I came in for a sports physical, but I really want to be tested for Huntington disease. My mom’s father died from Huntington when I was 8. My mom won’t really talk about it, but I know she doesn’t want to be tested. I have been doing some reading about Huntington disease, and I want to be tested. I mean, how can I plan my life if I don’t know how long I’m going to be able to enjoy it? —Sarah, age 16

LEARNING OUTCOMES

After reading this chapter, you will be able to do the following:

3.1 Explain the role of genetic and genomic concepts in health promotion, disease prevention, screening, diagnostics, selection of treatment, and monitoring of treatment effectiveness.

3.2 Elicit a family health history and construct a genetic pedigree.

3.3 Incorporate knowledge of genetic and genomic influences and risk factors into assessment, planning, and implementation of nursing care.

3.4 Integrate basic genetic and genomic concepts into child and family education.

3.5 Understand implications of genome science on the nursing role with particular attention to ethical, legal, and social issues.

3.6 Discuss the significance of recent advances in human genetics and genomics and their impact on healthcare delivery.
Completion of the Human Genome Project in 2003 heralded the dawn of the genomic era of health care. It has long been known that some diseases occur due to specific gene defects. Genetic diseases have traditionally been thought of as inherited diseases caused by a defect in a single gene. While “typical” genetic diseases have enormous health consequences for affected individuals and families, they have relatively little impact on the health of most people. The Human Genome Project decoded human deoxyribonucleic acid (DNA), revealing the sequence of its 3 billion “letters” (also called bases or nucleotides). Research associated with the Human Genome Project has revealed virtually all diseases to have a genetic component. The human genome is the entire DNA sequence of an individual, and the study of genomics takes a holistic view of gene function. Human genomics is the study of all DNA in the human genome, including how genes interact with each other and with environmental, psychosocial, and cultural factors. While essentially all diseases and health conditions have both genetic and environmental components, the genetic contribution to various diseases varies widely (Figure 3–1).

DNA is central to our state of health because of its role in determining the set of proteins an individual has available to carry out specific physiologic functions. There are about 21,000 genes in the human genome, and each gene directs the formation of one or more proteins (Lander, 2011). Proteins include enzymes, cell receptors, ion channels, structural molecules, antibodies, and other molecules necessary for biologic function. Good health is dependent on normal gene structure (or sequence) and normal gene function (or expression). Gene sequence, which is the order of the gene’s nucleotides or bases, determines whether a protein encoded by the gene has the correct amino acid sequence so that it can function normally. Normal gene function means that genes are expressed (i.e., translated and transcribed to make proteins) at the appropriate time and in appropriate amounts to support normal physiologic function. Gene expression, which is affected by all manner of environmental and epigenetic effects, is therefore just as important as gene sequence. Genetic abnormalities may cause too much or too little of a specific protein, or perhaps a dysfunctional protein, to be formed. Sometimes the altered protein is sufficient to cause disease; this is the case with traditional genetic diseases such as cystic fibrosis and sickle cell disease. More often, multiple genetic variations, together with environmental factors, increase risk for disease. Both traditional genetic disorders and common complex diseases such as heart disease, stroke, diabetes, and cancer are now known to be related to variation in gene sequence and gene expression. Research has uncovered many of the genetic and environmental factors that increase risk for disease, leading to development of new treatments that range in scope from promoting healthy lifestyles to specific genetic therapies. Knowledge gained from human genome research is anticipated to transform health care across the entire continuum of care, allowing care to be tailored to each person’s individual risk for disease. Genomic information is already being used to personalize health promotion and disease prevention, screening, treatment, and monitoring of treatment effectiveness (Green, Guyer, & National Human Genome Research Institute, 2011).

Nurses must be prepared to deliver genetically competent care in many healthcare settings to individuals, families, communities, and populations. Nurses in newborn nurseries and mother–baby units may be the first to suspect a newborn has a genetic condition. Pediatric nurses often care for children with genetic conditions, who may require frequent hospitalization. Nurses in general and specialty clinics must be prepared to help asymptomatic individuals and families who are increasingly seeking information about their risk for an inherited disease or condition. Parents who order direct-to-consumer genetic tests may bring questions about
their results to nurses. For these and other reasons, nurses must achieve genetic and genomic literacy in order to deliver competent care in the genomic era.

The translation of genetic and genomic knowledge to clinical care requires nurses to integrate new genetic knowledge into their nursing practice. This expectation has been formally established by the American Nurses Association (ANA) and the International Society of Nurses in Genetics (ISONG) in a joint statement, Genetics/Genomics Nursing: Scope and Standards of Practice. This document outlines the levels of genetic knowledge required of all registered nurses, including basic and advanced practice nurses in general practice as well as those who specialize in genetics nursing. In addition, a set of essential competencies in genetics and genomics has been defined and endorsed by nearly 50 nursing organizations. These competencies represent the minimal level of genetic and genomic competency expected of every registered nurse across all practice settings (Consensus Panel on Genetic/Genomic Nursing Competencies, 2009). Examples of nursing activities that reflect genetic and genomic competence include:

- Identifying risk for disease by collecting a family history and drawing a three-generation pedigree
- Helping individuals and families to understand the implications and limitations of genetic testing
- Administering gene-based therapies

Figure 3–1 Although the causes for nearly all diseases and health conditions have both genetic and environmental components, the relative contribution of genetic and environmental influences varies widely. At one end of the spectrum lie “traditional” genetic diseases, such as cystic fibrosis (CF). Although CF is caused by a gene alteration, its morbidity and mortality vary according to environmental effects such as medical management. On the other hand, AIDS is an infectious disease that will not occur without environmental exposure to the HIV virus. Still, there are genetic alterations that cause some people to be resistant to HIV infection. In type 2 diabetes, the genetic and environmental contributions are fairly equivalent.

