



# UNDERSTANDING GENETICS

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A NEW ENGLAND GUIDE FOR PATIENTS AND HEALTH PROFESSIONALS

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THE NEW ENGLAND PUBLIC HEALTH GENETICS EDUCATION COLLABORATIVE

The New England Genetics Guide for Patients and Health Professionals,  
produced as a partnership between the Genetic Alliance and  
the New England Public Health Genetics Education Collaborative

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## PREFACE

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Over the past few decades, advances in genetics and genomics have exceeded our greatest expectations and have revolutionized the way we think about health. While genetics has been traditionally associated with pregnancy, birth defects, and newborn screening, almost every disease is influenced in part by an individual's genetic make-up. Therefore, it is important to consider the impact of genetics for any condition throughout a patient's lifetime.

The purpose of this manual is to provide a genetics educational resource for patients and health professionals in the New England states and to increase awareness of specialty care in genetics. The manual opens with a basic introduction to genetic concepts followed by a description of the different types and applications of genetic tests. We also provide information about diagnosis of a genetic disease, family-history taking, newborn screening, and genetic counseling. We included helpful resources to assist in patient care, patient and professional education, and specialty genetics services in New England. At the end of each section, we provide a list of references to use if you desire additional information. In addition, we provide a series of consumer fact sheets to be copied and offered to patients. These take-home resources are critical to helping patients understand some of the basic concepts and applications of genetics.

The original manual was created by Genetic Alliance with funding from the District of Columbia Department of Health, through U.S. Department of Health and Human Services Health Resource and Services Administration, Grant #5 H91 MC 00228-03.

Genetic Alliance is an international coalition comprised of more than 600 advocacy, research, and healthcare organizations that represent more than 14 million people. With a 20-year history as a 501(c)(3) not-for-profit organization, Genetic Alliance is dedicated to improving the quality of life for everyone who is living with a genetic condition. Strategically situated at the crossroads of the genetics community, Genetic Alliance provides technical assistance to advocacy organizations, builds and sustains robust information systems to empower an active and dynamic network of stakeholders, and actively works for public policies that promote the translation of basic research into therapies and treatments. In particular, Genetic Alliance identifies solutions to emerging problems and works to reduce obstacles to rapid and effective translation of research into accessible technologies and services that improve human health.

With the increasing need for current knowledge about genetics, the New England Public Health Genetics Education Collaborative, made up of representatives from New England's six state public health departments, has committed to joint efforts and sharing resources in order that all in the region will have knowledge of genetics and its effects on health—toward the goal of improved health outcomes. A subcommittee of NERGG, Inc., the Collaborative supports the NERGG, Inc. mission to promote health of both children and adults by increasing the awareness of genetic concerns, the understanding of the role of genetics in healthcare, and the availability of appropriate services. Funding for this manual was provided by the U.S. Department of Health and Human Services, Health Resources and Services Administration, Grant U22MC03959-03-00 for Heritable Disorders to New England Regional Genetics Group (NERGG, Inc.).

The manual is available online at the NERGG, Inc. website, the Genetic Alliance website, and the individual state departments of public health websites in New England.





## CHAPTER 1 : GENETICS 101

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Understanding the underlying concepts of human genetics and the role of genes, behavior, and the environment will be important to appropriately collecting and applying genetic information and technologies during clinical care. This chapter provides some fundamental information about basic genetic concepts including cell structure, the molecular and biochemical basis of disease, major types of genetic disease, laws of inheritance, and the impact of genetic variation.

Almost every human trait and disease has a genetic component, whether inherited or by modifying the body's response to environmental factors such as toxins or behavioral factors such as exercise. Understanding the underlying concepts of human genetics and the interactive role of genes, behavior, and the environment will be important in improving disease diagnosis and treatment. This section presents a broad overview of concepts in basic genetics and the molecular and biochemical basis of disease.

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## 1.1 CELLS, GENOMES, DNA AND GENES

Cells are the fundamental working units of every living system. All the instructions needed to direct their activities are contained within a DNA (deoxyribonucleic acid) sequence. DNA from all organisms is made up of the same chemical units (base pairs) abbreviated as A, T, C, and G. The human genome (total composition of genetic material within a cell) is packaged into larger units known as chromosomes—physically separate molecules that range in length from about 50 million to 250 million base pairs. Human cells contain two sets of chromosomes, one set inherited from each parent. Each cell, except sperm and eggs, contains 23 pairs of chromosomes which consist of 22 autosomes (numbered 1 through 22) and one pair of sex chromosomes (XX or XY). Sperm and eggs contain half as much genetic material (in other words, only one copy of each chromosome).

