another gamete, further enhancing the genetic diversity that is possible at fertilization.

Chromosomal Alterations

Alterations in chromosomes sometimes occur during cell division (meiosis or mitosis) and are classified as alterations in either chromosome number or chromosome structure. The clinical consequences of both types of alterations vary according to the amount of DNA involved.

ALTERATIONS IN CHROMOSOME NUMBER

An increase or decrease in chromosome number is called **aneuploidy**. Aneuploidy is the result of an error during cell division, most often when **nondisjunction** occurs during meiosis. With nondisjunction, pairs of homologous chromosomes do not separate before migrating into egg or sperm cells. This creates a gamete with either two copies or no copies of a particular chromosome. When such a gamete is fertilized by a normal gamete with all 23 chromosomes, a **zygote** that is **monosomic** (missing one member of a chromosome pair) or **trisomic** (having three homologous chromosomes instead of the usual two) results.

Humans do not tolerate either extra or missing DNA very well, and most monosomic or trisomic conceptions result in early pregnancy loss. For example, Turner syndrome (45,X) is the only monosomic condition that is compatible with life. Trisomies involving chromosomes with small numbers of genes may result in live births. Down syndrome is the most common trisomy abnormality seen in children. The presence of the extra chromosome 21 produces distinctive clinical features and a variety of cognitive and physical impairments. Early intervention and clinical practice guidelines developed specifically for children with Down syndrome have improved their health and quality of life and extended their life expectancy (see Chapter 55). Babies are occasionally born with trisomy 13 (Patau syndrome) or trisomy 18 (Edwards syndrome). The prognosis for these conditions is extremely poor; most children die within the first 3 months of life because of cardiac and respiratory complications. However, about 8% to 10% of these children survive the first year; therefore, the family needs to plan for the possibility of long-term care of a severely affected infant (Wu, Springett, & Morris, 2013). It is not a coincidence that the three trisomy conditions that are not universally lethal involve duplication of chromosomes containing the smallest number of genes; other trisomies are lethal. (Pierce, 2014).

Mosaicism. Monosomy and/or trisomy can also occur during cell division (mitosis) after fertilization, resulting in an individual with two, or occasionally more, separate cell lines with different chromosomal makeup. This is known as **mosaicism**. The earlier in development the error occurs, the more cells that will be abnormal. The converse is also true. The degree to which a person is affected by this chromosomal error varies. For example, an individual with mosaic Down syndrome may have a higher intelligence level than children whose every cell has three copies of chromosome 21, and children who are mosaic for trisomy 13 or trisomy 18 tend to survive longer than children with the full trisomy.

Aneuploidies of the Sex Chromosome. In order to understand aneuploidies of the X and Y chromosome, the nurse should know that Y has few genes, none of which is critical to life. In contrast, the X chromosome has many critical genes that would be duplicated in females (compared to males) if it were not for a phenomenon called *X-inactivation*. Early in female embryonic development, within a week of fertilization, one of her X chromosomes is inactivated. This results in equalizing the expression of genes on the X chromosome between the two sexes. Because of X-inactivation and the lack of critical genes on the Y chromosome, aneuploidies involving sex chromosomes are much better tolerated than autosomal aneuploidies. The most common sex chromosome aneuploidies are Turner syndrome in females (45,X) and Klinefelter syndrome in males (47,XXY). Girls with Turner syndrome have short stature, may not develop secondary sex characteristics, and are usually infertile, while men with Klinefelter syndrome tend to be tall with reduced testosterone production, resulting in delayed puberty, breast enlargement, and infertility.

ALTERATIONS IN CHROMOSOME STRUCTURE

Abnormalities of chromosome structure involve only parts of the chromosome and generally occur in the form of an inversion, translocation, deletion, or duplication.

Inversion. A chromosomal **inversion** occurs when a chromosome breaks in two places and the piece between the breaks turns end-for-end and reattaches within the same chromosome. An inversion changes the DNA sequence for that portion of the chromosome. Inversion often results in *balanced* rearrangements because the amount of DNA in the chromosome remains normal. The clinical consequences of an inversion depend on how much chromosomal material is involved and where the inversion occurs. For example, an inversion that occurs between genes may have no effect on health, while an inversion within the gene that codes for factor VIII, a clotting factor, is an important cause of hemophilia A.

Translocation. **Translocation** occurs when two, usually nonhomologous, chromosomes exchange segments of DNA. A translocation that results in a correct amount of chromosomal material but a new arrangement is a *balanced translocation*. The individual who has a balanced rearrangement has all the chromosomal material present and therefore does not usually have any physical or mental disabilities. However, individuals with a balanced translocation are at high risk to produce gametes with unbalanced rearrangements. This leads to increased risk of pregnancy loss or having children with mental and/or physical disabilities owing to missing or extra genetic material. A common *unbalanced translocation* is responsible for about 4% of children diagnosed with Down syndrome (Schaaf, Zschocke, & Potocki, 2012). When a child with Down syndrome is born, it is important to determine if the cause is nondisjunction or translocation. Translocation, while unrelated to maternal age, carries a significantly greater recurrence risk with subsequent pregnancies. Clinically, the two types of Down syndrome are indistinguishable, and chromosome analysis is required to determine the cause.

Deletion and Duplication. Chromosomal alterations sometimes occur when unequal crossing over or abnormal segregation causes a chromosome to have a missing segment (deletion) or an additional segment (duplication) of genetic material. These are called *unbalanced* rearrangements. Conditions associated with unbalanced rearrangements may be incompatible with life or cause altered physical and/or mental development. An example is cri du chat syndrome, which is caused by a large deletion on chromosome 5. Children with cri du chat syndrome have microcephaly (a small head), significant intellectual disability, and an underdeveloped larynx, which causes a peculiar cry that sounds like a cat mewing (Schaaf et al., 2012).

Some deletions or duplications are too small to detect with a standard karyotype. These chromosome abnormalities, known as *microdeletions* and *microduplications*, can be detected by the use of a technology called *microarray comparative genomic*

hybridization (aCGH). An aCGH analysis compares a client's DNA to that of a normal control individual and detects not only aneuploidies and large structural changes, but also submicroscopic duplications, deletions, and unbalanced rearrangements in genes (ACOG, 2013). The higher resolution of aCGH makes it useful to detect disorders typically missed by conventional cytogenetic studies.

Genes

In addition to understanding chromosomal alterations, nurses must have knowledge of genes—what they are, their function, and the consequences of gene alterations. Nurses must also understand how gene alterations are inherited in order to design appropriate nursing interventions and teach the child, adolescent, and family at risk for or with a known genetic condition. Also, as genetic influences on common diseases are better understood, knowledge of gene function and inheritance has become increasingly relevant in health promotion and health maintenance.

GENE DISTRIBUTION

A **gene** is a small segment of a chromosome that can be identified with a particular function, most commonly protein production. In humans, protein-coding DNA is organized into about 21,000 genes (Lander, 2011), which are arranged along chromosomes in a linear order. The vast majority of human DNA lies between genes; it is believed that only about 1% of the human genome is actually represented by protein-encoding genes (McCarthy, McLeod, & Ginsburg, 2013).

Genes have a specific location on a designated chromosome; this is called the *genetic locus*. Gene mapping has documented the locus for most human genes. For example, it is known that the Huntington gene is located at the tip of chromosome 4, whereas the gene associated with cystic fibrosis is on chromosome 7.

Genes that reside on autosomes (i.e., chromosomes 1 through 22) come in pairs, with one copy on each homologous chromosome. Each gene copy, or **allele**, is inherited from a different parent; therefore, pairs of alleles likely have differences in their nucleotide sequence. These differences may be so minor that they do not affect gene function at all, or they may disrupt or totally disable the gene. An individual who has two functionally identical alleles of a gene is said to be **homozygous** (*homo* = same) for that gene. An individual whose alleles for a particular gene function differently is said to be **heterozygous** (*hetero* = different) for that gene.

GENES AND PROTEINS

The 21,000 genes in the human genome are responsible for encoding hundreds of thousands of proteins that carry out all physiologic functions. Proteins form structures, transmit messages between cells, fight infection, direct genes to turn on or off, metabolize nutrients and drugs, and sense light, taste, and smell. When proteins do not function normally, health may be impaired.

The order of amino acids in a particular protein is determine by the order of nucleotides in its encoding gene. Therefore, an alteration in the DNA sequence within a gene may disrupt the amino acid sequence in the protein product of that gene. Genes are described as being *altered* or *mutated* when a change has taken place in their nucleotide sequence. Such a change may or may not result in an altered protein product. A gene alteration that disrupts the order of amino acids in that gene's protein product is called a **mutation**. A protein with an incorrect amino acid may assume the wrong three-dimensional shape and, because protein function is dependent on protein shape (or configuration), the protein may not function as expected.

GENE EXPRESSION

A gene is said to be expressed when it is actively making protein. **Gene expression** can change moment to moment in response to thousands of intracellular and extracellular signals. An example is the mechanism that stimulates cells to produce insulin after eating a candy bar. After the candy bar is eaten, a gene on chromosome 11 directs pancreatic cells to produce and secrete insulin. Although the gene for producing insulin is present in all nucleated cells of the body, it is only functional in insulin-secreting pancreatic cells. The control of gene expression is complex and poorly understood. Changes in nucleotide sequence some distance from a gene may affect its activity in making protein. Smaller, non-DNA molecules are also involved in gene expression: These **epigenetic** effects can cause genes to be overexpressed (making more than expected protein product), underexpressed (making less than expected), or expressed at a time in development when the gene is normally inactive.

Each individual's particular set of genes represents his or her **genotype**. The observable, outward expression of an individual's entire physical, biochemical, and physiologic makeup, as determined by the person's genotype and environmental factors, is referred to as **phenotype**. Phenotype may be expressed as physical appearance such as curly or straight hair or physiologic function; for example, signs or symptoms of a disease.

MITOCHONDRIAL GENES

The vast majority of human genes reside on nuclear DNA that make up chromosomes in the cell nucleus, but mitochondria (organelles involved in energy metabolism, known as the "powerhouse" of the cell) also contain a small amount of DNA. Mitochondrial DNA (mtDNA) contains 37 genes (Turnpenny & Ellard, 2012). Because mitochondria are the sites for energy production, cells requiring large amounts of energy contain more mitochondria than other cells. mtDNA is inherited from the mother in a unique *matrilineal* pattern. This occurs because sperm's mitochondria are located in the tail, which detaches at fertilization. A woman with a mitochondrial gene mutation will consequently pass that mutation to all her children, whereas an affected man will not pass the mtDNA mutation to any of his children (Turnpenny & Ellard, 2012). Clinical manifestations occurring as a result of mitochondrial gene alterations primarily affect high-energy tissues such as brain and cardiac and skeletal muscle.

HUMAN GENETIC VARIATION

The Human Genome Project and other genetic studies have shown that humans are remarkably similar to each other at the DNA level. On average, any two humans vary in less than 1% of their nucleotide sequence. Much of human variation can be attributed to single nucleotide (or "single-letter") changes in DNA sequence. DNA sequencing of hundreds of individuals around the globe has shown that these single-nucleotide changes occur at several million sites (or loci) across the genome; the rest of the genome is identical in 99% of individuals. These single-letter variations are called **single nucleotide polymorphisms**, or SNPs (pronounced "snips"). Most SNPs are benign, although collectively they are thought to account for much phenotypic variation in appearance and risk for common diseases. SNPs have been mapped to the human genome, and the resulting SNP maps are of enormous value to researchers. For example, scientists studying the genetics of type 2 diabetes

mellitus have compared SNP patterns in large numbers of individuals with and without the disease to identify genetic variations associated with this common multifactorial disease. Such **genome-wide association studies** (GWAS) are uncovering the genetic contribution to common chronic conditions that cause most of the disease burden in developed countries.

In recent years, DNA research has identified **copy number variation** as an additional source of human genetic variation. In some individuals, stretches of DNA of variable size (up to 3 million bases and sometimes containing entire genes) are replicated one or more times. Copy number variants (CNVs) appear to be fairly common; on average, each person is believed to have about 100 CNVs of various sizes (Lander, 2011). A CNV that contains an entire gene may result in more than expected gene product. In some cases, copy number variation has been associated with disease or birth defects (Pierce, 2014).

Mutations and Disease

Mutations are gene alterations, and typically the term *mutation* is used to describe an alteration that threatens health. Mutations may cause the formation of an altered or defective protein or cause too much or too little protein to be made. Sometimes a mutation will cause protein to be formed at a time in development when that protein is not normally made.

Mutations can be inherited or acquired. Hereditary mutations are passed to offspring from one or both parents and are also known as *germline mutations* because the mutation exists in the reproductive cells or gametes. Consequently, the DNA in every cell of that offspring will have the mutation, which can then be transmitted to following generations.

Acquired, or somatic, mutations are DNA alterations that occur in an individual at any time throughout a lifetime after fertilization. They result from errors during cell division (mitosis) or from environmental influences such as radiation, toxins, or viral infections. Acquired mutations are also called *sporadic* or *de novo* mutations. Most cases of cancer, for example, are due to somatic mutations. Somatic mutations are not passed from one generation to another.