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Clinical Tip

ANA/ISONG Scope and Standards of Genetics/Genomics Nursing

The ANA/ISONG statement on the scope and standards of genetics and genomic nursing practice is as follows:

All licensed registered nurses, regardless of their practice setting, have a role in the delivery of genetics services and the management of genetic information. Nurses require genetics and genomics knowledge to identify, refer, support, and care for persons affected by, or at risk for manifesting or transmitting conditions or diseases with a genetic component. As the public becomes more aware of the genetic contribution to health and disease, nurses in all areas of practice are being asked to address basic genetics- and genomics-related questions and service needs.

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- Providing nondirective counseling to assist families who have questions or concerns about their reproductive risks
- Recognizing signs and symptoms, such as dysmorphic features or hypotonia, that may indicate a genetic condition in a newborn
- Anticipating variable responses among individuals to “standard” medication doses, due to pharmacogenetic effects
- Ensuring the delivery of genetically competent care for the child and family, for example, ensuring that a child about to start thiopurine treatment has completed pharmacogenetic testing
- Helping individuals and families to identify credible sources of genetic information
- Applying concepts of health promotion and health maintenance to assist children and families at increased risk to develop common chronic conditions, such as heart disease, to make informed lifestyle choices
- Partnering with families affected by genetic conditions, including providing advocacy, supporting the child’s and family’s decisions, teaching, facilitating appropriate referrals, clarifying information, and providing further information about available resources and services
- Partnering with the community to educate the public about genetics
- Supporting legislation to protect genetic information and to protect those with genetic conditions from discrimination
- Applying knowledge of the ethical, legal, and social implications of genetic information

Through informed application of fundamental genetic and genomic concepts, nurses can significantly improve the nursing care provided to children and their families. In fact, understanding and applying these concepts is an essential part of child and family nursing.
Impact of Genetic Advances on Health Promotion and Health Maintenance

Health promotion and health maintenance for children and their families are foundational for all nursing care (see Chapters 6 through 9). The genomic era offers a promise of personalized health care based on an individual’s or a population’s risk for disease, which varies according to the set of genes they inherited and a multitude of environmental factors to which they are exposed. Although some people may be aware that they carry an altered gene associated with a specific disease, most individuals do not know details of their genetic makeup or how their genetic inheritance influences their future health. This is particularly true for common conditions such as heart disease and diabetes, for which risk varies with inheritance of a number of altered genes and is modified by lifestyle factors such as diet and physical activity. Having specific knowledge about one’s genetic makeup and associated increased risk for disease provides a basis for health screening and may provide motivation for people to maintain a healthy lifestyle. Imagine, then, if people knew their statistical risks for inheriting or developing disease, based on their specific genotype. Health promotion and health maintenance teaching and nursing interventions would be targeted to individuals according to their disease risk. Children and families may experience increased motivation to adhere to lifestyle choices and health screenings that are personalized according to their disease risk. Personalized health care is a major goal in the genomic era (Feero & Guttmacher, 2014).

With knowledge of how genetic variations influence health, the pediatric nurse can ensure health teaching and early detection of complications from genetic conditions with emphasis on primary and secondary care interventions. For example:

- Nurses should ensure informed consent for newborn screening and provide teaching and support to families whose infants have positive screens.
- Nurses should recognize hypotonia (reduced muscle tone, limited voluntary movement, reduced strength, and joints with increased range of motion) in newborns and advocate for a referral for the infant to be evaluated by a genetic specialist (Prows, Hopkin, Barnoy, et al., 2013).
- A child who screens positive for scoliosis (see Chapter 29) should be assessed for axillary freckling and café au lait spots, due to the relationship between scoliosis and neurofibromatosis.
- Screening for Marfan syndrome (see Chapter 21) should be a part of all sports physicals, due to the lethal cardiovascular complication of aortic dilation. This can be accomplished by assessing for common characteristics such as myopia, scoliosis, tall stature, long fingers and thumbs, a hollow chest, and an arm span greater than the height.
- Nurses should both teach and support families regarding any specific interventions necessary to avoid complications in children with genetic conditions. Examples are the importance for children with phenylketonuria (PKU) to maintain a phenylalanine-free diet for life, and the need to maintain children with sickle cell disease (see Chapter 23) on penicillin.
- When caring for the child with Down syndrome (see Chapter 28), the pediatric nurse can help the parents shift from the more expected and traditional focus of disease management to health promotion and protection by teaching parents about the established guidelines for exams and screenings specific to children with Down syndrome.

Early diagnosis allows early intervention with health-promoting care specific to a genetic diagnosis, promoting achievement of maximal function, better health, and improved quality of life for children affected with genetic alterations. The pediatric nurse must be able to identify available community-based and genetic-based resources to assist the child or adolescent and the family with strategies to support both health promotion and health maintenance activities.

GENETIC BASICS

A basic knowledge of the cell, DNA, cell division, chromosomes, and genes is essential to deliver the genetic standard of care to children, adolescents, and their families. The cell is the basic unit of life and the working unit of all living systems. Life starts as a single cell, but the developed human body is made up of trillions of cells. These cells share common features such as a nucleus that contains 46 chromosomes 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, which 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.

Each cell nucleus 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 3–2 ●). Sperm and ova represent exceptions to the 23-pair rule, because each contains only a single chromosome from each homologous pair.

**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 oocytes (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 from an exchange or shuffling of material between homologous chromosomes inherited from the father and mother. This exchange results in new intact chromosomes that represent a patchwork of maternal and paternal genetic material. Only the Y chromosome does not have the ability to cross over, since it lacks a homologous mate. 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, paired 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.