Each chromosome contains many genes, the basic physical and functional units of heredity. Genes are specific sequences of bases that encode instructions on how to make proteins. The DNA sequence is the particular side-by-side arrangement of bases along the DNA strand (e.g., ATTCCGGA). Each gene has a unique DNA sequence. Genes comprise only about 29 percent of the human genome; the remainder consists of non-coding regions, whose functions may include providing chromosomal structural integrity and regulating where, when, and in what quantity proteins are made. The human genome is estimated to contain 20,000-25,000 genes.

Although each cell contains a full complement of DNA, cells use genes selectively. For example, the genes active in a liver cell differ from genes active in a brain cell since each cell performs different functions and therefore requires different proteins. Different genes can also be activated during development or in response to environmental stimuli such as an infection or stress.

## 1.2 MAJOR TYPES OF GENETIC DISEASE

Many, if not most, diseases have their roots in genes. Genes—through the proteins they encode—determine how efficiently foods and chemicals are metabolized, how effectively toxins are detoxified, and how vigorously infections are targeted. Genetic diseases can be categorized into three major groups: single-gene, chromosomal, and multifactorial.





Thousands of diseases are known to be caused by changes in the DNA sequence of single genes. A gene can be changed (mutated) in many ways resulting in an altered protein product that is unable to perform its function. The most common gene mutation involves a change or “misspelling” in a single base in the DNA. Other mutations include the loss (deletion) or gain (duplication or insertion) of a single or multiple bases. The altered protein product may still retain some function but at a reduced capacity. In other cases, the protein may be totally disabled by the mutation or gain an entirely new but damaging function. The outcome of a particular mutation depends not only on how it alters a protein’s function but also on how vital that particular protein is to survival.

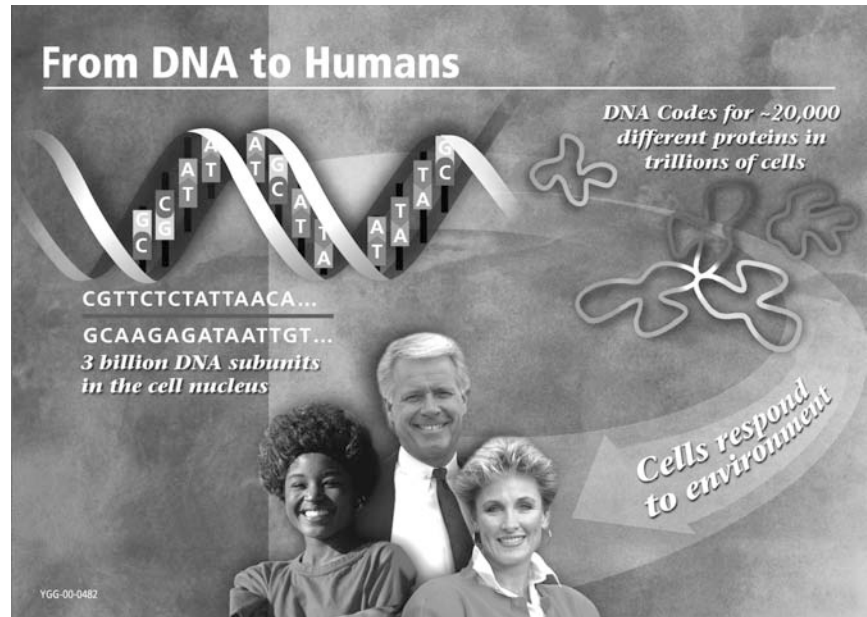


IMAGE CREDIT: U.S. Department of Energy Human Genome Program, <http://www.ornl.gov/hgmis>.

In addition, genetic diseases can be caused by larger changes in chromosomes. Chromosomal abnormalities may be either numerical or structural. The most common type of chromosomal abnormality is known as aneuploidy, an abnormal number of chromosomes due to an extra or missing chromosome. A normal karyotype (complete chromosome set) contains 46 chromosomes including an XX (female) or XY (male) sex chromosome pair. Structural chromosomal abnormalities include deletions, duplications, insertions, inversions, or translocations of a chromosome segment. [See Appendix H for more information about Chromosomal Abnormalities.]

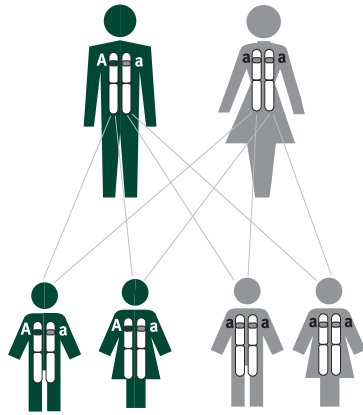
Multifactorial diseases are caused by a combination of genetic, behavioral and environmental factors. The underlying etiology of multifactorial diseases is complex and heterogeneous. Examples of these conditions include spina bifida, diabetes, and heart disease. While multifactorial diseases can recur in families, some mutations can be acquired throughout an individual’s lifetime such as in cancer. All genes work in the context of environment and behavior. Alterations in behavior or the environment, such as diet, exercise, exposure to toxic agents, or medications can all have influences on genetic traits.