SINGLE-GENE (MENDELIAN) MUTATIONS

Single-gene alterations are responsible for more than 5000 hereditary diseases such as cystic fibrosis, Duchenne muscular dystrophy, and phenylketonuria (PKU) (Online Mendelian Inheritance in Man [OMIM], 2014). Each of these disorders is relatively rare, although collectively they affect 1 of every 200 newborns (Schaaf et al., 2012). Although they are of enormous consequence to affected families, they constitute a relatively small portion of the total public health burden.

Genes vary enormously in size, but all are very long, containing tens of thousands or even hundreds of thousands of base pairs. Consequently, mutations can occur at various different loci within a gene and result in a wide variety of signs and symptoms. For example, the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene on chromosome 7 contains about 250,000 base pairs and encodes a protein that forms a chloride channel. More than 1000 different *CFTR* mutations that disrupt the chloride channel have been identified (Turnpenny & Ellard, 2012). Some of these mutations cause cystic fibrosis, while others are associated with milder disorders such as absence of the vas deferens, pancreatitis, and rhinosinusitis. Most genetic tests for cystic fibrosis will detect only the most common *CFTR* mutations.

Alterations as small as a single-nucleotide change are known to cause disease. Sickle cell disease is such a disorder: A single A-for-T substitution in the *HBB* gene causes an incorrect amino acid (valine) to be inserted at a site in the protein product (β-globin) normally occupied by a different amino acid (glutamic acid). The altered β-globin protein is then incorporated into hemoglobin molecules. Under conditions of low oxygen tension, the altered β-globin causes red blood cells to assume an abnormal, sickle-like shape. This leads to vascular occlusion and hemolytic anemia (Turnpenny & Ellard, 2012).

TRINUCLEOTIDE REPEAT DISORDERS

Some genetic disorders are caused by a phenomenon known as *trinucleotide repeat expansion*. This occurs at sites within a gene where the DNA sequence consists of adjacent three-nucleotide repeats such as CAGCAGCAG. These repeat sequences tend to expand during meiosis, a feature known as **anticipation**, resulting in a larger number of repeats in subsequent generations. A larger number of repeats may be associated with disease; typically, the larger the number of repeats, the more severe the condition. More than a dozen diseases result from trinucleotide repeat expansion, including Huntington disease, myotonic dystrophy, and Friedreich ataxia. Fragile X syndrome, the most common form of inherited cognitive disability, is a trinucleotide repeat disorder caused by an increased number of CGG trinucleotide repeats in the *FMR1* gene, located at a "fragile site" on the long arm of the X chromosome. The normal number of CGG repeats is up to 60. Individuals with a repeat number ranging between 60 and 200 have a *premutation* allele, meaning that the copy number can increase during meiosis. If the CGG repeat number increases to over 200, the individual (particularly males, who have only one X chromosome) can have the syndrome.

MULTIFACTORIAL DISORDERS

Most inherited traits, such as eye and skin color, are polygenic. That is, they occur as a result of variations on several genes. Most diseases and health conditions are polygenic as well, and the expression of those altered genes is often modified by environmental influences. Such conditions are said to be **multifactorial** and include many birth defects such as cleft lip and palate, pediatric conditions such as autism and asthma, and adult-onset conditions such as cancer and heart disease. Because the term *polygenic* does not imply the influence of the environment, the term *multifactorial* is preferred terminology. The relative contribution of genetic and environmental influences varies across disorders.

GENE ALTERATIONS THAT DECREASE RISK OF DISEASE

Although gene alterations are commonly associated with disease, they can also be helpful and decrease the risk of disease. For example, having a single copy of some genes known to cause autosomal recessive disorders can provide protection against disease. Individuals with a single altered copy of the gene associated with sickle cell disease are less likely to develop malaria. Another protective gene alteration involves a deletion in the *CCR5* gene, which encodes a cell receptor to which the HIV virus binds. Persons who have two copies of the altered *CCR5* gene are almost completely resistant to infection with HIV type 1, and those who are heterozygous for the deletion (have one copy of the altered gene) experience markedly delayed progression from the point of HIV infection to the development of AIDS (Barmania, Potgieter, & Pepper, 2013). As genome research continues, more beneficial gene alterations are being identified.

Principles of Inheritance

Knowledge of inheritance prepares the nurse to offer and reinforce genetic information to children, adolescents, and their families. Genetic knowledge may be important for nurses who assist clients with care management and reproductive decision making. Basic underlying principles of inheritance that nurses can apply to risk assessment and teaching include (a) nearly all genes are paired, (b) only one gene of each pair is transmitted (passed on) from each parent to an offspring, and (c) one copy of each gene in the offspring comes from the mother and the other copy comes from the father. Understanding of Mendelian patterns of inheritance is based on these principles.

Classic Mendelian Patterns of Inheritance

Single-gene, or monogenic, disorders are known as *Mendelian disorders* because they are predictably passed on from generation to generation following Mendel's laws of inheritance. More than 5000 monogenic disorders, most relatively rare, have been catalogued. Monogenic disorders that occur as a result of a mutation on an autosome (chromosome numbers 1 through 22) are commonly inherited in an autosomal dominant or autosomal recessive pattern. Disorders due to a mutation on one of the sex chromosomes are inherited in an X-linked, or rarely Y-linked, pattern. See Table 3–1 for a description of selected Mendelian disorders.

DOMINANT VERSUS RECESSIVE DISORDERS

For some disorders, the presence of a single altered gene allele is enough to cause disease; these disorders are said to be **dominant**. An individual who is heterozygous for a dominant disorder will therefore have (or express) the disorder despite the presence of one normally functioning allele. Other disorders occur only when both alleles of a gene pair are altered. In these **recessive** disorders, the gene product produced from a single unaltered gene is sufficient to perform the expected function and maintain homeostasis. Because most human genes reside on autosomes, the most common inheritance patterns are therefore called *autosomal dominant* or *autosomal recessive*. The nurse should realize, however, that the concept of dominant and recessive genes is most useful when considering the relatively rare, single-gene conditions inherited in classic Mendelian fashion.

AUTOSOMAL DOMINANT

More than half of the known Mendelian conditions are autosomal dominant (AD). Examples include neurofibromatosis, achondroplasia (dwarfism), Marfan syndrome, Huntington disease, and familial hypercholesterolemia. By definition, AD disorders involve altered genes on autosomes rather than the sex chromosomes X and Y. Disease occurs in AD disorders despite the presence of one unaltered gene, and most individuals with AD disorders are heterozygous for the disease-producing gene. Homozygous dominant conditions can occur, but they are generally much more severe or lethal and frequently result in early pregnancy loss. For example, the child who is born homozygous for achondroplasia (dwarfism with short stature and short limbs) is much more severely affected than a heterozygous child and usually will not survive early infancy.

Inheritance Risk in Autosomal Dominant Conditions. Because the mutation that causes an AD condition occurs on an autosome rather than a sex chromosome, males and females have an equal chance of being affected. There is a 50% chance that an affected parent will pass the altered disease-producing

TABLE 3–1 Selected Genetic Conditions Inherited in a Mendelian Pattern

GENETIC CONDITION	DESCRIPTION	INHERITANCE PATTERN
Achondroplasia	Abnormal bone growth resulting in short stature	Autosomal dominant More than 80% of cases represent a new mutation
Beta-thalassemia	Reduced synthesis of hemoglobin A resulting in anemia	Autosomal recessive
Cystic fibrosis	Complex multisystem disease leading to end-stage lung disease	Autosomal recessive
Duchenne muscular dystrophy	Progressive disease leading to atrophy of skeletal and/or cardiac muscle	X-linked recessive
Fragile X syndrome	Minimal-to-moderate intellectual disability due to trinucleotide repeat expansion	X-linked recessive Anticipation is demonstrated
Gaucher disease	Several subtypes, but all are lipid storage diseases due to enzyme deficiency	Autosomal recessive
Hemophilia A	Bleeding disorder due to deficient factor VIII clotting activity	X-linked recessive About 30% of cases represent a new mutation
Marfan syndrome	Connective tissue disorder with cardiovascular, ocular, and skeletal involvement	Autosomal dominant 25% of cases represent a new mutation
Neurofibromatosis (NF-1)	Variable expression with café au lait spots and benign cutaneous and subcutaneous neurofibromas	Autosomal dominant 50% of cases represent a new mutation
Phenylketonuria (PKU)	Enzyme deficiency results in accumulation of phenylalanine, inhibiting brain and cognitive development	Autosomal recessive
Sickle cell disease	Abnormal hemoglobin causes vaso-occlusive events and chronic anemia	Autosomal recessive
Tay-Sachs disease	Fatal neurodegenerative disorder of lipid accumulation due to enzyme deficiency	Autosomal recessive

Note: Information adapted from Online Mendelian Inheritance in Man. Retrieved March 14, 2014, from http://omim.org/

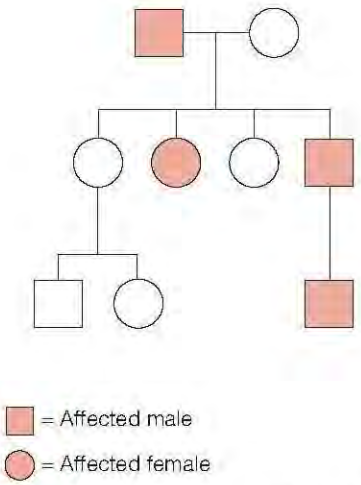

Figure 3–2 Autosomal dominant pedigree. One parent is affected. Statistically, 50% of offspring will be affected, regardless of sex.

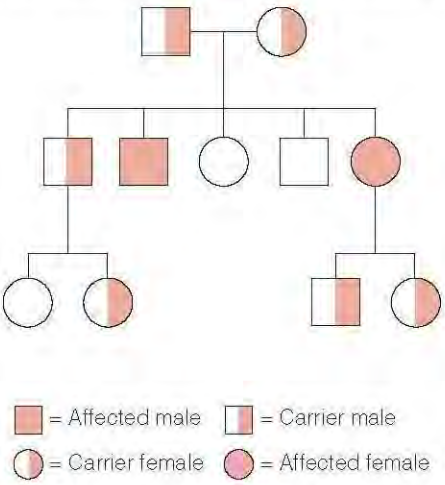

Figure 3–3 Autosomal recessive pedigree. Both parents are carriers. Statistically, 25% of offspring will be affected, regardless of sex.

gene on to a child. Nurses must remember and teach families that no matter how many of a couple's previous children inherited the altered gene, each pregnancy is an independent event with a 50% chance of having an affected child. Family histories will often reflect this 50% inheritance rate as well as both males and females being affected. An affected child always has an affected parent, who in turn also has an affected parent (Figure 3–2). See *Clinical Tip*. Exceptions to this inheritance pattern occur when the condition is due to a spontaneous new mutation, as discussed later in this chapter.

Clinical Tip

When examining a genetic pedigree, the nurse should recognize the following characteristics of autosomal dominant inheritance:

1. Both males and females are affected.
2. Males and females are usually affected in equal numbers.
3. An affected child will have an affected parent, and/or all generations will have an affected individual (appearing as a vertical pattern of affected individuals on the family pedigree).
4. Unaffected children of an affected parent will have unaffected offspring.
5. A significant proportion of isolated cases are due to a new mutation.

AUTOSOMAL RECESSIVE

Autosomal recessive (AR) conditions occur when both copies of the same gene in an individual are altered. Generally, AR conditions are more severe and have an earlier onset than conditions with other patterns of inheritance. Examples of AR conditions include cystic fibrosis, sickle cell disease, Tay-Sachs disease, and most inborn errors of metabolism. Like AD disorders, AR conditions involve genes on one of the 22 autosomes. A condition is called "recessive" when two altered gene copies gene are needed to express the condition. A child born with a recessive condition has therefore inherited one altered gene from each parent. Both parents are **carriers** of the condition (Figure 3–3). Usually carriers do not exhibit signs or symptoms; however, exceptions to this general rule are increasingly being discovered. Sickle cell disease (SCD) provides an example: Although individuals with a single copy of the altered gene are usually asymptomatic, they can develop symptoms in situations of extreme physical exertion, dehydration, or high altitude (Bender & Hobbs, 2012). The heterozygous, or carrier, state for SCD (known as sickle cell trait) actually affords some evolutionary benefit because a single copy of the altered gene provides some resistance to malaria. Individuals whose ancestors are from malaria-endemic areas are therefore more likely to carry an altered sickle cell gene. Because carrier status usually confers no symptoms, parents are often unaware of their carrier status until they have an affected child.

Because individuals who are related are more likely to be carriers for the same rare AR conditions, children born to parents who are genetically related have an increased risk to inherit a recessive condition. Therefore, **consanguinity** should be identified when taking a family history. See *Clinical Tip*. See *Developing Cultural Competence: Consanguineous Marriages* below.