In general, humans do not tolerate either extra or missing DNA very well. Most monosomic or trisomic conceptions result in early pregnancy loss. For example, Turner syndrome is the only monosomic condition that is compatible with life. Trisomies involving chromosomes with small numbers of genes may result in live births. Examples are trisomy 13 (Patau syndrome), trisomy 18 (Edwards syndrome), and trisomy 21 (Down syndrome). Each of these aneuploidies produces clinical features that vary according to the chromosome that is duplicated. It is not a coincidence that the three nonlethal trisomic conditions involve duplication of chromosomes containing the smallest number of genes (Pierce, 2014).

**Mosaicism.** Monosomy and/or trisomy can also occur during mitosis, 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, individuals with mosaic Turner syndrome may show varying degrees of infertility or short stature, and an individual with mosaic Down syndrome may have a higher intelligence level than children whose every cell has three copies of chromosome 21.

**Structural Chromosomal Alterations**

**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.

**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, caused by a large deletion on chromosome 5. Children with cri du chat have microcephaly (a small head), significant intellectual disability, and a peculiar cry during infancy that sounds like a cat mewing (Schaaf, Zschocke, & Potocki, 2012).

**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 due to missing or extra genetic material. In about 4% of cases of Down syndrome, the extra chromosome 21 is due to a translocation (Schaaf, Zschocke, & Potocki, 2012). When a child with Down syndrome is born, it is important to conduct a chromosome study to determine if the cause is nondisjunction or translocation. Translocation, while unrelated to maternal age, carries a significantly greater recurrence risk with subsequent pregnancies.

**Genes**

In addition to understanding chromosomal alterations, the nurse must have knowledge of genes—what they are, their function, and the consequences of gene alterations. The nurse must understand the inheritance of gene alterations 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 chronic disease are better understood, knowledge of gene function and inheritance has become increasingly relevant in health promotion and health maintenance.

A **gene** is a small segment of a chromosome that can be identified with a particular function, most commonly protein production. Each chromosome contains many genes arranged in a linear order. 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 don’t 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. As previously discussed, genes on the sex chromosomes of males are unpaired, because the X and Y chromosomes contain different genes.

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 are described as **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 does not change the protein product is called a polymorphism or silent mutation. Other changes in nucleotide sequence, perhaps at a locus some distance from the gene itself, may affect gene expression—a gene’s 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. 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 curvy or straight hair or physiologic function, for example, signs or symptoms of a disease.

**Function and Distribution of Genes**

It is believed that only about 1% of the human genome is actually represented by genes (McCarthy, McLeod, & Ginsburg, 2013). The vast majority of human DNA does not encode proteins. In humans, protein-coding DNA is organized into about 21,000 genes (Lander, 2011); each individual's particular set of genes represents his or her genotype. These 21,000 genes are responsible for encoding hundreds of thousands of proteins that carry out all physiologic functions. An error, or mutation, in a gene can disrupt the order of amino acids that make up that gene's protein product. 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. Proteins are highly specialized and perform virtually all cellular functions. They 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.

Gene activity in making proteins (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 eating, 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.

**Mitochondrial Genes**

Chromosomes in the cell nucleus are not the only site where genes reside. 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. Mitochondrial DNA 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 female with a mitochondrial gene mutation will consequently pass that mutation to all her children, whereas an affected male 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 single nucleotide changes occur at about 15 million sites (or loci) across the genome (The 1000 Genomes Project Consortium, 2010); the rest of the genome is identical in 99% of individuals. These single letter variations are called single nucleotide polymorphisms (SNPs) or SNPs (pronounced “snips”). Most SNPs are benign, although collectively they account for much phenotypic variation in appearance and risk for disease. 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).

**Gene Alterations and Disease**

An alteration in the DNA sequence of a gene may cause a defective protein to be formed, which may have clinical significance. Gene alterations can be inherited, or they can be acquired. Mutations inherited from one or both parents (hereditary mutations) 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 gene alteration, which can then be transmitted to following generations.

The second kind of gene alteration is an acquired, or somatic, mutation. These are mutations that occur in the DNA of cells of an individual at any time throughout a lifetime. 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 alterations are responsible for more than 5,000 hereditary diseases such as cystic fibrosis, Duchenne muscular dystrophy, and phenylketonuria (Online Mendelian Inheritance in Man [OMIM], 2014). Each of these disorders is relatively rare, although collectively they affect 1 of every 200 newborns (Schaaf, Zschocke, & Potocki, 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 multiple 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 1,000 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 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).

In other situations, multiple gene alterations along with environmental factors contribute to disease or health conditions. These conditions are said to be multifactorial. Most common chronic disorders, including hypertension, heart disease, type 2 diabetes, and most cancers, are multifactorial, as are several birth defects. Alterations in regulatory genes may also occur. Regulatory elements are stretches of DNA sequence, usually located between genes, that control gene expression or activity in making proteins. They include gene promoters, enhancers, silencers, and other control mechanisms and are important in maintaining homeostasis. Mutation of a regulatory gene might lead to the loss of expression of a gene, unexpected expression in a tissue in which it is usually silent, or a change in the time when a gene is expressed. Small, non-DNA molecules are also known to affect gene function; these epigenetic factors are of great interest in genetics research.

**Gene Alterations That Decrease Risk of Disease**

Although gene mutations 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 sickle cell disease (SCD) gene 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 (Jorde, Carey, & Bamshad, 2010). 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 in assisting patients 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**

Conditions that are caused by a mutation or alteration of a single gene are known as monogenic or single-gene disorders. More than 5,000 known single-gene disorders have been catalogued, with detailed information posted to a searchable public database, the Online Mendelian Inheritance in Man (OMIM, 2014). Single-gene disorders are known as Mendelian disorders, because they are predictably passed on from generation to generation following Mendel’s laws of inheritance. Monogenic disorders that occur due to a mutation on an autosome (chromosome numbers 1 through 22) are most 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 occasionally Y-linked, pattern. See Table 3–1.