### 1.3 LAWS OF INHERITANCE

The basic laws of inheritance are important in order to understand patterns of disease transmission. Single-gene diseases are usually inherited in one of several patterns depending on the location of the gene (for example, chromosomes 1-22 or X and Y) and whether one or two normal copies of the gene are needed for normal protein activity. There are five basic modes of inheritance for single-gene diseases: autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive, and mitochondrial.

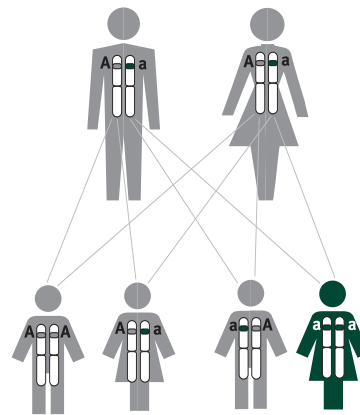
Genetic diseases caused by chromosomal abnormalities are generally not inherited, but usually occur as random events during the formation of reproductive cells. Below is a sample pedigree of each type of inheritance pattern and overview of family history patterns:

■ Affected      ■ Unaffected



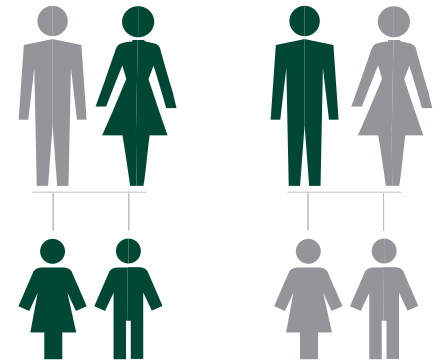
#### AUTOSOMAL DOMINANT

- Individuals carrying one mutated copy of a gene in each cell will be affected by the disease
- Each affected person usually has one affected parent
- Tends to occur in every generation of an affected family



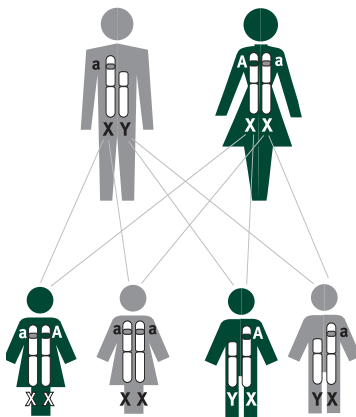
#### AUTOSOMAL RECESSIVE

- Affected individuals must carry two mutated copies of a gene
- Parents of affected individual are usually unaffected and each carry a single copy of the mutated gene (known as carriers)
- Not typically seen in every generation.



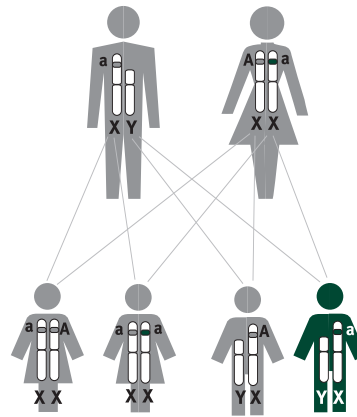
#### MITOCHONDRIAL

- Only females can pass on mitochondrial conditions to their children (maternal inheritance)
- Both males and females can be affected
- Can appear in every generation of a family



#### X-LINKED DOMINANT

- Females are more frequently affected than males
- Fathers cannot pass X-linked traits to their sons (no male-to-male transmission)



#### X-LINKED RECESSIVE

- Males are more frequently affected than females
- Families with an X-linked recessive disorder often have affected males, but rarely affected females, in each generation
- Both parents of an affected daughter must be carriers
- Only mother must be carrier of affected son (fathers cannot pass X-linked traits to their sons.)



## 1.4 GENETIC VARIATION

All individuals are 99.9 percent the same with respect to their DNA sequence. Differences in the sequence of DNA among individuals are called genetic variation. Genetic variation explains some of the differences among people, such as physical traits and also whether a person has a higher or lower risk for certain diseases. Genetic variation is referred to as mutations or polymorphisms. While mutations are generally associated with disease and relatively rare, polymorphisms are more frequent and their clinical significance is not as straightforward. Single nucleotide polymorphisms (SNPs) are DNA sequence variations that occur when a single nucleotide is altered. SNPs occur every 100 to 300 bases along the 3-billion-base human genome. A single individual may carry millions of SNPs.