Clinical Tip

When examining a genetic pedigree, the nurse should recognize the following characteristics of autosomal recessive inheritance:

1. Both males and females are affected.
2. Males and females are usually affected in equal numbers.
3. An affected child will have an unaffected parent but may have affected siblings (appearing as a horizontal pattern of affected individuals on the family pedigree).
4. The condition may appear to skip a generation.
5. The parents of the affected child may be consanguineous (close blood relatives).
6. The family may be descendants of an ethnic group that is known to have a more frequent occurrence of a certain genetic condition.

Inheritance Risk in Autosomal Recessive Conditions. Because AR conditions do not involve genetic material on the sex chromosomes, males and females have an equal chance

Developing Cultural Competence **Consanguineous Marriages**

In the United States, marriage between related individuals is generally taboo. In Western medicine, there is a well-recognized concern that a child conceived by people who are related by blood may have an increased risk for birth defects. In many other cultures, however, marriage of first cousins and others who are related by blood is customary or even preferred. Historically, consanguineous marriage has offered a number of social benefits, including stronger family ties, relative ease in finding a suitable partner, support for the woman's status, better relationships with in-laws, and better care for people in old age. In times of high overall infant mortality, the increased risk for passing on serious or life-threatening recessive disorders was likely to be overshadowed by the social security that came with a consanguineous marriage. Today, genetic counseling involves identifying consanguinity and offering risk information, carrier testing, and nondirective counseling.

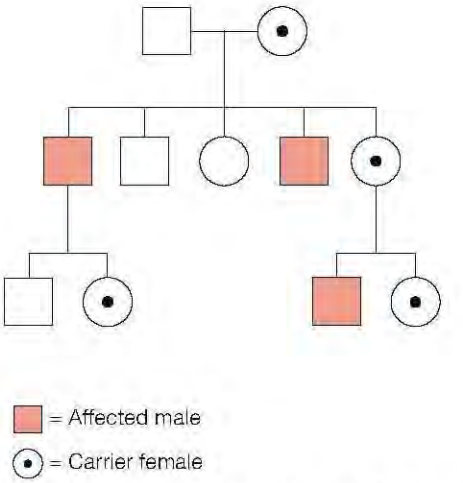

Figure 3–4 X-linked recessive pedigree. The mother is the carrier. Statistically, 50% of male offspring will be affected, and 50% of female offspring will be carriers.

of inheriting the altered genes and exhibiting the condition. When both parents are carriers of an autosomal recessive gene alteration, each pregnancy presents the same inheritance risks. Each child born to carrier parents has a 25% chance of inheriting two copies of the altered gene and having the condition, a 50% chance of inheriting only one altered gene copy and being a carrier, and a 25% chance of inheriting both unaltered genes and thus neither being affected nor being a carrier. Remembering that each pregnancy is an independent event, these probability percentages remain constant with each pregnancy, no matter how many affected or unaffected children a family already has. This is often a difficult concept for parents to grasp, and the nurse should carefully evaluate the parent's level of understanding of this important detail about inheritance.

The transmission percentages stated previously apply when both parents are carriers of an autosomal recessive condition. Percentages will change if only one parent is a carrier or if a parent is homozygous for the condition. The nurse must be able to teach a parent about these simple inheritance percentages.

X-LINKED

X-linked conditions are the result of an altered gene on the X chromosome. Examples include hemophilia A and Duchenne muscular dystrophy. Most X-linked conditions are recessive; that is, the presence of a normal allele is sufficient to maintain health. Recall, however, that the sex chromosomes are unevenly represented in males and females. Males, with their single X chromosome, have just one copy of each gene that resides on the X chromosome. Any altered X gene will consequently be expressed in males because an unaltered allele is not present for "backup." Females have two copies of each X gene, and the unaltered gene usually compensates for an altered allele, making the female a carrier. This is not the case, however, in X-linked dominant disorders. Such disorders are rare, the most common being vitamin D–resistant rickets. In X-linked dominant conditions, heterozygous females can be affected. Otherwise, the inheritance pattern is the same as X-linked recessive inheritance (Figure 3–4). See *Clinical Tip*.

Clinical Tip

When examining a genetic pedigree, the nurse should recognize the following characteristics of X-linked inheritance:

1. More males will be affected than females.
2. An affected male will have all carrier daughters.
3. There is no male-to-male inheritance.
4. Affected males are related by carrier females.
5. Females may report varying milder symptoms of the condition.
6. A new sporadic case could occur owing to a new mutation.

Recall also that one of the X chromosomes in females is inactivated early in development. Although the inactivation of either the maternal or paternal X chromosome is random in a given cell, every daughter cell (through mitosis) will have the same X chromosome inactivated. Females therefore have a mosaic pattern of X chromosome expression; some of their cells will express genes on the paternal X, and other cells will express genes on the maternal X. Females who inherit altered genes on an X chromosome show variable expression because the gene alteration will be present in only some cells. Expression of symptoms can vary from extremely mild to a full manifestation of the condition. For example, female carriers of X-linked ocular albinism may have pigment deficiencies of their irises and ocular fundi (Turnpenny & Ellard, 2012).

Inheritance Risk in X-Linked Conditions. In families with X-linked disorders, a pattern of maternal transmission is seen. Females who are carriers of X-linked conditions have a 50% chance of passing the altered gene to their offspring. Any daughter who receives the altered gene is likely to receive an unaltered X chromosome from her father and therefore be a carrier like her mother. Sons of carrier mothers, however, have no backup X chromosome. Therefore, a son who inherits the altered X will display the condition and go on to pass that altered X to each of his daughters, who will then be carriers of the altered gene. A male can never transmit an altered gene on the X chromosome to his sons because only Y chromosomes are transmitted from fathers to sons.

Y-LINKED DISORDERS

Because the Y chromosome has very few genes, alterations on the Y chromosome are not often associated with health problems. The Y chromosome does contain genes associated with spermatogenesis, and alterations in those genes can cause male infertility (Turnpenny & Ellard, 2012).

Variability in Classic Mendelian Patterns of Inheritance

In addition to classic Mendelian inheritance patterns, nurses must be prepared to help families understand several other concepts that affect the risk for inheriting a genetic disorder. These concepts include the following common variations in traditional Mendelian patterns of inheritance.

PENETRANCE

Penetrance is the probability that a gene will be expressed phenotypically. It is an "all-or-none" concept; a gene is considered to be penetrant if it is expressed to any degree. Penetrance can be measured in the following way. In a certain group of individuals with the same genotype, what percentage of them will exhibit any signs or symptoms of the condition? If the number is less than 100%, then that condition is said to show *reduced* or *incomplete penetrance*. For example, both achondroplasia and Huntington disease exhibit 100% penetrance because every individual with one copy of the altered gene will exhibit signs and symptoms of the disease.

VARIABLE EXPRESSION

The term *expressivity* is used to describe the degree to which a phenotype is expressed. When people with the same genetic makeup (genotype) exhibit signs or symptoms with varying degrees of severity, the phenotype is described as showing *variable expression*. Variable expression is common in the autosomal dominant condition neurofibromatosis type 1 (NF-1). Although neurofibromatosis has 100% penetrance, members of the same affected family often exhibit marked variation in degree of signs or symptoms (Friedman, 2012).

NEW MUTATIONS

When there is no previous family history of a condition, the disease may be caused by a spontaneous new mutation. A new mutation is said to be sporadic or de novo. Mutation rates have been estimated for a number of inherited disorders and vary widely due to a number of factors, only some of which are understood. Diseases with high new mutation rates include NF-1, achondroplasia, Duchenne muscular dystrophy, and hemophilia A and B. Determining whether a genetic condition is due to an inherited or a de novo mutation has important implications in calculating a family's recurrence risk.

IMPRINTING

The expression of a few genetic conditions varies depending on whether the altered gene is inherited from the mother or the father. This differential gene expression is due to genomic **imprinting**. Imprinting takes place before gametes are formed, when certain genes are chemically marked as having maternal or paternal origin. After conception, the imprint controls gene expression so that only one allele, either maternal or paternal, is expressed. If the unsilenced (active) allele carries a mutation, disease may result. A well-studied example of imprinting involves a deletion in a gene on chromosome 15 that causes two very different disorders depending on whether the altered gene comes from the mother or the father. Prader-Willi syndrome, characterized by hypotonia in infancy, excessive eating habits leading to obesity, and mild-to-moderate intellectual disability, is due to a deletion on chromosome 15 that is inherited from the father. Angelman syndrome is due to a similar deletion in the same gene on chromosome 15, but it is inherited from the mother. The clinical presentation is very different. Individuals with Angelman syndrome have severe intellectual disability, absent speech, an uncoordinated gait, seizures, and a happy, sociable disposition (Schaaf et al., 2012).

Multifactorial Inheritance

Multifactorial conditions aggregate in families but do not follow the characteristic Mendelian patterns of inheritance seen with single-gene conditions. Multifactorial conditions often present with highly variable severity. Neural tube disorder, for example, ranges from spina bifida occulta to myelomeningocele to anencephaly. Often, more severe defects reflect a greater number of altered genes. Some multifactorial conditions show a sex bias. Pyloric stenosis, for example, is more common in males, whereas cleft palate is more common among females. When a member of the less commonly affected sex shows the condition, a greater number of altered genes are thought to be present. This situation confers a higher risk for recurrence of the disorder for clients and their relatives. Recurrence risk varies among multifactorial conditions but is usually less than that of Mendelian conditions. Recurrence risk is calculated from population studies and expressed as a percentage; for some disorders, recurrence risk is not easily predicted. Recurrence risk varies according to the number of affected family members, the degree of relationship, and sometimes the severity of the defect. As examples, the recurrence risk for cleft lip or cleft palate in a family with one affected child is 4%, while recurrence risk for pyloric stenosis is as high as 10% (Turnpenny & Ellard, 2012).

Although most congenital malformations are multifactorial (Table 3–2), a careful family history should always be taken because occasionally cleft lip and palate, certain congenital heart defects, and other malformations are inherited as autosomal dominant or recessive traits. Adult-onset disorders such as type 2 diabetes, hypertension, some heart diseases, and some mental illness, are also included in the multifactorial inheritance group.

Genetic Testing

Many health professionals work together in the screening, diagnosis, identification, and treatment of genetic disorders. The goals of collaborative care are early diagnosis through assessment and testing, development of an effective treatment plan combined with psychosocial support to enhance coping, and referral to a genetic specialist when needed.

Genetic tests are useful to diagnose disease, predict risk of future disease, inform reproductive decision making, and manage client care. The landscape of genetic testing is changing rapidly. New methodologies have expanded the number of conditions for which genetic testing is available and reduced the cost. Genetic nurses express concern that genetic tests are becoming available very quickly with little regulation of the companies offering them. For example, some genetic testing is offered directly to consumers

TABLE 3–2 Common Birth Defects and Conditions With a Multifactorial Cause

Neural tube defects	A neural tube defect (NTD) is a condition that occurs early during fetal development with incomplete closure of the neural tube. Severity of the disorder varies, depending on which part of the tube does not close. Anencephaly, meningomyelocele, and spina bifida are examples of NTD. Recurrence risk is increased in families with an affected child, but that risk can be modified by maternal dietary folic acid supplementation (Turnpenny & Ellard, 2012).
Congenital heart defects	Most congenital heart defects are thought to be of multifactorial cause. A number of genes have been associated with patent ductus arteriosus, atrial or ventricular septal defects, and other heart defects. In some states, newborn screening for critical congenital heart disease is performed routinely using pulse oximetry (Bradshaw & Martin, 2012).
Cleft lip and palate	Cleft lip and/or palate (CL/P) occur as a result of failure of bony fusion early in gestation. While rare gene mutations can cause CL/P, most cases are thought to be multifactorial. The more severe the malformation, the higher the family's recurrence risk is for future pregnancies (Tobias, Connor, & Ferguson-Smith, 2011).
Autism spectrum disorder	Although the etiology of autism spectrum disorder remains poorly understood, most experts believe it to be multifactorial. Twin studies suggest a strong genetic component, with 60%–90% concordance between identical twins. A number of environmental influences have been suspected to influence the development of autism as well, including environmental exposures, viral infections, and maternal stress (Johnson, Giarelli, Lewis, et al., 2013).

without benefit of oversight by a healthcare provider, nor is counseling or follow-up uniformly provided. Individuals may make hard and irrevocable life-altering decisions after receiving test results, so accuracy and reliability, along with professional counseling, are essential (Beery & Workman, 2012). Guidelines regarding who should be tested and when to test are available for some genetic conditions. However, new knowledge accumulates rapidly, and recommendations for practice often lag behind research findings by several years.

Nurses must have knowledge of available genetic tests and their implications to assist clients and their families as they weigh choices regarding genetic testing. Genetic testing can be done for screening or diagnostic purposes, can detect both chromosomal and gene-based alterations, and can be done across development, from early in the prenatal period to any time after birth. Some genetic testing is done on specimens obtained noninvasively, such as a cheek swab or peripheral blood sample; other tests require invasive procedures such as amniocentesis or biopsy. See Box 3–1.

Box 3–1 What Is a Genetic Test?