**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.

**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 gene alteration in AD conditions occurs on an autosome rather than a sex chromosome, both 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 gene on to a child. Nurses must remember and teach families that each pregnancy is an independent event with a 50% chance of an affected child, no matter how many of a couple’s previous children inherited the altered gene. 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. 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.

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 autosomal dominant disorders, AR conditions involve genes on one of the 22 autosomes. A condition is called “recessive” when two copies of the altered 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. 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 resistance to malaria. Individuals whose ancestors are from malaria-endemic areas are therefore more likely to carry an altered sickle cell gene. See Developing Cultural Competence: Ancestral or Ethnic Groups and Autosomal Recessive Inheritance. Because carrier status usually confers no symptoms, parents are often unaware of their carrier status until they have an affected child.
Clinical Tip

Autosomal Dominant Mendelian Inheritance Characteristics
When gathering a family history, the nurse should assess for any of 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.

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 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. Recall 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 generally compensates for an altered allele, making the female a carrier.

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. See Clinical Tip.

X Inactivation. Early in embryonic life, within a week of fertilization, one of the X chromosomes inherited by females is inactivated. This process results in equalizing the expression of X-linked genes in the two sexes. Each female receives an X chromosome from her mother (maternal X) and one from her father (paternal X). The inactivation of either the maternal or paternal X chromosome is random. However, once that X has been inactivated in any given cell, all the cell’s descendants (through mitosis) contain the same inactive X chromosome. Therefore, females are mosaic for X-linked genes; some cells will express genes from the maternal X chromosome, whereas other cells will express genes from the paternal X. Females who inherit altered genes on an X chromosome therefore 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 iris and ocular fundus (Turnpenny & Ellard, 2012).

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 risk for inheriting a genetic disorder. These concepts include the following common variations in traditional Mendelian patterns of inheritance.

Clinical Tip

Autosomal Recessive Mendelian Inheritance Characteristics
When gathering a family history, the nurse should assess for any of 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.
Penetrance is the probability that a gene will be expressed phenotypically. It is an “all or none” concept in that a gene is considered to be penetrant if it is expressed to any degree (Jorde, Carey, & Bamshad, 2010). 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 Expressivity**

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 (NF-1). Although neurofibromatosis has 100% penetrance, members of the same affected family often exhibit variation in degree of signs or symptoms (Friedman, 2012).

**New Mutation**

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 neurofibromatosis type 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.

**Anticipation**

Anticipation is said to occur when successive generations in a family exhibit earlier onset of symptoms and more severe signs and symptoms of certain diseases. Anticipation occurs in disorders characterized by unstable repeat expansions, which are DNA sequences that consist of repeating units of three or more nucleotides, for example CAGCAG . . . CAG. Repeat units have a tendency to expand, or accumulate repeats, during meiosis, especially during spermatogenesis. As a result, the number of repeats tends to increase in successive generations. More than a dozen diseases, most neurologic in nature, result from unstable repeat expansions. These include Huntington disease,
fragile X syndrome, and myotonic dystrophy (Schaaf, Zschocke, & Potocki, 2012).

**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, Zschocke, & Potocki, 2012).

**Uniparental Disomy**

In cases of uniparental disomy, the child inherits both copies of a chromosome pair (or homologous parts of a chromosome pair) from the same parent instead of one copy from each parent. If there are no altered genes on these chromosomes, the child may not be affected by this event. However, if the chromosomes contain an altered gene for an autosomal recessive disease, the child will receive both altered genes and express the disease. For instance, if a child inherits two altered copies of chromosome 7 from a mother who is a carrier for cystic fibrosis, the child will then exhibit signs and symptoms of cystic fibrosis.

**Multifactorial Inheritance**

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. These are called multifactorial conditions 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.

Multifactorial conditions aggregate in families but do not follow the characteristic Mendelian patterns of inheritance seen with single-gene conditions. 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). See Table 3–2.

**COLLABORATIVE CARE**

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.

**Diagnostic Procedures**

Genetic testing is available for both chromosomal and gene-based alterations, and the entire landscape of genetic testing is changing rapidly. New methodologies have not only expanded the number of conditions for which genetic testing is available, but, to an even greater degree, reduced the cost. Increasingly,
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 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).

genetic testing is offered directly to consumers, who receive limited counseling about test results. Patients and families are likely to have limited or incorrect understanding about the types of genetic tests available and what information those tests are able and not able to provide, and they may access unreliable sources for information. Further, interpreting results of genetic testing can be complex. As described later in this chapter, a test for cystic fibrosis may be reported as negative, but the significance of that finding depends on how many of the multiple CF-causing mutations were included in the test. The pediatric nurse needs knowledge of available genetic tests and their implications to assist patients and their families as they weigh choices regarding genetic testing. See Box 3–1.

**Recommendations for Genetic Testing.** Genetic tests are useful to diagnose disease, predict risk of future disease, inform reproductive decision making, and manage patient care. 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.

**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. Genetic testing uses a variety of methods and may analyze DNA, products of DNA, or other substances that indicate a genetic defect. DNA can be analyzed on a number of levels, from karyotyping an entire set of chromosomes to examining a specific gene for a mutation. Tests of DNA products (RNA or proteins) are sometimes done to measure gene function or expression. Some genetic tests measure metabolites that accumulate when individuals lack a specific enzyme due to a gene mutation.

It is especially important for the pediatric nurse to understand the difference between screening tests, which are used in populations to find individuals at risk for a disorder, and diagnostic tests, which are required to make a diagnosis. Newborn screening is carried out on most newborns in developed countries and provides a means to identify children who may have a genetic disease such as a metabolic or endocrine disease or hemoglobinopathy. Many of these disorders are exceedingly rare. In recent years, a laboratory technique called tandem mass spectrometry has allowed greatly expanded newborn screening with little increase in laboratory cost. Issues around expanded newborn screening are of considerable interest, in part due to issues of follow-up. Even the most specific of screening tests will result in false-positive results, which must be followed up with a diagnostic test. The cost of follow-up testing is significant both in terms of parental anxiety and financial burden (DeLuca, Zanni, Bonhomme, et al., 2013). See Chapter 7 for further description of newborn screening.