While some genetic variation may cause or modify disease risk, others may result in no increased risk or a neutral presentation. For example, genetic variants in a single gene account for the different blood types A, B, AB and O. Understanding the clinical significance of genetic variation is a complicated process because of our limited knowledge of which genes are involved in a disease or condition, and the multiple gene-gene and gene-behavior-environment interactions likely to be involved in complex, chronic diseases. New technologies are enabling faster and more accurate detection of genetic variants in hundreds or thousands of genes in a single experiment.

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**National Library of Medicine, *Genetics Home Reference—Your Guide to Understanding Genetic Conditions.*** Available at <http://ghr.nlm.nih.gov/>

**Online Mendelian Inheritance in Man.** Available at <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>





## CHAPTER 2 : DIAGNOSIS OF A GENETIC DISEASE

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All diseases have a genetic component. However, the extent to which genes contribute to disease varies and much remains to be learned. Advances in understanding the genetic mechanisms behind these diseases enable the development of early diagnostic tests, new treatments, or interventions to prevent disease onset or minimize disease severity. This chapter provides information about the importance of clinical signs such as family history that may be suggestive of a genetic disease, the different uses of genetic testing, and the different types of genetic diseases.

All diseases have a genetic component. Mutations may be inherited or developed in response to environmental stresses such as viruses or toxins. The ultimate goal is to use this information to treat, cure, or if possible, prevent the development of disease.

## 2.1 HISTORY AND PHYSICAL EXAMINATION

The diagnosis of a genetic disease requires a comprehensive clinical examination composed of three major elements:

1. a physical examination
2. a detailed medical family history
3. clinical and laboratory testing if available.

While primary care providers may not always be able to make a definitive diagnosis of a genetic disease, their role is critical in collecting a detailed family history, considering the possibility of a genetic disease in the differential diagnosis, ordering testing as indicated and when available, appropriately referring patients to genetic specialists.

## 2.2 RED FLAGS FOR GENETIC DISEASE

There are several factors that raise the possibility of a genetic disease in a differential diagnosis. One major factor is the occurrence of a condition among family members that is disclosed when the family history is obtained (see Chapter 3 on Pedigree and Family History Taking). The occurrence of the same condition in more than one family member (particularly first-degree relatives), multiple miscarriages, stillbirths, and childhood deaths are all suggestive of a genetic disease. Additionally, family history of common adult conditions (heart disease, cancer, dementia) that occur in two or more relatives at relatively young ages may also suggest a genetic predisposition.

Other clinical symptoms that are suggestive of a genetic disease include developmental delay/mental retardation and congenital abnormalities. Dysmorphologies, often involving the heart and face, as well as growth problems are suggestive of a genetic disorder caused by an inherited mutation, a spontaneous mutation, a teratogen exposure, or unknown factors. While these clinical features may be caused by a number of factors, genetic conditions should also be considered as part of the differential diagnosis, particularly if the patient expresses several clinical features together that might be indicative of a syndrome (for example, mental retardation, distinct facies, and heart defect). Some physical features may appear unique or slightly different than the average such as wide-set or droopy eyes, flat face, short fingers, and tall stature. While these rare and seemingly mild features may not immediately be suggestive of a genetic disease to a primary care provider, an evaluation by a genetics specialist may be helpful in ruling in/out a genetic disease.



IMAGE CREDIT: U.S. Department of Energy Human Genome Program, <http://www.ornl.gov/hgmis>.



While many genetic conditions appear during childhood, a genetic condition should not entirely be ruled out in adolescents or adults. Often a genetic disease can remain undetected for several years until an event such as puberty or pregnancy triggers the onset of symptoms or the accumulation of toxic metabolites manifests in disease. In these cases, a detailed family history and physical examination should be performed and a referral made to a genetics specialist if indicated.

## 2.3 USES OF GENETIC TESTING

Genetic tests can be used for many different purposes some of which are listed in Table 2.1.

- **Newborn screening** is the most widespread use of genetic testing [See Chapter 4 for more information about newborn screening]. Almost every newborn in the U.S. is screened for several genetic diseases. Early detection of these diseases can lead to interventions to prevent the onset of symptoms or minimize disease severity.
- **Carrier testing** can be used to help couples to learn if they carry—and thus risk passing to their children—an allele for a recessive condition such as cystic fibrosis, sickle cell anemia, and Tay-Sachs disease. This type of testing is typically offered to individuals who have a family history of a genetic disorder and to people in ethnic groups with an increased risk of specific genetic conditions. If both parents are tested, the test can provide information about a couple's risk of having a child with a genetic condition.
- **Prenatal diagnostic testing** is used to detect changes in a fetus's genes or chromosomes. This type of testing is offered to couples with an increased risk of having a baby with a genetic or chromosomal disorder. A tissue sample for testing can be obtained through amniocentesis or chorionic villus sampling. [See Appendix E for more information.]
- Genetic tests may be used to confirm a **diagnosis** in a symptomatic individual or used to monitor **prognosis** of a disease or response to treatment.
- **Predictive or predispositional** genetic testing can identify individuals at risk of getting a disease prior to the onset of symptoms. These tests are particularly useful if an individual has a family history of a specific disease and an intervention is available to prevent the onset of disease or minimize disease severity. Predictive testing can identify mutations that increase a person's risk of developing disorders with a genetic basis, such as certain types of cancer.