A genetic test involves the analysis of chromosomes, DNA, RNA, genes, or gene products (e.g., enzymes and other proteins) to detect variations related to disease or health. Whether a laboratory method is considered a genetic test also depends on the intended use, claim, or purpose of a test. For example, amino acid analysis to detect metabolic disorders such as phenylketonuria (PKU) is considered a genetic test, but the use of this same analysis to monitor general nutritional status is not (U.S. Department of Health and Human Services, 2008).

Categories of Genetic Tests

Genetic tests have been used for some time to detect heritable conditions that are passed from generation to generation. There are several categories of genetic testing, each with a unique purpose. See Table 3–3.

TABLE 3–3 Categories of Genetic Tests

TYPE OF TEST	DESCRIPTION
Diagnostic testing	Used to establish a diagnosis of a genetic disorder in an individual who is symptomatic or has had a positive screening test.
Prenatal testing	Testing to identify a fetus with a genetic disease or condition. Some prenatal testing is offered routinely; other testing may be initiated on account of family history or maternal factors.
Newborn screening	Testing of a newborn to identify the presence of a condition that requires immediate initiation of treatment to prevent death or disability.
Preimplantation testing	Following in vitro fertilization (IVF), testing to identify embryos with a particular genetic condition.
Carrier testing	Testing in an asymptomatic individual to identify carrier status for a genetic condition.
Presymptomatic and predictive testing	Offered usually to asymptomatic individuals to detect genetic conditions that occur later in life. • *Presymptomatic testing* detects mutations that, if present, are likely or certain to eventually cause symptoms (an example is Huntington disease). • *Predictive, or predispositional, testing* detects mutations that increase the likelihood that symptoms will develop (such as *BRCA1* and *BRCA2*).

It is especially important for nurses to understand the difference between a screening test and a diagnostic test, which lies in the purpose of the test. Screening tests are population-based tests designed to find individuals at risk for a disorder. They are designed to be very sensitive; that is, to find every case. Sensitive tests, however, will sometimes be positive in individuals who do not have the disorder; that is, false-positive tests do occur. For that reason, a positive screening test must be followed by a diagnostic test. Newborn screening provides an excellent example. Most newborns in developed countries are screened for a variety of genetic diseases, most rare. Recent advances in laboratory technology have allowed greatly expanded newborn screening with little increase in cost, and newborns in some states are tested for more than 40 rare conditions. Each positive screening test must be followed by a diagnostic test. Fortunately, most positive screening tests are falsely positive, but the cost of follow-up testing is significant both in terms of parental anxiety and financial burden (DeLuca, Zanni, Bonhomme, et al., 2013).

Diagnostic tests are performed to confirm a diagnosis when a child is suspected of having a specific disorder based on clinical presentation or screening test results.

Diagnosing Chromosomal Alterations

Cytogenetics describes the microscopic examination of chromosomes to reveal large alterations such as additions, deletions, breaks, and rearrangements or rejoinings (translocations). Prenatally, amniocentesis and chorionic villi sampling (CVS) can be undertaken to provide specimens for cytogenetic examination. After a child is born, chromosomal diagnostic examination can be accomplished with a blood, skin, or buccal cell sample. Cytogenetic testing includes karyotyping, as described earlier in this chapter, and molecular cytogenetic techniques, which are capable of detecting submicroscopic DNA variations too small to be seen on a karyotype.

Diagnosing Gene Alterations

Recent advances in molecular genetic technology along with the mapping of the human genome have resulted in tremendous expansion of available genetic testing. Genetic testing is currently available for nearly 3000 diseases, with new tests constantly being added (Lander, 2011). DNA-based tests involve sophisticated new technology that permits the detection of DNA sequence changes as small as a single nucleotide. These tests can be performed on blood, bone marrow, amniotic fluid, fibroblast cells of the skin, or buccal cells from the mouth. Genetic testing can examine DNA (to determine specific nucleotide sequence), RNA (to measure gene expression), or proteins (to analyze gene products). Some tests can be performed quickly; others require several days to weeks, or occasionally several months, before results are reported.

Genes are very long DNA sequences made up of hundreds of thousands of nucleotides (or base pairs). Alterations at various sites along a gene may alter its function and cause disease. As an example, the *CFTR* gene (which in an altered form causes cystic fibrosis) is 230,000 base pairs long, and nearly 2000 different *CFTR* mutations have been identified (Cystic Fibrosis Mutation Database, 2014). Most of these mutations are exceedingly rare; the most common (named delta F508) is found in about two thirds of affected individuals (De Boeck, Zolin, Cuppens, et al., 2014). Although DNA testing is capable of detecting any of these alterations in DNA sequence, it is not feasible to test for all of them. Currently available *CFTR* tests detect from about 23 to 98 different mutations. The chance of missing an uncommon mutation therefore varies depending on which test is selected. Also, mutation detection rates are higher in people of European ancestry than other populations. Therefore, a "negative" CF test must be interpreted with caution and an eye on how many mutations were included in the test. This is just one of the limitations of genetic testing that nurses must understand in order to provide genetically competent care. See *The Role of the Nurse in Genetic Testing* section below.

Other Genetic Tests

Tests are available to measure gene expression, For example, **microarray analysis** can detect levels of messenger RNA in cells, which indicates which genes are "turned on" or being expressed. Microarray analysis is especially useful to examine tumor cells.

Often, genetic tests do not examine DNA directly, but are biochemical tests for gene products or metabolites of gene products. Most newborn screening tests are biochemical. For example, PKU is caused by an alteration in the gene encoding the enzyme phenylalanine hydroxylase (PAH), which breaks down dietary phenylalanine. The PKU test actually measures phenylalanine levels, which are markedly elevated in individuals with PKU. Many of these biochemical tests have been in use for years.

Prenatal Testing

Nurses who care for childbearing families may be responsible for counseling about prenatal testing for congenital or inherited conditions. Screening and invasive diagnostic testing for chromosome abnormalities should be available to all women who present for prenatal care before 20 weeks of pregnancy regardless of maternal age. Nurses therefore require current information and sufficient expertise to explain testing to families. Women should be counseled regarding the differences between screening and diagnostic testing. For example, noninvasive screening tests, such as nuchal translucency ultrasound and maternal serum screening, are designed to assess a pregnancy's risk of chromosomal abnormalities or a neural tube defect. If the risk is increased above a specific cutoff, the woman is offered invasive prenatal diagnosis. These diagnostic techniques, such as amniocentesis and CVS, obtain cells from the pregnancy to rule out or diagnose a chromosomal abnormality or certain genetic disorders. They are associated with a small risk of pregnancy complications, including miscarriage.

Several methods of prenatal testing are currently available. The tests are used for different purposes and involve varying degrees of risk.

GENETIC ULTRASOUND

Ultrasound may be used to assess the fetus for genetic or congenital problems. With ultrasound, one can visualize the fetal head for abnormalities in size, shape, and structure. Craniospinal defects (anencephalus, microcephaly, hydrocephalus), thoracic malformations (diaphragmatic hernia), gastrointestinal malformations (omphalocele, gastroschisis), renal malformations (dysplasia or obstruction), and skeletal malformations (caudal regression, conjoined twins) are just some of the disorders that have been diagnosed in utero by ultrasound.

Screening by ultrasound for congenital anomalies is best done at 16 to 20 weeks, when fetal structures have developed completely. With the addition of a fetal nuchal translucency measurement at 10 to 14 weeks, there is high correlation with fetal chromosomal abnormalities (Gilbert, 2011). The nuchal translucency is a fluid-filled space at the back of the fetal neck. An increased amount of fluid is associated with an increased risk for chromosomal abnormalities, birth defects, genetic syndromes, and poor pregnancy outcome—the larger the nuchal translucency, the higher the risk for abnormalities. There is no

information documenting harm to the fetus or long-term effects with exposure to ultrasound. However, there is no guarantee of complete safety; therefore, the practitioner and the parents must evaluate the risks against the benefits on an individual basis.

MATERNAL SERUM SCREENING

Measuring specific hormones and proteins in the maternal serum during the first and/or second trimester can determine the risk for Down syndrome, trisomy 18, or open spina bifida. In the first trimester, the nuchal translucency measurement is often added to improve the detection rate for Down syndrome and trisomy 18. Detection and false-positive rates vary depending on the type of screening test that is performed and sometimes the laboratory that performs the screening.

NONINVASIVE PRENATAL TESTING

Noninvasive prenatal testing (*NIPT*) for chromosomal abnormalities, which examines fetal DNA circulating in maternal serum, is now available. Approximately 3% to 13% of the circulating DNA in a woman's plasma is derived from the placenta (ACOG/SMFM, 2012). Several laboratories have developed techniques to quantify fetal DNA fragments as early as 9 to 10 weeks of gestation in order to detect some of the common trisomies (including Down syndrome, trisomy 18, and trisomy 13). NIPT shows greater sensitivity and specificity than traditional maternal serum screening but is not yet meant to replace diagnostic testing such as amniocentesis or CVS. NIPT has limitations, including limited data on low-risk pregnancies, twin gestations, and pregnancies with a vanishing twin as well as concerns about false-positive results due to maternal or placental mosaicism (ACOG/SMFM, 2012). At this time, NIPT is used as a screening test and is recommended primarily for women of advanced maternal age or other indications of a high-risk pregnancy such as fetal ultrasound findings suggestive of aneuploidy; history of prior pregnancy with trisomy 21, trisomy 18, or trisomy 13; or positive maternal serum screening. Clients with abnormal NIPT results, or those with other factors suggestive of a chromosomal abnormality, should receive genetic counseling and be given the option of standard confirmatory diagnostic testing (Devers et al., 2013).

GENETIC AMNIOCENTESIS AND CVS

Methods of prenatal diagnosis include genetic amniocentesis and CVS. Figure 3–5 illustrates these two procedures. Both tests collect cells derived from fetal origin and are therefore invasive. With amniocentesis, a needle is inserted into the amniotic fluid under continuous ultrasound guidance and a small amount of amniotic fluid is collected. Fetal cells can then be cultured and tested. With CVS, a tiny amount of placental tissue of fetal origin is obtained by inserting a needle through either the abdomen or cervix. While amniocentesis is offered after 15 weeks of gestation, CVS can be performed after 9 weeks. A variety of tests can be performed on the fetal cells collected from either procedure.

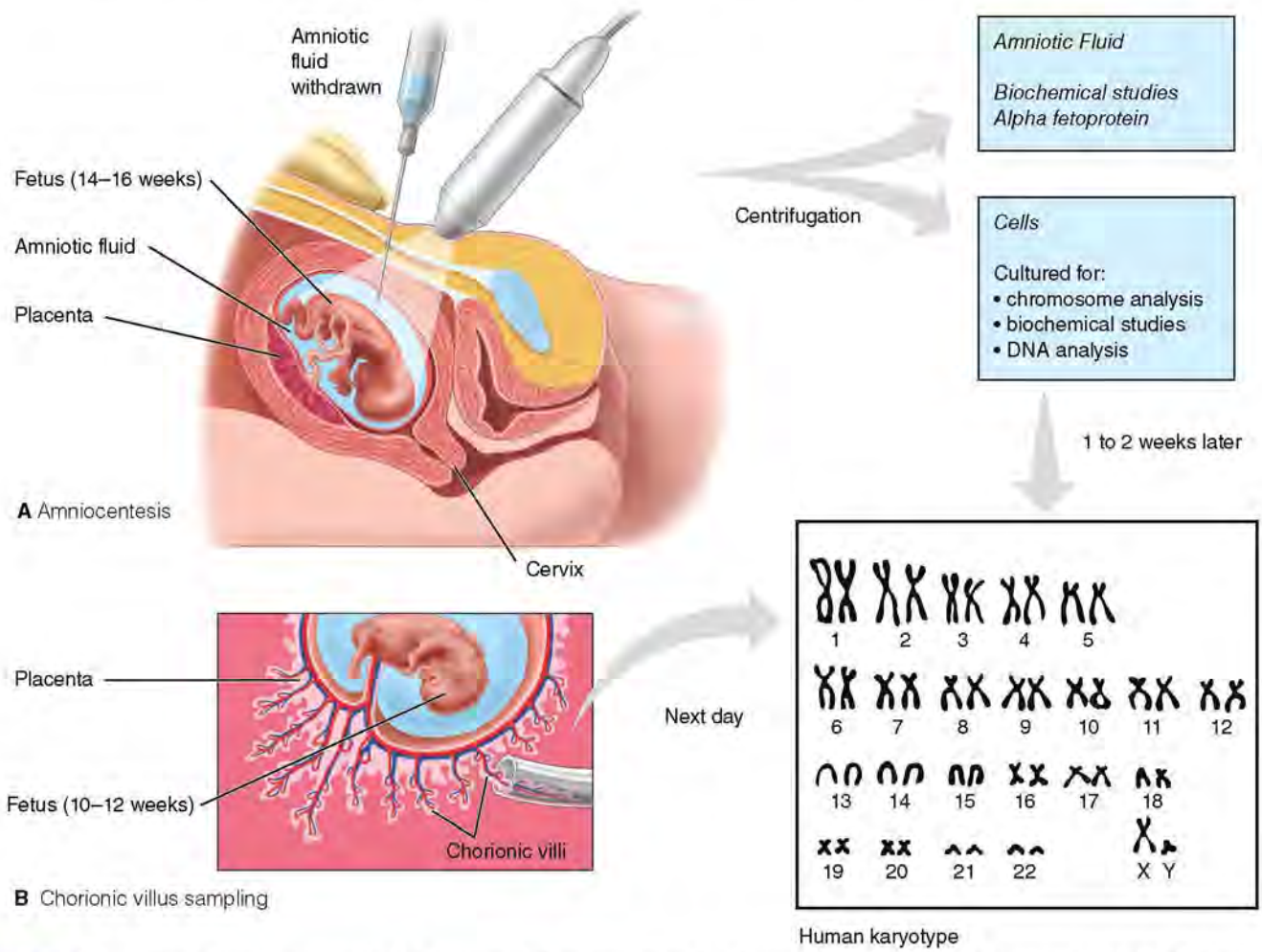

Figure 3–5 *A,* **Genetic amniocentesis for prenatal diagnosis can be done after 15 weeks' gestation. Fetal cells are cultured and tested; results take 7 to 14 days.** *B,* **Chorionic villus sampling is done after 9 weeks' gestation; results take 1 to 3 days.**