Diagnostic tests are performed to confirm a diagnosis in a symptomatic child or adult. Diagnostic tests may be ordered when a child is suspected of having a specific disorder based on clinical presentation or screening test results. Diagnostic testing is sometimes carried out prenatally to identify genetic disease such as a trisomy in a fetus.

**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, which are too small to be seen on a karyotype.

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**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 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).

**Table 3–3 Categories of Genetic Tests**

<table>
<thead>
<tr>
<th>Type of Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic testing</td>
<td>Used to establish a diagnosis of a genetic disorder in an individual who is symptomatic or has had a positive screening test.</td>
</tr>
<tr>
<td>Prenatal testing</td>
<td>Testing to identify a fetus with a genetic disease or condition. Some prenatal testing is offered routinely; other testing may be initiated due to family history or maternal factors.</td>
</tr>
<tr>
<td>Newborn screening</td>
<td>Testing of a newborn to identify the presence of a condition that requires immediate initiation of treatment to prevent death or disability.</td>
</tr>
<tr>
<td>Preimplantation testing</td>
<td>Following in vitro fertilization (IVF), testing to identify embryos with a particular genetic condition.</td>
</tr>
<tr>
<td>Carrier testing</td>
<td>Testing in an asymptomatic individual to identify carrier status for a genetic condition.</td>
</tr>
<tr>
<td>Presymptomatic and predictive testing</td>
<td>Offered usually to asymptomatic individuals to detect genetic conditions that occur later in life.</td>
</tr>
</tbody>
</table>

- **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).
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 3,000 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 2,000 different CFTR mutations have been identified (Cystic Fibrosis Mutation Database, 2011). Most of these mutations are exceedingly rare; the most common (named delta F508) is found in about two thirds of affected individuals (Castellani, Cuppens, Macek, et al., 2008). 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 patients 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 later in this chapter.

Tests of gene expression are available as well. 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.

Other genetic tests examine gene products or metabolites of gene products, rather than the makeup of the gene itself. One example is a biochemical test for PKU. PKU is caused by an alteration in the gene encoding the enzyme phenylalanine hydroxyase (PAH), which breaks down dietary phenylalanine. The PKU test actually measures phenylalanine levels, which are markedly elevated in individuals with PAH deficiency. Many of these biochemical tests have been in use for years.

Quality and Accuracy of Genetic Tests
Genetic nurses express concern that genetic tests are becoming available very quickly with little regulation of the companies offering them. The quality, accuracy, and reliability of genetic test results are not measured against any common standard. Of perhaps greater concern is the interpretation of genetic test results. Even if a test per se is accurate and reliable, companies are free to apply their own criteria to interpret the results. Growth in direct-to-consumer marketing of genetic tests has resulted in increasingly accessible and affordable testing without the benefit of oversight by a healthcare provider. In most cases, little or no education is provided for the individual undergoing testing, 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).

NURSING MANAGEMENT
By simply integrating genetic and genomic concepts into assessment, observation, and history gathering, the pediatric nurse can improve the standard of care delivered and have a positive impact on the child and family. The pediatric nurse

Clinical Tip
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 patient undergoing testing. The contrasting viewpoint points out that other information is also predictive (consider blood cholesterol and risk for cardiovascular disease) and stigmatizing (for example, 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 taking the exceptionalist view, providing protection against discrimination based on genetic information and penalties for violating genetic privacy (U.S. Department of Health and Human Services, 2008). These laws were implemented in response to public 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 due to 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, or GINA) was implemented in November 2009. As a federal law, GINA offers protection to Americans in all states.
does not need to be a genetic expert, but baseline knowledge and heightened awareness of genetic and genomic issues will support appropriate assessment and referral to genetic specialists as needed.

**Family Risk Assessment**

**Genetic Family History**

While gathering a family history, the nurse must look for genetic information that might indicate the need for referral to a genetic specialist. Examples that would indicate a family may benefit from a genetic referral include a family history of conditions known or suspected to be genetic, several family members with the same condition, intellectual disability or learning difficulties, dysmorphic features or congenital anomalies, neonatal or pediatric death of unknown cause, recurrent miscarriage, or established genetic carrier status.

**Pedigrees**

Pediatric nurses and all other health professionals should know how to collect a three-generation family history, record the history in a pedigree, and “think genetic.” 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 3–3 ●). Standard format and nomenclature for pedigrees, which includes multiple symbols (Figure 3–4 ●), have been adopted (Bennett, French, Resta, et al., 2008). 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 (see Clinical Tip for Steps in Drawing a Pedigree). 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, risk assessment, 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 quickly see what history and background information has been collected.

It is important to gather a three-generation family pedigree even if the nurse believes this is a first occasion of the condition within a family. A condition without any identifiable inheritance pattern on the pedigree may be due to a new mutation or variable expressivity. Throughout the process of gathering family history assessment data, the nurse must protect family confidentiality at all times. 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 the parents’ inability to remember conditions that have been surgically repaired and then forgotten. Parents may fail to report conditions thought not to be genetic or that have been attributed...
incorrectly to other causes. Also, parents may be reluctant to 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 that allows individuals to easily record and save their information, as well as print their family pedigree.

**Genetic Physical Assessment**

The pediatric nurse in any healthcare setting should also “think genetic” when performing physical assessment (see Chapter 5). An early finding by the nurse will provide the child and family with an opportunity for a genetic referral and more specialized health care.