Table 2.1  
Uses of Genetic Tests

- Newborn Screening
- Carrier Testing
- Prenatal Diagnosis
- Diagnostic/Prognostic
- Predictive/Predispositional

## 2.4 TYPES OF GENETIC TESTING

Several different methods are currently used in genetic testing laboratories. The type of test will depend on the type of abnormality that is being measured. In general, three major types of genetic testing are available: cytogenetic, biochemical, and molecular testing.

*2.4.1 Cytogenetic Testing.* Cytogenetics involves the examination of whole chromosomes for abnormalities. Chromosomes of a dividing human cell can be clearly analyzed under a microscope. White blood cells, specifically T lymphocytes, are the most readily accessible cells for cytogenetic analysis since they are easily collected from blood and are capable of rapid division in cell culture. Cells from other tissues such as bone marrow (for leukemia), amniotic fluid (prenatal diagnosis), and other tissue biopsies can also be cultured for cytogenetic analysis.



Following several days of cell culture, chromosomes are fixed, spread on microscope slides, and then stained. The staining methods for routine analysis allow each of the chromosomes to be individually identified. The distinct bands of each chromosome revealed by staining allow for analysis of chromosome structure.

**Table 2.2 Types of Protein Changes Resulting in Altered Function**

- No protein made
- Too much or too little protein made
- Misfolded protein made
- Altered active site or other critical region
- Incorrectly modified protein
- Incorrectly localized protein (build-up of protein)
- Incorrectly assembled protein

**2.4.2 Biochemical Testing.** The enormous numbers of biochemical reactions that routinely occur in cells require different types of proteins. Several classes of proteins exist to fulfill multiple functions, such as enzymes, transporters, structural proteins, regulatory proteins, receptors, and hormones. A mutation in any type of protein can result in disease if the mutation results in failure of the protein to correctly function (see Table 2.2 for types of protein alterations that may result in disease).

Clinical testing for a biochemical disease utilizes techniques that examine the protein instead of the gene. Tests can be developed to directly measure protein activity (enzymes), level of metabolites (indirect measurement of protein activity), and the size or quantity of protein (structural proteins). These tests require a tissue sample in which the protein is present, typically blood, urine, amniotic fluid, or cerebrospinal fluid. Because proteins are more unstable than DNA and can degrade quickly, the sample must be collected, stored properly, and shipped promptly according to the laboratory's specifications.

**2.4.3 Molecular Testing.** For small DNA mutations, direct DNA testing may be the most effective method, particularly if the function of the protein is not known and a biochemical test cannot be developed. A DNA test can be performed on any tissue sample and requires very small amounts of sample. Some genetic diseases can be caused by many different mutations, making molecular testing challenging. For example, more than 1,000 mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene can cause cystic fibrosis (CF). It would be impractical to sequence the entire CFTR gene to identify the causative mutation since the gene is quite large. However, since the majority of CF cases are caused by approximately 30 mutations, this smaller group of mutations is first tested before more comprehensive testing is performed.

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**Scriver CR, Beaudet AL, Sly WS, Valle D** (eds.). *The Molecular and Metabolic Basis of Inherited Disease*. New York: McGraw-Hill, 2001.

**Thompson MW, McInnes RR, Willard HE.** *Thompson & Thompson: Genetics in Medicine*, 5th Edition. Philadelphia: W.B. Saunders Company, 1991.







## CHAPTER 3 : PEDIGREE AND FAMILY HISTORY TAKING

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Health care professionals have known for a long time that common diseases—like heart disease, cancer, and diabetes—and even rare diseases—like hemophilia, cystic fibrosis, and sickle cell anemia—can run in families. If one generation of a family has high blood pressure, it is not unusual for the next generation to have similarly high blood pressure. Therefore, family history can be a powerful screening tool and has often been referred to as the best “genetic test.”

Both common diseases and rare diseases can run in families. Therefore, family history can be a powerful screening tool. Family history should be updated on each visit and patients should be made aware of its significance to their health.

### 3.1 IMPORTANCE OF FAMILY HISTORY

Family history holds important information about an individual's past and future life. Family history can be used as a diagnostic tool and help guide decisions about genetic testing for the patient and at-risk family members. If a family is affected by a disease, an accurate family history will be important to establish a pattern of transmission. In addition, a family history can even help to exclude genetic diseases, particularly for common diseases in which lifestyle and environment play strong roles. Lastly, a family history can identify potential health problems that an individual may be at increased risk for in the future. Early identification of increased risk can allow the individual and health professional to take steps to reduce risk by implementing lifestyle changes and increasing disease surveillance.