Both procedures carry a small risk for pregnancy complications, including infection and miscarriage. Although invasive diagnostic testing should be available to all women (ACOG, 2007), testing is frequently targeted to women who meet one or more of the following criteria:

1. *Maternal age 35 or older.* Women ages 35 or older are at greater risk for having children with chromosomal abnormalities. Chromosomal abnormalities because of maternal age include trisomy 21, trisomy 13, trisomy 18, XXX, or XXY. A woman's risk for having an infant with a chromosomal abnormality increases from less than 1 in 1000 at age 21 years to about 1 in 350 at age 35 and 1 in 30 at age 46 (Schaaf et al., 2012).
2. *Previous child born with a chromosomal abnormality.* Young couples who have had a child with a trisomy 21, 18, or 13 have an approximately 1% to 2% risk of a future child having a chromosomal abnormality.
3. *Parent carrying a chromosomal abnormality (balanced translocation).* A woman who carries a balanced 14/21 translocation has a risk of approximately 10% to 15% that her children will be affected with the unbalanced translocation of Down syndrome; if the father is the carrier, there is a 2% to 5% risk.
4. *Mother carrying an X-linked disease.* In families in which the woman is a known or possible carrier of an X-linked disorder such as hemophilia A or B or Duchenne muscular dystrophy, the risk of an affected male fetus is 50%. Now DNA testing may make it possible to identify affected males from nonaffected males in some disorders.
5. *Parents carrying an inborn error of metabolism that can be diagnosed in utero.* Inborn errors of metabolism disorders are detectable in utero by DNA analysis or biochemical testing; these include Fabry disease, galactosemia, Gaucher disease, homocystinuria, Hunter syndrome, Hurler syndrome, Krabbe disease, Lesch-Nyhan disease, maple syrup urine disease, metachromatic leukodystrophy, methylmalonic aciduria, Niemann-Pick disease, Pompe disease, and Tay-Sachs disease.
6. *Both parents carrying an autosomal recessive disease.* When both parents are carriers of an autosomal recessive disease, there is a 25% risk for each pregnancy that the fetus will be affected. Autosomal recessive diseases identified by amniocentesis are hemoglobinopathies such as sickle cell disease, thalassemia, and cystic fibrosis.
7. *Family history of neural tube defects.* Genetic amniocentesis is available to couples who have had a child with neural tube defects or who have a family history of these conditions, which include anencephaly, spina bifida, and myelomeningocele. Neural tube defects are usually multifactorial traits.
8. *Positive screening test.* When the first- or second-semester maternal screening test and/or ultrasound exam indicates the fetus may be affected with an aneuploidy or neural tube defect, further testing may be offered. This may be in the form of a more accurate noninvasive test (NIPT) or an invasive diagnostic test such as CVS or amniocentesis. For further discussion see Chapter 13.

PERCUTANEOUS UMBILICAL BLOOD SAMPLING

Percutaneous umbilical blood sampling (PUBS), also called *cordocentesis,* involves drawing blood from the umbilical vein under direct ultrasound guidance. It can be performed after 18 weeks' gestation and allows rapid chromosomal diagnosis and other genetics studies, but its use has diminished as other technologies have become more readily available.

Nursing Management

Nurses are on the front line of client care and need to be competent in genetic- and genomic-related health care. Specific competencies are expected of all professional nurses. These competencies include eliciting a genetic family history and depicting it in a pedigree; identifying current, credible genetic information; identifying clients and families who might benefit from referral to a genetic expert; and managing genetic information (Consensus Panel on Genetic/Genomic Nursing Competencies, 2009). This section focuses on the roles of nurses in the care of clients and families with genetic health issues.

Assessing Genetic Risk

All professional nurses should incorporate awareness of genetic risk into the assessments they perform. "Thinking genetic" is important throughout health assessment, in collecting the health history, performing the physical assessment, and interpreting assessment findings.

ASSESSING REPRODUCTIVE RISK

Nursing care for the childbearing family includes identifying women who may be at increased risk to have a child with a genetic disorder. Nurses should be aware of risk factors that indicate a couple may benefit from a genetic referral or consideration for prenatal testing. Annual examinations and other clinic appointments provide opportunities to identify women whose family history or other factors indicate risk. If couples with genetic risk factors are planning to conceive, the nurse may encourage them to consider genetic counseling before discontinuing contraception. See *Health Promotion: Couples Who May Benefit From Prenatal Diagnostic Testing* below.

Health Promotion **Couples Who May Benefit From Prenatal Diagnostic Testing**

- Women ages 35 or older at time of birth
- Couples with a balanced translocation (chromosomal abnormality)
- Family history of known or suspected Mendelian genetic disorder (e.g., cystic fibrosis, hemophilia A and B, Duchenne muscular dystrophy)
- Couples with a previous child with chromosomal abnormality
- Couples in which either partner or a previous child is affected with, or in which both partners are carriers for, a diagnosable metabolic disorder
- Family history of birth defects and/or intellectual disability (e.g., neural tube defects, congenital heart disease, cleft lip and/or palate)
- Ethnic groups at increased risk for specific disorders (see *Developing Cultural Competence: Genetic Screening Recommendations for Various Ethnic and Age Groups* below)
- Couples with history of two or more first-trimester spontaneous abortions
- Women with an abnormal maternal serum alpha-fetoprotein (MSAFP or AFP) test
- Women with a teratogenic risk secondary to an exposure or maternal health condition (e.g., diabetes)

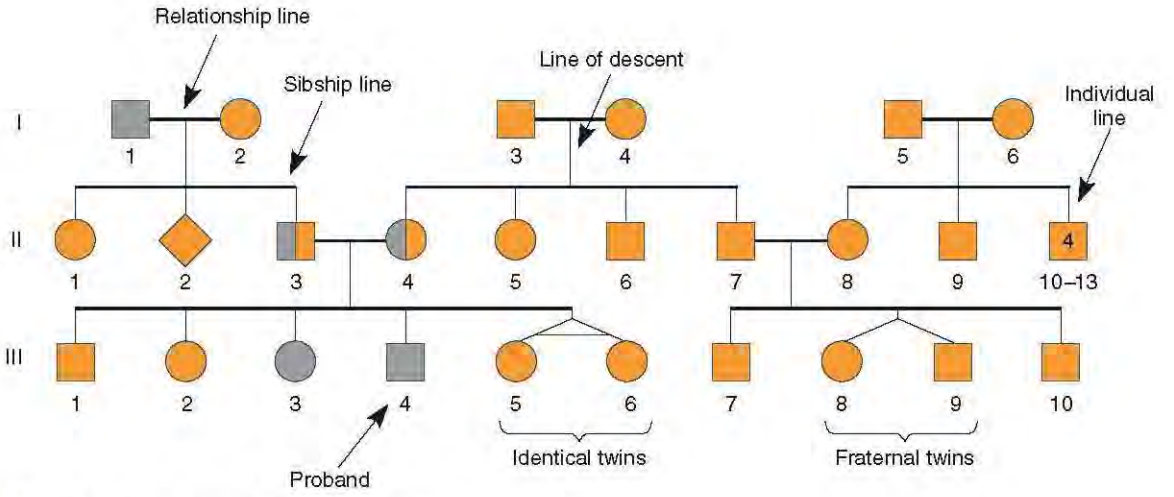

Figure 3–6 Sample three-generation pedigree.

FAMILY HISTORY AND THE GENETIC PEDIGREE

An expectation of all professional nurses is that they know how to collect a three-generation family history and record the history in a pedigree using standard symbols and terminology. Information to document in a family history includes:

- First name of all family members with age or year of birth
- Any medical conditions or diseases including age at diagnosis
- Age and cause of death
- Infertility or no children by choice
- Pregnancy complications with gestational age indicated
- Adoption status
- Ancestry
- Consanguinity

A **pedigree** is a graphic representation or diagram of a family's medical history and genetic relationships. Figure 3–6 shows a sample pedigree. Standard format and nomenclature for pedigrees, which includes multiple symbols (Figure 3–7), have been adopted (Bennett, 2010). A pedigree is constructed around a designated "index" patient, called the **proband** (if he or she is affected with the genetic disorder of interest) or **consultand** (if he or she seeks genetic counseling without being known to have the disorder). A finished pedigree provides a clear, visual representation of a family's medical data and biologic relationships at a glance. A pedigree identifies affected individuals in the immediate and extended family and can identify family members who might benefit from a genetic consultation. A pedigree can also illustrate patterns of inheritance and clusters of multifactorial conditions. On the basis of the pedigree, genetic referral and/or reproductive risk teaching for the individual and family can occur. The visual nature of a pedigree enhances a family's learning and can be used to clarify misunderstandings or misconceptions about inheritance. If completed correctly and comprehensively, a pedigree allows all healthcare professionals working with the child or family to see quickly what history and background information has been collected.

Throughout the process of gathering family history information, the nurse must protect family confidentiality. A pedigree is different from a personal health history in that it reflects information about multiple individuals, which greatly increases the risk for harm if confidentiality is broken. A pedigree may reveal sensitive details that include infertility problems, reproductive decisions, or misassigned paternity that may not be known by a current partner or other family members. Other sensitive issues include pregnancies conceived by technology, a history of suicides, drug or alcohol abuse, and same-sex relationships.

Challenges inherent in recalling the family history include failure to report conditions thought not to be genetic or attributed to other causes, or to recall conditions that have been surgically repaired and forgotten. Also, clients may be reluctant to

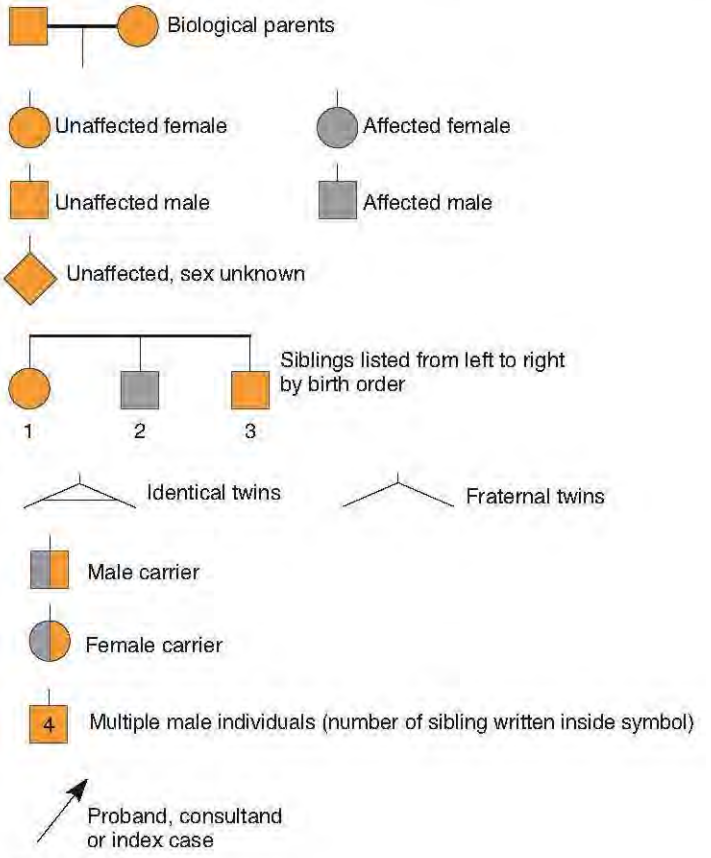

Figure 3–7 Selected standard symbols for use in drawing a pedigree.

reveal sensitive information, particularly information unknown to other family members.

Families are encouraged to collect and record their own family history in a form that can be shared within the family as well as with healthcare providers. The U.S. Surgeon General's Family History Initiative is a national campaign to promote the collection of family histories. The Initiative provides a web-based program entitled "My Family Health Portrait" that allows individuals to easily record and save their information, as well as print their family pedigree.