**Major and Minor Anomalies**

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 patient 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 infants 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 is the cause of a variety of anomalies that can appear 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, Zschocke, & Potocki, 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 (Table 3–4). 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,
Principles of Inheritance

The Role of the Nurse in Genetic Testing

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 patients and families. Finally, as with all aspects of delivering genetic nursing care, privacy and confidentiality are paramount.

Clinical Tip

Steps in 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 3–4 ●).
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 3–4 ●).
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.


so that dysmorphic facial features are more easily identified (Figure 3–5 ●). By advocating for a genetic referral, the pediatric nurse can make a difference in the child’s state of health.

Clinical Tip
Genetic Testing Issues of 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 clearly understand why a genetic test is being done.

In general, four reasons have been suggested to consider genetic testing of minors. The first is if the testing offers an immediate medical benefit for the child in terms of disease prevention or early treatment. Newborn screening is an example of testing designed to promote the health of children, and consensus statements by several professional groups

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Table 3-4  Selected Dysmorphic Physical Features*

<table>
<thead>
<tr>
<th>Skull</th>
<th>Externities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymmetric head/face</td>
<td>An abnormally positioned feet</td>
</tr>
<tr>
<td>Brachycephaly (short, broad head shape) (See Figure 27–15.)</td>
<td>Arachnodactyly (long fingers or toes)</td>
</tr>
<tr>
<td>Brachycephaly (short fingers or toes)</td>
<td>Brachydactyly (short fingers or toes)</td>
</tr>
<tr>
<td>Craniosynostosis (premature closing of skull sutures)</td>
<td>Camptodactyly (permanent flexion of fingers or toes)</td>
</tr>
<tr>
<td>Flattened or prominent occiput</td>
<td>Clinodactyly (curved fingers or toes, most often the fifth finger)</td>
</tr>
<tr>
<td></td>
<td>Edema of the hands or feet</td>
</tr>
<tr>
<td></td>
<td>Extremely long/thin or short extremities</td>
</tr>
<tr>
<td></td>
<td>Fontanels too large or small</td>
</tr>
<tr>
<td></td>
<td>Frontal bossing (prominent central forehead)</td>
</tr>
<tr>
<td></td>
<td>Microcephaly or macrocephaly</td>
</tr>
<tr>
<td></td>
<td>Micrognathia (small jaw)</td>
</tr>
<tr>
<td></td>
<td>Prognathism (projection of jaw beyond that of the forehead)</td>
</tr>
<tr>
<td></td>
<td>Hypoplastic (very small) or absent nails</td>
</tr>
<tr>
<td></td>
<td>Hypotonia (diminished muscle tone)</td>
</tr>
<tr>
<td></td>
<td>Loose joints</td>
</tr>
<tr>
<td></td>
<td>Polydactyly (extra fingers and/or toes)</td>
</tr>
<tr>
<td></td>
<td>Rocker bottom feet</td>
</tr>
<tr>
<td></td>
<td>Single transverse palmar crease (See Figure 5–46.)</td>
</tr>
<tr>
<td></td>
<td>Syndactyly (webbing between fingers and toes)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ears</th>
<th>Hair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear tags or pits</td>
<td>Excessive body hair</td>
</tr>
<tr>
<td>Ears that are posteriorly rotated</td>
<td>Unusual hairline or hair distribution</td>
</tr>
<tr>
<td></td>
<td>Large section of white hair in otherwise pigmented hair</td>
</tr>
<tr>
<td></td>
<td>Sparse or brittle hair</td>
</tr>
<tr>
<td></td>
<td>Hypoplastic (very small) or absent nails</td>
</tr>
<tr>
<td></td>
<td>Hypotonia (diminished muscle tone)</td>
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<tr>
<td></td>
<td>Loose joints</td>
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<td></td>
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<tr>
<td></td>
<td>Syndactyly (webbing between fingers and toes)</td>
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</table>

<table>
<thead>
<tr>
<th>Eyes</th>
<th>Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue sclera</td>
<td>Axillary freckling (See Figure 27–16.)</td>
</tr>
<tr>
<td>Different colored eyes</td>
<td>Café au lait spots (See Figure 27–16.)</td>
</tr>
<tr>
<td>Down-slanting eyes</td>
<td>Excessive skin</td>
</tr>
<tr>
<td>Epicanthal folds inconsisitent with ethnicity (See Figure 5–14.)</td>
<td>Extremely loose or thin skin</td>
</tr>
<tr>
<td>Extreme hyperopia (farsightedness)</td>
<td>Hirsutism (excessive hair)</td>
</tr>
<tr>
<td></td>
<td>Hyperelastic skin</td>
</tr>
<tr>
<td></td>
<td>Leaf-shaped white markings</td>
</tr>
<tr>
<td></td>
<td>Syndactyly (webbing between fingers and toes)</td>
</tr>
<tr>
<td></td>
<td>Hirsutism (excessive hair)</td>
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<tr>
<td></td>
<td>Hyperelastic skin</td>
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<td></td>
<td>Leaf-shaped white markings</td>
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<td></td>
<td>Syndactyly (webbing between fingers and toes)</td>
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<table>
<thead>
<tr>
<th>Mouth</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleft lip with or without cleft palate (See Figure 25–3.)</td>
<td>Abdominal wall defect</td>
</tr>
<tr>
<td>Large or small tongue</td>
<td>Ambiguous genitalia</td>
</tr>
<tr>
<td>Misshapen, missing, or extra teeth</td>
<td>Cryptorchidism (undescended testicle)</td>
</tr>
<tr>
<td></td>
<td>Hernia (inguinal or umbilical)</td>
</tr>
<tr>
<td></td>
<td>Hypospadias</td>
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<tr>
<td></td>
<td>Hypogonadism</td>
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<tr>
<td></td>
<td>Obesity</td>
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<td></td>
<td>Scoliosis</td>
</tr>
<tr>
<td></td>
<td>Seizures</td>
</tr>
<tr>
<td></td>
<td>Short, webbed neck</td>
</tr>
<tr>
<td></td>
<td>Single umbilical artery</td>
</tr>
<tr>
<td></td>
<td>Small or widely spaced nipples</td>
</tr>
<tr>
<td></td>
<td>Multiple fractures</td>
</tr>
<tr>
<td></td>
<td>Unusual cry (catlike/mewing, hoarse, weak)</td>
</tr>
<tr>
<td></td>
<td>Unusually tall or short stature</td>
</tr>
<tr>
<td></td>
<td>Webbed neck</td>
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*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.
support mandatory offering of newborn screening for 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, Gargouri, Alberti, et al., 2011). Genetic counseling and informed consent are essential prior to predictive genetic testing in minors (Ross et al., 2013).