While many of the well-known genetic disorders are of childhood onset, many complex, adult-onset conditions can also run in families. For example, about 5 to 10 percent of all breast cancers are hereditary. These cancers may be caused by mutations in particular genes, such as BRCA1 or BRCA2. An individual may be at high risk of hereditary breast cancer and genetic testing should be considered if her family history includes more than one first-degree (mother, sister, or daughter) or second-degree relative (aunt, grandmother, or niece) with breast or ovarian cancer, particularly if the diagnosis of breast or ovarian cancer in those relatives was at a young age (50 or younger).

Another example of an adult-onset disease that can be inherited is Alzheimer's disease. Although most of Alzheimer's disease cases are sporadic, a small number are hereditary. Hereditary Alzheimer's disease is an extremely aggressive form of the disease and typically manifests before the age of 65. Three genes that cause early-onset Alzheimer's disease have been identified.

Notwithstanding the importance of family history to help define occurrence of a genetic disorder within a family, it should be noted that some genetic diseases are caused by spontaneous mutations, such as for single gene disorders like Duchenne muscular dystrophy and hemophilia A, as well as for most cases of Down syndrome, chromosomal deletion syndromes, and other chromosomal disorders. Therefore, a genetic disorder cannot be ruled out in the absence of a family history.



## 3.2 HOW TO TAKE A FAMILY MEDICAL HISTORY

A basic family history should include three generations. To begin taking a family history, start by asking the patient about his/her health history and then ask about siblings and parents.

Questions should include:

1. General information such as names and birthdates
2. Family's origin or racial/ethnic background
3. Health status
4. Age at death and cause of death of each family member
5. Pregnancy outcomes of the patient and genetically-related relatives

It may be easier to list all the members of the nuclear family first and then go back and ask about the health status of each one. After you have taken the family history of the patient's closest relatives, go back one generation at a time and ask about aunts, uncles, grandparents, and first cousins.

## 3.3 PEDIGREES

One way to record a family history is by drawing a family tree called a "pedigree." A pedigree represents family members and relationships using standardized symbols (see below). As patients relate information to you about their family history, a pedigree can be drawn much quicker than recording the information in writing and allows patterns of disease to emerge as the pedigree is drawn. Since the family history is continually changing, the pedigree can be easily updated on future visits. Patients should be encouraged to record information and update their family history regularly.

### PEDIGREE SYMBOLS



**Male**



**Female**



**Adopted**



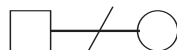
**Deceased**  
Diagonal line used to show that a person has died.



**Pregnancy loss**  
Include the number of weeks if known.



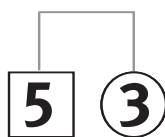
**Still birth**  
Include the number of weeks if known.



**Divorced/not together**  
Diagonal line used to show parents are divorced or not together.

### WHAT IF THERE IS LIMITED INFORMATION ABOUT FAMILY MEMBERS?

1. If you do not know names and ages of family members, but do know the number of boys and the number of girls, you can do this:



**Example:** This shows that there are 5 boys and 3 girls.

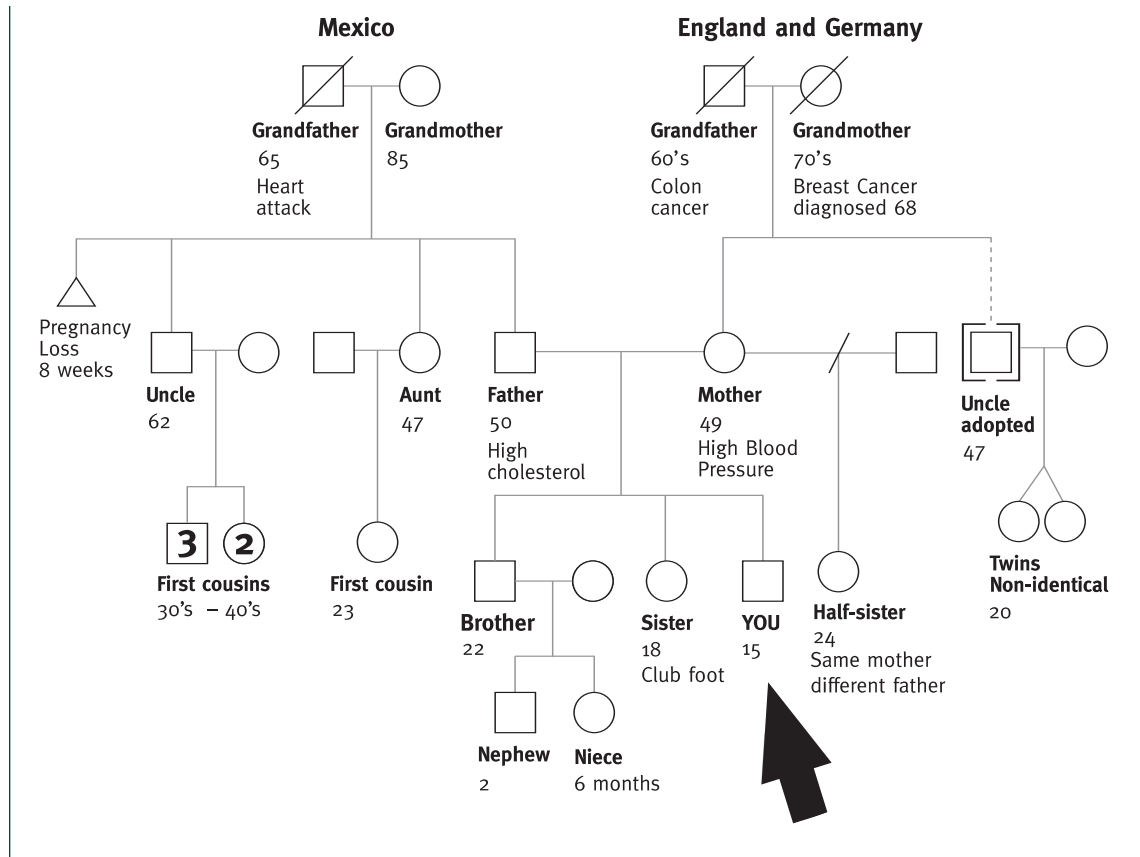
2. If you do not know the number of boys and the number of girls, use diamond with number inside it (if total is known) or "?".



**Example:** This shows that there are 8 children.

The sample pedigree below contains information such as age or date of birth (and, for all deceased family members, age at death and cause of death), major medical problems with age of onset, birth defects, learning problems and mental retardation, and vision loss/hearing loss at a young age. For family members with known medical problems, ask whether they smoke, what their diet and exercise habits are if known, and if they are overweight.

### SAMPLE PEDIGREE



### SELECTED REFERENCES

American Society for Human Genetics. (2004). *Your Family History*.

<http://www.ashg.org/genetics/ashgeduc/007.shtml>

Bennett RL. *The Practical Guide to the Genetic Family History*. New York: Wiley-Liss, Inc. 1999.

Centers for Disease Control and Prevention. Office of Genomics and Disease Prevention. Using Family History to Promote Health. <http://www.cdc.gov/genomics/public/famhistMain.htm>

Genetic Alliance. (2004). *Taking a Family History*.

[http://www.geneticalliance.org/ws\\_display.asp?filter=fhh](http://www.geneticalliance.org/ws_display.asp?filter=fhh)

March of Dimes—Genetics and Your Practice <http://www.marchofdimes.com/gyponline/index.bm2>

My Family Health Portrait <http://familyhistory.genome.gov>

U.S. Department of Health and Human Services. (2004) U.S. Surgeon General's Family History Initiative. <http://www.hhs.gov/familyhistory/>





## CHAPTER 4 : NEWBORN SCREENING

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Almost every child born in the United States undergoes state-mandated newborn screening. For each state, a small blood sample (“heel stick”) is collected from each newborn within 48 hours of birth and sent to a laboratory for testing for a panel of medical conditions. Newborn screening programs screen for an ever-increasing number of conditions, including phenylketonuria (PKU), sickle cell disease, and hypothyroidism. Every year, about 3,000 newborns test positive for one of these conditions. In the event that a newborn screens positive, early medical intervention can reduce the severity of the condition and possibly even prevent symptoms from occurring. This chapter provides an overview of newborn screening programs in New England.

In the U.S., about 3,000 newborns test positive each year for a medical condition detected via newborn screening. Currently, the conditions screened in each state vary; efforts are underway to develop a national newborn screening program. This chapter provides an overview of the newborn screening programs and procedures in the six New England states.

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#### 4.1 THE IMPORTANCE OF NEWBORN SCREENING TESTS

By law, all newborns are tested for several rare but serious medical conditions. Babies with these conditions may look healthy at birth. If not treated, these conditions can cause health problems such as mental retardation, slow growth, and even death. With treatment, these problems may be prevented.

#### 4.2 TESTING PROCEDURE AND FOLLOW-UP

A nurse or other medical professional will take a few drops of blood from the baby's heel. This blood sample is sent to a newborn screening laboratory. The blood should be drawn after the baby is 24 hours old, but before the baby leaves the hospital.

The baby's doctor will contact the parent(s) if the results are positive for one of the screened conditions. Follow-up testing may be required.