Clinical Tip

Follow these steps when drawing a pedigree:

I. Organization

1. Begin recording data in the middle of the sheet of paper (to allow enough room for both the maternal and paternal sides of the family).
2. Use only standard pedigree symbols (see Figure 3–7).
3. Place the male individual in a couple on the left of the relationship line; the paternal side of the family will also be on the left side of the paper.

II. Determining Family Relationships

1. Determine relationships within the family by asking questions such as:
   - Do you have a partner or are you married?
   - How many biologic brothers and sisters do you have?
   - How many children do you have? Are they with the same partner?
   - Do all the children have the same biologic father?
   - Do your siblings share the same mother and father as you?
2. Referring to "the baby's father or mother" can be helpful until the relationship between parents is established.
3. Referring to a "union" if marriage does not exist can also help communication.

III. Who Should or Should Not Be Included

1. To ensure accuracy, the pedigree should include the parents, offspring, siblings, aunts, uncles, grandparents, and first cousins of the individual seeking counseling.
2. Detailed information about the spouses of the proband's family can be omitted unless there is a history of some kind of disorder or condition.
3. Eliminating persons or information that does not contribute any valuable information can help keep the pedigree small and more manageable.

IV. Recording the Family History

1. It may be useful to determine the approximate size of the family, to plan spacing on paper.
2. Begin the drawing with the proband (the person who is seeking counseling or is affected with the genetic condition). Mark the proband with an arrow.
3. Then add the symbols for the brothers and sisters of the proband and an individual line for each. Connect the individual lines with a sibship line and add a line of descent, the relationship line for the parents, and symbols for parents of the proband.
4. Repeat this step for children of the proband and children of the proband's siblings.
5. Continue with symbols for all immediate relatives of the proband's parents and grandparents. Record ancestry or country of origin of the first generation at the top of the page.
6. Mark each symbol to designate relevant information (see Figure 3–7).
7. Create a key to contain all information relevant to interpretation of the pedigree.
8. The pedigree should include at least three generations.
   - Mark each generation with a Roman numeral along the left side of the paper with the first generation marker (I) at the top.
   - Each person in a generation should fall along the same imaginary horizontal line.
9. The pedigree should include:
   - Half-siblings, pregnancy losses, stillbirths, previous marriages, and adopted children
   - The reason for taking the pedigree (e.g., developmental disability, dysmorphology)
   - The name of the family historian (person relaying the information)

V. Other

1. **Consanguinity** may be suspected if the historian repeatedly gives the same last name on both sides of the family. Ask if any relatives in the family have ever had a child together.

VI. Completing the Pedigree

1. When completed, the pedigree should be dated and signed with the name, credentials, and position of the person drawing it.

Source: Data from Bennett, R. L. (2010). *The practical guide to the genetic family history* (2nd ed.). Copyright © 2010 John Wiley & Sons. Reproduced with permission of John Wiley & Sons, Inc.

GENETIC PHYSICAL ASSESSMENT

Nurses caring for newborns and children in any setting should also "think genetic" when performing physical assessment. An early finding by the nurse will provide the child and family with an opportunity for a genetic referral and more specialized health care. **Dysmorphology** refers to the study of human congenital defects or abnormalities of body structure that begin before birth. Traditionally, congenital anomalies have been included under the umbrella of genetic disorders whether they occur due to a gene alteration or another cause of abnormal embryonic or fetal development. Dysmorphic anomalies can occur anywhere in the body, but are perhaps most often associated with facial features. As a routine part of client assessment, the nurse should screen for both minor and major anomalies. A **minor anomaly** or malformation is an unusual morphologic feature that in itself is of no serious medical or cosmetic concern to the individual or family. The presence of a single minor anomaly is relatively common, occurring in approximately 10% of newborns, and is usually of no consequence (Turnpenny & Ellard, 2012). Some minor anomalies are merely family traits or are present in certain ethnic groups. Minor anomalies include such traits as wide-set eyes, single palmar creases, café au lait patches, low anterior hairline, preauricular (in front of the ears) pits and tags, broad face, or mild proportionate short stature. Examples of variations associated with ethnic origin include upward-slanting eyes or prominent epicanthal folds among individuals of Asian descent.

The appearance of multiple minor anomalies in an infant is of greater concern. Fewer than 1% of newborns have two minor anomalies, and fewer still have three or more. But of those newborns who do have multiple minor anomalies, many will also have a major anomaly or an underlying genetic condition. Therefore, the nurse who notes multiple minor anomalies in a newborn

or child should consider the possibility of a major anomaly or an underlying genetic condition and advocate for a genetic referral. For example, a newborn who is hypotonic and has a single palmar crease with up-slanting eyes that do not resemble his parent's eyes should be evaluated for Down syndrome.

About 2% to 3% of all children have a **major anomaly**, defined as a serious structural defect present at birth that may have severe medical or cosmetic consequences, interfere with normal functioning of body systems, lead to a lifelong disability, or even cause an early death. Congenital heart defects, cleft lip and/or palate, myelomeningocele, duodenal atresia, and craniosynostosis are considered major anomalies, as is developmental disability. Some major anomalies are present at birth but are not apparent, such as deafness, various skeletal dysplasias, and some types of congenital heart defects (Turnpenny & Ellard, 2012).

A **syndrome** is a collection of multiple anomalies, major or minor, that occur in a consistent pattern and have a common cause. For example, Down syndrome causes a variety of anomalies in multiple body systems, including the eyes, ears, hair, mouth and tongue, heart, and brain. A **sequence** is a collection of anomalies that occur as a chain of events initiated by a single problem. As an example, Potter sequence begins with prenatal failure of renal development, which leads to small amounts of amniotic fluid, which in turn causes growth restriction. An **association** is a group of abnormalities of unknown cause that occur together more often than is expected by chance (Schaaf et al., 2012).

The nurse can identify clues to genetic problems by examining the child and considering the physical characteristics of the parents and other family members (see *Assessment Guide: The Child With Selected Dysmorphic Physical Features* below). Nurses may even ask to look at family photographs and examine them for common dysmorphic features and family traits. Several standardized craniofacial measurements have been defined, and tables are available displaying normal values according to age, so that dysmorphic facial features can be more easily identified. Figure 3–8 depicts some standard measurements used in describing facial features. By advocating for a genetic referral, the nurse can make a difference in the child's state of health.

The Role of the Nurse in Genetic Testing

For childbearing families, genetic screening is routinely offered in the prenatal and newborn periods and is commonly performed in the diagnostic workup for children with a variety of health problems or concerns. Many people have misconceptions about genetic testing. Nurses play an important role in teaching parents and children about the implications and limitations of genetic tests to ensure that they make informed decisions. The nurse should promote communication, autonomy, and privacy when helping families. Recognizing that genetic testing affects families, and not just individuals, the nurse should use a family perspective when assisting parents and children who are making decisions about genetic testing. Not all family members will want to know their genetic risks. All voices should be heard, and each family member's decision should be respected, whether it is to participate in genetic testing or to decline. To ensure autonomy, a nondirective approach is critical; nurses must take care to avoid imposing their own values or personal opinions onto clients and families. Finally, as with all aspects of delivering genetic nursing care, privacy and confidentiality are paramount.

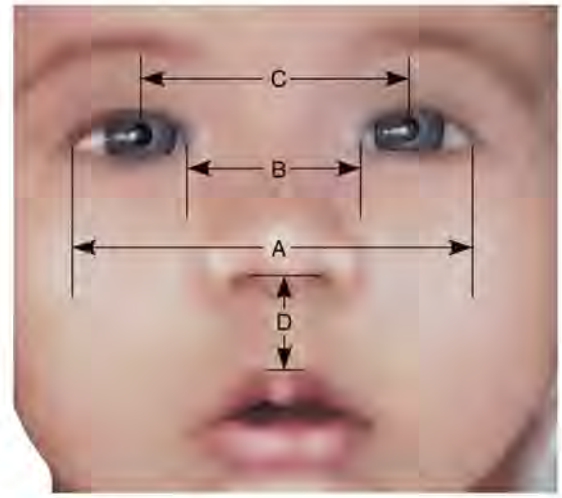

Figure 3–8 **Classic facial measurements for genetic assessment with a focus on facial features. *A*, Outer intercanthal distance. *B*, Intercanthal distance. *C*, Interpupillary distance. *D*, Philtrum length.**

PRENATAL GENETIC TESTING

It is essential that couples be informed before any prenatal testing is done, whether that testing is routine screening or diagnostic testing. Counseling should address the reason for the test, the potential outcomes and follow-up tests that may be indicated based on those outcomes, potential risks and benefits of testing, and limitations and implications. The nurse must recognize the emotional impact on the family of a decision to undergo or not to undergo genetic testing and ensure that any decision to undergo prenatal testing is based on autonomous decision making and informed consent.

Every pregnancy has a 3% to 4% risk of resulting in an infant with a birth defect. When an abnormality is detected or suspected before birth, an attempt is made to determine the diagnosis by assessing the family health history (via the pedigree) and the pregnancy history and by evaluating the fetal anomaly or anomalies via ultrasound. After experts on a specific disorder have been consulted, healthcare professionals can then present the parents with options. Treatment of prenatally diagnosed disorders may begin during the pregnancy, thus possibly preventing irreversible damage. In light of the philosophy of preventive health care, information that can be obtained prenatally should be made available to all couples who are expecting a baby or who are contemplating pregnancy.

With the advent of diagnostic techniques such as amniocentesis, at-risk couples who would not otherwise have a first child or additional children can decide to conceive. Following prenatal diagnosis, a couple can decide not to have a child with a genetic disease. For many couples, prenatal diagnosis is not a solution because they choose not to prevent the genetic disease by aborting the fetus. The decision about whether to use prenatal diagnosis can only be made by the family. Even when termination is not an option, prenatal diagnosis can give parents an opportunity to prepare for the birth of a child with special needs, contact the families of children with similar problems, or access support services before the birth.

Client Advocacy (or Considerations) in Prenatal Testing. The aim of prenatal screening is to provide prospective parents with information about the health of their fetus. Maternal serum screening is a noninvasive procedure that has become a

ASSESSMENT GUIDE | The Child With Selected Dysmorphic Physical Features*

Skull	Asymmetric head/face	Fontanels too large or small
	Brachycephaly (short, broad head shape) (See Figure 54–11.)	Frontal bossing (prominent central forehead)
	Craniosynostosis (premature closing of skull sutures)	Microcephaly or macrocephaly
	Flattened or prominent occiput	Micrognathia (small jaw)
		Prognathism (projection of jaw beyond that of the forehead)
Extremities	Abnormally positioned feet	Hypoplastic (very small) or absent nails
	Arachnodactyly (long fingers or toes)	Hypotonia (diminished muscle tone)
	Brachydactyly (short fingers or toes)	Loose joints
	Camptodactyly (permanent flexion of fingers or toes)	Polydactyly (extra fingers and/or toes)
	Clinodactyly (curved fingers or toes, most often the fifth finger)	Rocker bottom feet
		Single transverse palmar crease (See Figure 33–33.)
	Edema of the hands or feet	Syndactyly (webbing between fingers and toes)
	Extremely long/thin or short extremities	
Ears	Ear tags or pits	Hearing loss
	Ears that are posteriorly rotated	Low-set or malformed ears
Hair	Excessive body hair	Large section of white hair in otherwise pigmented hair
	Unusual hairline or hair distribution	
		Sparse or brittle hair
Eyes	Blue sclera	Extreme myopia (nearsightedness)
	Different colored eyes	Hypertelorism (widely spaced eyes)
	Down-slanting eyes	Hypotelorism (closely spaced eyes)
	Epicanthal folds inconsistent with ethnicity (See Figure 33–7.)	Short palpebral fissures (distance between inner and outer canthus of eyes)
	Extreme hyperopia (farsightedness)	Up-slanting eyes (See Figure 33–8.)
Skin	Axillary freckling	Hirsutism (excessive hair)
	Café au lait spots	Hyperelastic skin
	Excessive skin	Leaf-shaped white markings
	Extremely loose or thin skin	Syndactyly (webbing between fingers and toes)
Mouth	Cleft lip with or without cleft palate (See Figure 51–1.)	Early loss of teeth
	Large or small tongue	Late eruption of teeth
	Misshapen, missing, or extra teeth	Smooth or abnormal philtrum
		Thin upper lip
Other	Abdominal wall defect	Seizures
	Ambiguous genitalia	Short, webbed neck
	Cryptorchidism (undescended testicle)	Single umbilical artery
	Hernia (inguinal or umbilical)	Small or widely spaced nipples
	Hypospadias	Multiple fractures
	Hypogonadism	Unusual cry (catlike/mewing, hoarse, weak)
	Obesity	Unusually tall or short stature
	Scoliosis	Webbed neck

**This list is not all-inclusive, but is meant to increase the nurse's awareness of assessment findings that may be significant and require a referral to a genetic specialist.*

routine aspect of prenatal care. Usually, screening provides reassurance, but when screening tests are abnormal, parents must make decisions about issues that they never may have considered. Within a short time of a receiving a positive screening result, for example, parents must decide whether to have invasive diagnostic testing. Informed decision making requires acquiring significant knowledge about various testing procedures and their respective risks, limitations, and benefits, and about the disorders for which testing is being performed. As parents learn this new information, they consider the potential impact of a genetic diagnosis on their child and their family, often in the context of their perceived moral duty regarding responsible parenthood and safeguarding the health and well-being of their family. Nurses have a critical role in encouraging clients to make informed decisions and in providing sufficient information to support informed consent. Distinct challenges are associated with this role.