A second kind of situation occurs when an adolescent is facing a reproductive decision of his or her own. If the adolescent has a family history of a genetic condition, he or she may be interested in genetic testing such as carrier screening that offers no specific medical benefit to the adolescent other than family planning. Recall Sarah, the young woman in the opening scenario who wanted to be tested for Huntington disease. Might genetic testing affect her reproductive decisions?

A third situation occurs when a parent or child requests 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. In the genetics community, 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.

Finally, 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 genomic knowledge and increasing availability of genomic testing have blurred the issues around testing in minors. Consider, for example, carrier screening. It is generally agreed that when carrier status is identified on newborn screening, those results should be communicated to the family (Ross et al., 2013). While routine carrier testing when carrier status has no medical relevance during minority 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. Predispositional testing, which can be ordered direct-to-consumer (i.e., without benefit of professional guidance), 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 two to three 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 genomics medicine, but clear guidelines have yet to be established.

The pediatric nurse must be aware of these potential situations and know that decisions to perform genetic tests on children and adolescents are not made easily. Unless the potential benefits of testing outweigh the potential harms to the child, a genetic test is not justified and should be postponed until the child is capable of making an informed decision. Amidst a rapidly changing landscape of genomic testing, and recognizing the difficult issues and lack of consensus around genetic testing in children and minors, the genetics community is working to develop standardized practice recommendations to guide clinical decision making (Ross et al., 2013).

Communication with the child and family about genetic testing should include an assessment of the positive and negative outcomes of the test. Are there existing treatments for the condition being tested? What are the potential psychologic issues associated with a positive or negative test? Who will be affected by the test results? Will the test results be shared with extended
family members? The nurse has an important role in educating adolescents and parents about issues around genetic testing to ensure that they are making informed decisions. The nurse should also consider the decision-making ability of the child. There is little consensus regarding the age at which children may be able to take part in a decision-making process involving genetic testing, and it is imperative for the nurse to be an advocate for the child.

Ensuring Informed Consent for Genetic Testing The pediatric nurse is responsible for alerting children and their 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 patients to sign; rather, nurses must ensure patients 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.

Ensuring Confidentiality and Privacy for Genetic Testing Issues of confidentiality and privacy are of particular concern when genetic information is involved. Results of genetic tests can be far reaching beyond usual concerns about health information. Tests may reveal information about other family members who did not consent to testing and who may not want to know (or have other family members know) that information. Current legal protection of genetic information is limited to health insurance and employment, but other concerns remain. Can genetic information be released to the courts, military, schools, or adoption agencies? Would a child with a known gene alteration for Huntington disease be offered a college scholarship for the best law school? The technology that has made genetic testing possible has far outpaced the ability of health policy makers and legislators to put in place systems to protect genetic information. Nurses should not only be diligent about protecting patients’ genetic information, but should discuss with patients and families the potential implications when sensitive test results are shared, either intentionally or inadvertently. Such anticipatory guidance is a key nursing role in patient advocacy (Consensus Panel, 2009).

Psychosocial Issues Pediatric nurses must be prepared to assist children and families to manage anxiety around 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, problems may occur and the pediatric 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 disturbed 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 family members may unconsciously form lowered expectations for the child or adolescent. Nurses must use counseling interventions to assist patients to process, adjust to, and use genetic information (ANA/ISONG, 2007).

Planning and Implementation The pediatric nurse is responsible for comprehensively delivering the standard of care to children and families, while being aware of limitations of his or her own knowledge and expertise (Consensus Panel, 2009). Although nurses without specialized training and credentialing in genetics are not expected to assume the role of genetic professionals, they do have critical roles in providing genomic health care. Often, nurses have more direct patient interaction than other health professionals and maintain a particularly high level of trust with patients. Nurses therefore are well positioned to recognize a patient or family who may be at increased risk for a genetic condition. In general, nurses are expected to (a) integrate genetic and genomic concepts into a comprehensive nursing assessment including documenting that history in the form of a pedigree, (b) recognize significant genomic information in the family history, (c) apply knowledge of local or regional services to explain available genetic services to patients, and (d) facilitate a genetic referral when appropriate (Consensus Panel, 2009; Jacobs & Patch, 2013).

Genetic Referrals and Counseling After gathering assessment data that incorporate genetic concepts, the pediatric nurse is able to partner with children and their families by initiating a referral to genetic specialists if there are indicators for a genetic referral (see Clinical Tip). The nurse should provide the family with information about the advantages of a referral to a genetic specialist and the disadvantages of not following through with the referral. The nurse should inform the child and family that a genetic referral can provide information and answer questions they may have concerning genetic health.
Families should be encouraged to address all their concerns with the genetic specialist, who will be able to answer questions regarding genetic conditions, inheritance, availability of treatment, and economic, insurance, and future implications of genetic conditions. Initiating or facilitating the referral of a child with a suspected genetic problem to a geneticist, genetic clinical nurse specialist, or genetic clinic is an expected nursing responsibility in the same way as referrals to a dietitian or a social worker. When in doubt, the pediatric nurse should contact the advanced practice genetic clinical nurse, genetic counselor, or geneticist to discuss concerns.