- Most clients have limited health literacy related to prenatal screening, particularly in the face of evolving technology.
- Most clients also have limited understanding of the conditions for which testing is done. For example, life with Down syndrome has changed in many ways in recent

years, and up-to-date information is required for families to make informed decisions about continuing the pregnancy and either keeping the child, placing the child for adoption, or terminating the pregnancy (Van Riper, 2012).

- First-trimester screening is carried out early in pregnancy, limiting opportunities for informed consent. Still adjusting to a new pregnancy, women and their partners may be unprepared to face the emotional impact should a test result be abnormal.
- Although prenatal testing may establish a diagnosis, for example, of Down syndrome, results cannot provide specific information about the level of intellectual ability or health status of the fetus.
- Attitudes about the purpose of prenatal screening vary widely. Research indicates some women accept prenatal screening with little thought, expecting a reassuring outcome. Others have the test to gain information about the pregnancy, with no thought of intervening should the outcome be abnormal. Still others consider the purpose of a screening test to inform decisions around pregnancy termination (Fisher, 2012).
- Multiple considerations—ethical, legal, social, cultural, and religious—affect decision making related to reproductive health and must be balanced to achieve the most appropriate decision about prenatal screening.

To provide competent care, nurses must assess each client's knowledge, attitudes, and values about prenatal diagnosis and tailor the information they share in order to provide individualized care.

POSTNATAL GENETIC TESTING

Newborn screening is the most common postnatal genetic test being performed routinely to identify newborns at high risk of a variety of disorders which require immediate intervention. The panel of tests included in newborn screening has expanded greatly in recent years and varies from state to state. Although informed consent should be a part of any genetic testing, in most states newborn screening is mandated and written consent is not required. Parents are likely, therefore, to have little information about the tests that are performed or the meaning of a positive test. Nurses therefore have a key role in teaching parents about newborn screening and that a positive test does not mean that their newborn has a genetic condition. Diagnostic testing is always required to confirm a positive screening test. Most often, a positive screening test represents a false-positive result and the diagnostic test is normal.

When a child is born with anomalies, has a stormy newborn period, or does not progress as expected, a genetic evaluation may be warranted, and testing may confirm a genetic diagnosis. Questions concerning genetic disorders (cause, treatment, and prognosis) are most often first discussed in the newborn nursery or during the infant's first few months of life. To make an accurate diagnosis, the geneticist consults with other specialists, reviews the current literature, and evaluates all the available information before arriving at a diagnosis and plan of action.

One cannot expect a couple who has just learned that their child has a birth defect or genetic condition to take in any information concerning risks with future pregnancies. However, the couple should never be "put off" from genetic counseling for so long that they conceive another affected child because of lack of information. The nurse can inform parents that genetic counseling is available before they attempt to have another child.

GENETIC TESTING FOR MINORS

In order to support, advocate for, and educate children, adolescents, and their families, the pediatric nurse must have knowledge of issues related to genetic testing of minor children. Parents may request genetic testing for their minor children without foreseeing the consequences associated with a positive finding. Nurses have a critical role in providing information and anticipatory guidance for families considering genetic testing.

The primary focus of genetic testing in children is to promote the child's well-being, and guidelines generally recommend that genetic testing in children only be conducted if the results would affect medical management soon after testing. With this in mind, nurses should help families to understand clearly why a genetic test is being done.

Newborn screening is an example of testing designed to offer an immediate medical benefit for the child in terms of disease prevention or early treatment. Consensus statements by several professional groups support the mandatory offering of newborn screening to parents of all children (Ross, Saal, David, et al., 2013). Diagnostic genetic testing for children with symptoms of a genetic condition is also broadly supported because establishing a diagnosis informs health management for the child as well as reproductive decision making by the family. Predictive testing in asymptomatic children for conditions that cause morbidity at a young age or for specific health promotion, screening, or treatment is also recommended. An example is familial adenomatous polyposis (FAP). Children with a family history of FAP should be tested for the altered gene because screening by colonoscopy is recommended for affected individuals during adolescence (Munck et al., 2011). Genetic counseling and informed consent are essential prior to predictive genetic testing in minors (Ross et al., 2013).

In contrast to the above scenarios, a parent or child may request predictive genetic testing for future planning in the absence of any immediate benefit. This situation may arise with inherited adult-onset disorders such as Huntington disease, certain cancers, or familial (early-onset) Alzheimer disease. An older child who has a relative with such a disorder may wish to know whether he or she carries the altered gene to plan for a life career or to make relationship decisions such as marriage. Parents sometimes request predictive or carrier testing for their children who are well below reproductive age. Among genetics professionals, there is widespread consensus that predictive genetic testing for minors in the absence of targeted preventive, surveillance, or treatment interventions should be deferred until a child reaches the age of majority (Ross et al., 2013). In most states that age is 18 years.

Occasionally, a family member may request genetic testing for a child when the test results are entirely for the benefit of another family member, with no direct benefit to the child. This may occur during DNA linkage studies, in which multiple blood samples from both affected and unaffected individuals within a family are analyzed and compared to identify a specific DNA alteration for diagnosing a genetic condition in that particular family. Another example is genetic testing for the purpose of human leukocyte antigen (HLA) matching

prior to stem cell donation. Because HLA-matched siblings are often preferred as stem cell donors, parents may request this testing, which offers no clinical benefit for the child but may benefit immediate family members. Such testing is supported by consensus in pediatric and genetic communities (Ross et al., 2013).

In recent years, advances in genetic knowledge and increasing availability of genetic testing have blurred the issues around testing in minors. Consider, for example, carrier screening. While routine carrier testing of minors is not recommended, carrier screening may be appropriate for adolescents under certain circumstances. Examples are sickle cell trait screening for some athletes and carrier screening for adolescents who are pregnant or considering reproduction. Sometimes, carrier status is identified on newborn screening, creating an issue regarding testing in minors. Although carrier status in a newborn is rarely clinically significant, it is generally agreed that carrier status should be communicated to the family (Ross et al., 2013). Predispositional testing is also complex. Consider a child who is tested and found to have a genetic predisposition to type 2 diabetes. Typically, the disease risk is moderately elevated—perhaps 2 to 3 times the population risk. Does knowledge of that genetic test have immediate medical benefit for the child? Does the potential benefit outweigh any harm that may accompany the knowledge? Issues such as these are of great interest in genomic medicine, but clear guidelines have yet to be established.

ENSURING INFORMED CONSENT AND CONFIDENTIALITY FOR GENETIC TESTING

Nurses are responsible for alerting clients and families of their right to make an informed decision prior to *any* genetic testing, with consideration of the special circumstances arising from the family's social, cultural, and community life. All genetic testing should be voluntary, and it is the nurse's responsibility to ensure that the consent process includes discussion of the risks and benefits of the test, including any physical or psychologic harm, as well as potential societal injury due to stigmatization or discrimination. Ross et al. (2013) suggest using a consent process similar to that conducted before an elective medical procedure. Providing informed consent involves more than just presenting a form and asking clients to sign; rather, nurses must ensure clients fully understand both the process of the testing and potential implications (Badzek, Henaghan, Turner, et al., 2012). For example, tests may reveal unexpected genetic alterations unrelated to the indication for which the test was ordered, and the management of such **incidental findings** should be explained during the consent process. The nurse should be aware that health insurance policies may not cover genetic testing, which is often very expensive. Even if the insurance benefit will cover the test, and despite protections afforded by law, many individuals are fearful of discrimination based on genetic test results that are included in their medical record. The pediatric nurse should inform the child and the family of their right to know who will have access to the genetic test results and of legal protections against genetic discrimination. See *Professionalism in Practice: ELSI.*

PSYCHOSOCIAL ISSUES IN GENETIC TESTING

Nurses must be prepared to assist clients and families to manage anxiety associated with genetic testing. Uncertainty and stress associated with making a decision to undertake genetic testing may extend into weeks or even months before results are available. That stress may be increased or relieved once test results are known. Although receiving favorable test results may decrease anxiety for the family or the individual, potential problems do occur and the nurse must be prepared to address them. Concerns about carrier status may interfere with development of intimacy and interpersonal relationships. A positive test result may lead to feelings of unworthiness and disturb self-image. Survivor guilt may affect children with negative results if their siblings are positive. Younger children may blame themselves, thinking they did or said something to cause the gene alteration. The adolescent carrying a gene alteration for a late-onset disease may have an increased tendency for risky behaviors. The adolescent who has inherited an altered disease-producing gene may foster resentment toward the parent who carries the altered gene. Parental guilt may exist for passing the altered gene to the child. Finally, parent–child bonds may be altered if parents become either overprotective or overly permissive. The parent and other

Professionalism in Practice ELSI

Since its inception, the National Human Genome Research Institute has designated a percentage of its budget to examining the ethical, legal, and social implications (ELSI) of genetic and genomic information. Genetic testing raises many questions that have been addressed by ELSI. Genetic exceptionalism, the idea that genetic information should be treated differently than other health information, continues to be a subject of great interest and little consensus. Proponents of genetic exceptionalism point out that genetic information is unique and deserving of special consideration and protection because it is predictive, is potentially stigmatizing, and may reveal information about family members other than the client undergoing testing. The contrasting view points out that other information is also predictive (consider blood cholesterol and risk for cardiovascular disease) and stigmatizing (e.g., information about sexually transmitted infections).

Federal health privacy protection, as mandated under the federal Health Insurance Portability and Accountability Act (HIPAA) privacy rule, does not afford special protection to genetic information, treating it as being no more sensitive than other health-related information. However, by 2008, the majority of states had enacted legislation to protect people from discrimination based on genetic information and penalties for violating genetic privacy. These laws were implemented in response to concerns that individuals might be reluctant to seek potentially beneficial genetic testing without some guarantee about the confidentiality, privacy, and security of that information. For example, an individual may have health coverage for a genetic test but be unwilling to submit the claim because of concerns about the insurance company "owning" the information in the test result. Federal legislation to prohibit discrimination based on genetic information in health insurance and employment (the Genetic Information Nondiscrimination Act [GINA]) was implemented in November 2009. As a federal law, GINA offers protection to Americans in all states.

TEACHING HIGHLIGHTS | Nursing Responsibilities in Genetic Counseling

The nurse in genetic counseling is responsible for the following:

- Identify families at risk for genetic problems.
- Determine how the family perceives the genetic problem and what information they wish before proceeding.
- Assist families in acquiring accurate information about the specific problem.
- Act as a liaison between the family and genetic counselor.
- Assist the family in understanding and dealing with information received.
- Provide information on support groups.
- Aid families in coping with this crisis.
- Provide current, credible genetic information.
- Assure continuity of nursing care to the family.

family members may unconsciously form lowered expectations for the child or adolescent. Nurses must use counseling interventions to assist clients to process, adjust to, and use genetic information.

The Role of the Nurse in Genetic Referral

When the nursing assessment reveals a client may benefit from referral to a genetic specialist, the nurse is expected to partner with the client and facilitate the referral. This is a nursing responsibility in the same way as a referral to a dietitian or social worker. *Genetic counseling* is a communication process in which a genetic counselor, physician, or specially trained and certified nurse helps a family or individuals understand and adapt to the medical, psychologic, and familial implications of genetic contributions to disease (National Society of Genetic Counselors, 2005, reaffirmed 2011). Genetic specialists are able to answer questions regarding genetic conditions, inheritance, availability of treatment, and economic, insurance, and future implications of genetic conditions.

Genetic counseling referral is advised for any of the following categories:

- *Congenital abnormalities.* These include *developmental, cognitive, and intellectual disabilities*. Any couple who has had a child or a relative with a congenital malformation may be at increased risk and should be so informed. If a developmental, cognitive, or intellectual disability of unidentified cause has occurred in a family, there may be an increased risk of recurrence. In some cases, the genetic counselor will identify the cause of a malformation as a teratogen. The family should be aware of teratogenic substances so they can avoid exposure during any subsequent pregnancy.
- *Familial disorders.* Families should be told that certain diseases may have a genetic component and that the risk of their occurrence in a particular family may be higher than that in the general population. Such disorders as diabetes, heart disease, cancer, and mental illness fall into this category.
- *Known inherited diseases.* Families may know that a disease is inherited but not know the mechanism or the specific risk for them. An important point to remember is that family members who are not at risk for passing on a disorder should be as well informed as family members who are at risk.
- *Metabolic disorders.* Any families at risk for having a child with a metabolic disorder or biochemical defect should be referred for genetic counseling. Because most inborn errors of metabolism are autosomal recessively inherited, a family may not be identified as being at risk until the birth of an affected child.
- *Chromosomal abnormalities.* As discussed previously, any couple who has had a child with a chromosomal abnormality may be at increased risk of having another child similarly affected. This group includes families in which there is concern about a possible translocation.

When facilitating referral to a genetic specialist, the nurse should educate the client or family so they know what to expect during and after a genetic evaluation. Before the first visit, the client will usually be contacted to provide a detailed medical and family history. The client should be prepared to give as exact a family history as possible so that a detailed three-generation pedigree can be constructed. Information concerning ancestry will also be collected because some genetic disorders are more common among certain groups or individuals from a particular geographic area. (See *Developing Cultural Competence: Genetic Screening Recommendations for Various Ethnic and Age Groups* below.)

Clients should be informed that a genetic consultation visit can last several hours. During the appointment, a genetic clinical nurse, genetic counselor, and/or physician will perform an initial interview with the parents and their child. A geneticist will examine the child and possibly the parent(s) in order to establish an accurate diagnosis. Photos may be taken and tests may be ordered. The specialist will often provide preliminary information based on the data at hand, although a definitive diagnosis may not be possible at the initial visit.

After the completion of testing and careful analysis of all data, the geneticist or genetic counselor will discuss the findings with the parents and/or child and make recommendations. This may occur at a subsequent visit. The discussion will include the diagnosis (if known), the probable course of the disorder, and available management options. The inheritance pattern for the disorder and risk of recurrence with future pregnancies will also be discussed. The remainder of the counseling session is spent discussing the course of action that seems appropriate to the family in view of the risk and family goals. For couples who desire to become parents or who want a subsequent child, options include prenatal diagnosis, early detection and treatment, preimplantation genetic diagnosis or other assisted reproductive therapies, delayed childbearing until prenatal diagnosis is available or a disease can be detected and treated early to prevent irreversible damage, or, in some cases, adoption. When the parents have

Developing Cultural Competence **Genetic Screening Recommendations for Various Ethnic and Age Groups**

Background of Population at Risk	Disorder	Screening Test	Definitive Test
Ashkenazi Jewish, French-Canadian, Cajun	Tay-Sachs disease	Decreased serum hexosaminidase-A or DNA mutation analysis	Chorionic villus sampling (CVS) or amniocentesis for hexosaminidase-A assay or DNA mutation analysis
Ashkenazi Jewish	Cystic fibrosis, Canavan disease, familial dysautonomia, several other disorders	DNA mutation analysis	CVS or amniocentesis for DNA mutation analysis
African; Hispanic from Caribbean, Central America, or South America; Arab, Egyptian; Asian Indian	Sickle cell disease	Presence of sickle cell hemoglobin; confirmatory hemoglobin electrophoresis	CVS or amniocentesis for DNA mutation analysis
Greek, Italian	Beta-thalassemia	Mean corpuscular volume less than 80%; confirmatory hemoglobin electrophoresis	CVS or amniocentesis for DNA mutation analysis
Southeast Asian (Vietnamese, Laotian, Cambodian), Filipino	Alpha-thalassemia	Mean corpuscular volume less than 80%; confirmatory hemoglobin electrophoresis	CVS or amniocentesis for DNA mutation analysis or gene deletion studies
Women over age 35 (all ethnic groups)	Chromosomal trisomies	Prenatal serum and/or ultrasound screening	CVS or amniocentesis for cytogenetic analysis
Women of any age (all ethnic groups; particularly suggested for women from British Isles, Ireland)	Neural tube defects and selected other anomalies	Maternal serum alpha-fetoprotein (MSAFP)	Amniocentesis for amniotic fluid alpha-fetoprotein (AFP) and acetylcholinesterase assays
Caucasian (northern European, Celtic population), Ashkenazi Jewish	Cystic fibrosis	DNA mutation analysis of the cystic fibrosis transmembrane regulation (CFTR) gene	CVS or amniocentesis for DNA mutation analysis

completed the counseling sessions, the counselor sends them and the referring provider a letter detailing the contents of the sessions. The parents should keep this document for reference.

Genetic healthcare providers present the individual and the family with information to promote informed decisions. They are also sensitive to the importance of protecting the individual's autonomy. A challenge during any visit to a genetic specialist is in providing nondirective counseling. Families should be permitted to make decisions that are not influenced by any biases or values from the nurse, counselor, or geneticist. Many families are accustomed to practitioners and nurses providing direction and guidance in their decision making, and families may be uncomfortable with a nondirective approach. They may believe that the nurse or healthcare provider is withholding very bad news. Health professionals should present all indicated options and discuss the positive and negative aspects of each option, employing therapeutic listening and communication skills.

After genetic counseling, the nurse with the appropriate knowledge of genetics is in an ideal position to help couples review what has been discussed during the counseling sessions and to answer any additional questions they might have. As families return to daily living, the nurse can provide helpful information on the day-to-day aspects of caring for a child, answer questions as they arise, support parents in their decisions, and refer families to other health and community agencies.

Clinical Tip

The following are indications for pediatric referral to a genetic specialist:

- If the child or family reports a known or "believed" genetic condition in the family
- Single major or multiple minor congenital anomalies
- Dysmorphic features that are not familial
- Developmental delay or regression
- A known or suspected metabolic disorder
- Speech problems
- Learning disability
- Failure to thrive
- Delays in physical growth, unusual body proportions, or low muscle tone
- Abnormal or delayed development of secondary sex characteristics or sex organs
- Short or extremely tall stature
- Blindness or cataracts in infants or children
- Deafness
- Hypotonia in an infant or child
- Seizures in newborns or infants
- Skin lesions such as café au lait spots

The Role of the Nurse in Genetic Teaching, Psychosocial Care, and Advocacy

Nurses must be prepared to educate clients and families about genetic disorders. Consideration of a client's cultural and religious beliefs and values is important to teaching. Gene alterations may be viewed as uncontrollable, as occurring secondary to cultural beliefs such as a stranger looking at the infant, or as a "punishment." A family's readiness to learn can be influenced by cultural or religious beliefs and values. Obtaining educational materials in the primary language of the child or family will help facilitate the teaching–learning experience.

The nurse must be aware of common inheritance misconceptions such as a parent's belief that with a 25% recurrence risk, after one child is affected the next three children will be unaffected, or with a 50% recurrence risk every other child will be affected. The recurrence risk *for each pregnancy* should be continually stressed by the nurse. Families often believe that certain family members have inherited a genetic condition because they look like or "take after" a relative with a genetic condition. When new gene alterations or mutations are found or even discussed, families will often express surprise. Because no one else in the family has the condition, they perceive the trait or condition cannot be inherited. Helping families to understand genetic concepts about inheritance is fundamental to delivering competent genetic nursing care.

In order to provide holistic care, the nurse should identify the psychosocial needs and expectations of the child and family, as well as their cultural, spiritual, value, and belief systems. Denial of a genetic diagnosis is common, and nurses must be aware of the family's state of acceptance. Nurses must often help alleviate anxiety or guilt in the child or family. Anxiety related to uncertainty is common when awaiting diagnosis or test results, but individuals also experience anxiety from not understanding the future implications of a confirmed genetic disease. Guilt may be associated with knowledge of a genetic condition being "in the family." It is important for the nurse to reassure parents that the genetic condition is not the result of something they did or did not do during pregnancy. The nurse should encourage open discussion and free expression of fears and concerns. Guilt and shame are common as a family deals with the loss of the expectation and dream of a healthy child, grandchild, niece, or nephew. Reinforce to parents that genetic alterations are caused by changes within a gene and not by superstitions related to sin or other cultural beliefs. As mothers, fathers, and extended family members provide continuous care for the individual with a genetic condition, depression can result. Depression can also occur in the individual with the condition. The nurse must maintain awareness of the possibility of depression and be proactive in obtaining support for the individual or family.

The nurse also is responsible for assessing the family's coping mechanisms and available family, spiritual, cultural, and community support systems. The nurse can refer the individual or family to a support group; however, it is important to have permission from the child or family before providing a support group with their names and contact information. Electronic sources of genetic information abound and are unregulated; many of them are proprietary, offering expensive genetic testing that may have little scientific basis. Nurses should help families to select and evaluate credible websites and online discussion groups.

Another key role for the nurse is to help families with the often difficult task of communicating genetic information such as inheritance patterns to extended family members. Cultural values of autonomy and privacy come into play when a person considers whether to communicate genetic information to extended family members who may also carry the altered gene. Family members often have difficulty understanding that some genetic conditions have variable expressivity. Members of the extended family often feel shock and profound guilt upon learning that they carry the gene alteration that has caused their loved one to have a genetic condition.

The nurse must continually advocate for the child and family and support their decisions even if the decisions contradict the nurse's own ideals and morals. Therefore, careful self-assessment of feelings is essential for the nurse to recognize when one's own attitudes and values may affect care (Consensus Panel on Genetic/Genomic Nursing Competencies, 2009). Coping with genetic revelations and making genetic-related treatment decisions are difficult activities for everyone. The nurse must remember that families will need resources and support and also help in gathering information about reproductive options.

Evaluation

Expected outcomes of delivering nursing care with a genetic focus include:

- The child and family will make informed and voluntary decisions related to genetic health issues.
- The child and family will accurately identify:
  - Basic genetic concepts and simple inheritance risk probabilities
  - What to expect from a genetic referral
  - The influence of genetic factors in health promotion and health maintenance
  - Social, legal, and ethical issues related to genetic testing

Vision for the Future

Nurses are often the primary caregivers to whom children and their families turn for information, guidance, and clarification of ideas. Genetic and genomic competency among nurses is essential, not only to provide direct care but also to function as informed members of the community and greater society. As more information about the genome science becomes available to consumers—in areas such as **pharmacogenomics**, gene therapy, ethics, genetic engineering, and stem cell research—the role of nurses not only remains vital but also increases in breadth. For example, research in pharmacogenetics is leading to prescribing medications based on an individual's genomic profile. As that testing becomes the standard of care for more medications, the nurse's role expands to ensure the testing is completed and to explain results and implications to families. Nurses must acquire foundational understanding of genetic and genomic concepts, maintain currency as genomic discovery is translated to practice, and be ready to discuss trends and changes with children, adolescents, and their families.

Focus Your Study

- Nurses must understand basic concepts of genetics and genomics to deliver the expected standard of nursing care.
- When cell division does not occur as expected, chromosomal alterations in autosomes or sex chromosomes can result.
- Large chromosomal alterations can be seen in a karyotype.
- Mosaicism may cause varied clinical manifestations of chromosomal alterations.
- Gene structure or sequence is critical to the formation of proteins, which are necessary to carry out all physiologic functions.
- Alterations in gene sequence can cause the production of proteins that do not function as expected, which may threaten health.
- Different forms of a gene that occupy the same place on a pair of chromosomes are alleles.
- An individual may be identified as heterozygous or homozygous for a single gene.
- Some gene alterations cause disease, and some protect individuals from disease.
- Mitochondrial gene alterations are inherited from the mother and are primarily involved in high-energy organs such as skeletal muscles, brain, and heart muscle.
- Knowledge of the principles of inheritance allows the nurse not only to offer and reinforce genetic information to children, adolescents, and their families but also to assist them in managing their care and in making reproductive decisions.
- Multifactorial conditions do not follow Mendelian inheritance patterns.
- Several types of genetic tests are available and vary in intended use, implications, and limitations.
- Nurses have an important role in educating clients about genetic testing, promoting informed decision making, and obtaining informed consent.
- Genetic testing of minors has particular implications that require careful consideration.
- The nurse must be aware of the ethical, social, legal, cultural, and spiritual issues related to the delivery of genetic care.
- Basic genetic nursing involves initiating a referral to genetic specialists.

Clinical Reasoning in Action

SOURCE: Lane Oatey/Blue Jean Images/Getty Images.

Jessica Chan, age 30, is 12 weeks pregnant with her first child. She presents to the clinic with her spouse, Brian, for follow-up after a maternal serum screening test and ultrasound, which indicate an increased risk for Down syndrome. She appears anxious and is intermittently tearful. She describes their pregnancy as being planned, a source of great joy and little concern until hearing about her positive screening test. "To tell you the truth, I thought that blood test was just routine and never gave it any thought. And when we had our ultrasound, we were both just so happy to see our baby!" she says.

Although Jessica and Brian have both heard of Down syndrome, neither has personally known a person or even a family in which there is a member with Down syndrome. "We don't know what to do," says Jessica. "What are our options?"

1. How will you explain the implications and limitations of positive screening tests?
2. Jessica asks about additional tests that might provide more specific information without threatening her pregnancy. What would you tell her?
3. Jessica asks you about amniocentesis and CVS, which she was told could determine for sure whether their baby has Down syndrome. What would you tell her about those two procedures?
4. If Jessica chooses to have further testing, what particular challenges are associated with obtaining informed consent?
5. How can you tailor Jessica's and Brian's care based on their knowledge, attitudes, and values?

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