**Family Preparation for Genetic Referrals and Genetic Counseling**

Not knowing what to expect from a genetic referral is common, and fear of the unknown may cause anxiety for both the child and family. To facilitate a genetic referral to genetic specialists, the pediatric nurse should educate the child and family so they know what to expect during and after a genetic evaluation.

Usually before the first genetic evaluation visit, the parents will be contacted to provide a detailed medical and family history and to make an appointment for genetic consultation. The parent should be prepared to give as exact a family history as possible so that a detailed three-generation pedigree can be constructed. The parents should be informed that a genetic consultation 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. Tests may be ordered. These may include chromosome analysis, DNA-based testing, radiographs, biopsy, biochemical tests, developmental testing, or linkage studies. After the exam and the completion of any applicable testing, the geneticist or genetic counselor will discuss the findings with the parents and/or child and make recommendations. The discussion will include the natural history of the condition, its pattern of inheritance, current preventive or treatment options, and risks to the child or family. The visit will include opportunities for questions and answers and assessment and evaluation of the family’s understanding. It is typical for information retention to be very low for a family facing a new genetic diagnosis. This makes it imperative for the nurse to reinforce genetic concepts at a later time when the individual or family is ready.

As the visit concludes, the child and parents can expect that appropriate referrals will be made, available services will be discussed, and a follow-up visit may be scheduled. A summary of the information is usually sent to the family. The child’s healthcare provider will receive a report if requested by the individual or parents.

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 nondirectional 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.

**Family Teaching**

The pediatric nurse must be aware of available genetic resources and participate in education about genetic disorders and health promotion and prevention. Informing children and their families of what to expect from a genetic referral and clarifying and reinforcing information obtained during a genetic referral or genetic test results are also important.

Cultural and religious beliefs and values of the individual and family must be assessed by the nurse prior to teaching. Genetic 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.

### 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
Helping families to understand these genetic concepts is fundamental to delivering competent genetic nursing care.

Psychosocial 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. See Chapter 28.

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.

Managing Care Through Advocacy The pediatric 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, 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

VISIONS 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.
1. All diseases and health conditions have both genetic and environmental influences.
2. Single-gene (Mendelian) diseases are typically rare and occur when specific genes are altered; environmental influences usually contribute minimally to the disease process.
3. Complex (multifactorial) diseases and health conditions are common and usually occur when multiple gene alterations collectively increase disease risk; environmental influences usually have significant impact, which can be negative or protective.
4. Understanding the molecular mechanisms by which gene alterations affect health provides new targets and strategies for preventing, diagnosing, and treating disease.
5. Genomic health care applies knowledge about an individual’s genetic and environmental risk factors to improve his or her health.

Learning Outcome 3.1: Explain the role of genetic and genomic concepts in health promotion, disease prevention, screening, diagnostics, selection of treatment, and monitoring of treatment effectiveness.

Learning Outcome 3.2: Elicit a family health history and construct a genetic pedigree.

Learning Outcome 3.3: Incorporate knowledge of genetic and genomic influences and risk factors into assessment, planning, and implementation of nursing care.

Learning Outcome 3.4: Integrate basic genetic and genomic concepts into child and family education.

Learning Outcome 3.5: Understand implications of genome science on the nursing role with particular attention to ethical, legal, and social issues.

Learning Outcome 3.6: Discuss the significance of recent advances in human genetics and genomics and their impact on healthcare delivery.
Clinical Reasoning in Action

Recall 16-year-old Sarah from the chapter opening scenario. While at the sports clinic for a routine physical, she questions the nurse about being tested for Huntington disease. Huntington disease (HD) is a progressive disorder of motor, cognitive, and psychiatric disturbances. Symptoms typically present between age 35 and 44 years, with a median survival time of 15 to 18 years after onset. HD is inherited in an autosomal dominant pattern. Sarah’s maternal grandfather died from HD. Sarah has been reading about HD and is interested in being tested. Her mother strongly objects; she does not want to know her own Huntington status.

Sarah’s mother, Diane, is of western European Caucasian descent. Sarah’s knowledge about her father is limited. She knows that he is a third-generation Filipino American but has no medical information on him or his extended family. Sarah’s grandmother on her mother’s side has three sisters and two brothers. The two brothers died of myocardial infarctions at the ages of 37 and 55 years, respectively. Sarah’s maternal grandfather had no brothers but had two sisters. Her maternal grandfather died at age 62 years of Huntington disease. The sisters are alive and well and have no medical problems.

Diane has two brothers and two sisters. She is the youngest of the siblings. Her oldest brother, Ken, was diagnosed 10 years ago with Huntington disease at age 41 years. Ken has two daughters ages 21 and 25 years. Sarah is very close to these cousins, and she knows that they have no medical problems beyond seasonal allergies and migraine headaches. Brian and his wife Sally adopted a son, Dave, with Down syndrome, and he is 19 years old. Sarah’s brother is age 12 years and does not have any medical problems.

1. What further data would you gather from Sarah before referring her to a genetic specialist?
2. What are the signs and symptoms of Huntington disease? The prognosis? Is it linked to any ethnic group?
3. Create a family pedigree for Sarah based on the family information she has provided. What does the pedigree reveal, and what nursing actions would you plan for Sarah?
4. What are the implications for Sarah’s family if her test is positive for HD? What if her result is negative?
5. Should Sarah be tested at this time? Give a rationale for your answer.

References


References


The 1000 Genomes Project Consortium. (2010). A map of human genome variation from population scale sequencing. *Nature*, 467(7319), 1061–1073. DOI: 10.1038/nature09534