#### 4.3 RETESTING

Sometimes, a baby needs to be tested again. This does not necessarily mean that a medical condition is present. Retesting may need to be done if:

- The blood sample was taken before the baby was 24 hours old
- There was a problem with the way the blood sample was taken
- The first test showed a possible medical condition

The baby's doctor or the state's newborn screening program will contact the parent(s) if retesting is necessary. It is important to get this testing done right away.



## 4.4 TESTS PERFORMED

The tests that are done vary from state to state. In general, the conditions that are tested for fall into one of the following groups:

- Metabolic conditions, which affect how the body processes food
- Endocrine conditions, which affect the levels of important hormones
- Hemoglobin conditions, which affect the blood and cause anemia, infections, and other health problems
- A pulmonary condition, which affects growth and the lungs

For information on the diseases tested for in a particular state, contact that state's newborn screening program. Testing for more conditions may be available at other laboratories for a fee.

## 4.5 TREATMENT

The treatment for each condition is different and may include a special diet, hormones, and/or medications. It is very important to start the treatment of affected infants as soon as possible.

## 4.6 NEWBORN SCREENING PROGRAMS

### Connecticut

State of Connecticut,  
Department of Public Health  
410 Capitol Avenue, MS #11 MAT  
P.O. Box 340308  
Hartford, CT 06134-0308  
(860) 509-8081  
[www.dph.state.ct.us/bch/nbs/nbs.htm](http://www.dph.state.ct.us/bch/nbs/nbs.htm)

### Maine

Maine Newborn Screening Program  
11 Statehouse Station  
286 Water Street  
Augusta, ME 04333  
(207) 287-5357  
[www.maine.gov/dhhs/boh/cshn/cshn](http://www.maine.gov/dhhs/boh/cshn/cshn)

### Massachusetts

New England Newborn Screening Program  
University of Massachusetts Medical School  
305 South Street  
Jamaica Plain, MA 02130-3515  
(617) 983-6300  
[www.umassmed.edu/nbs](http://www.umassmed.edu/nbs)

### New Hampshire

Maternal & Child Health Section  
29 Hazen Drive  
Concord, NH 03301  
(603) 271-4225  
[www.dhhs.state.nh.us/dhhs/mch.htm](http://www.dhhs.state.nh.us/dhhs/mch.htm)

### Rhode Island

Rhode Island Department of Health  
3 Capitol Hill, Room 302  
Providence, RI 02908-5097  
(800) 942-7434  
[www.health.ri.gov/genetics/newborn.php](http://www.health.ri.gov/genetics/newborn.php)

### Vermont

Division of Health Improvement,  
Children with Special Health Needs  
108 Cherry Street, P.O. Box 70  
Burlington, VT 05402  
(802) 951-5180

## 4.7 NEWBORN HEARING SCREENING

Hearing loss is a common condition that is present in as many as 1 in every 300 babies. When hearing loss goes undetected, even for just a year or two, serious delays in speech and language can result. When hearing loss is discovered in infancy, treatment can be started early enough to prevent or lessen these delays.

Each of the six New England states has a program to provide hearing screening to all newborns. Five states (all except Vermont) have a law mandating this screening. Babies are usually screened in the first few days of life, before they are discharged from the hospital. The testing, which is quick and painless, is done by one of two methods: otoacoustic emissions (OAE) or automatic brainstem response (ABR). Both of these methods involve placing tiny earplugs in the ear canals or earphones on the ears and using a computer to measure the baby's reactions to sound. Babies who do not pass the first screening are retested and may be referred to an audiologist (hearing specialist).



## 4.8 NEWBORN HEARING SCREENING PROGRAMS

### Connecticut

State of Connecticut,  
Department of Public Health  
410 Capitol Avenue, MS #11 MAT  
P.O. Box 340308  
Hartford, CT 06134-0308  
(860) 509-8081  
[www.dph.state.ct.us/bch/ehdi/b\\_unhs.htm](http://www.dph.state.ct.us/bch/ehdi/b_unhs.htm)

### Maine

Maine Newborn Hearing Program  
11 Statehouse Station  
286 Water Street  
Augusta, ME 04333  
(207) 287-5357  
[www.maine.gov/dhhs/bob/cshn/cshn](http://www.maine.gov/dhhs/bob/cshn/cshn)

### Massachusetts

Massachusetts Universal Newborn Hearing  
Screening Program  
Bureau of Family and Community Health  
250 Washington Street  
Boston, MA 02108  
(800) 882-1435  
[www.mass.gov/dph/fch/unhspl/index.htm](http://www.mass.gov/dph/fch/unhspl/index.htm)

### New Hampshire

Early Hearing Detection and Intervention  
Program (EHDI)  
Maternal & Child Health Section  
29 Hazen Drive  
Concord, NH 03301  
(603) 271-1037  
[www.dhhs.state.nh.us/dhhs/mch.htm](http://www.dhhs.state.nh.us/dhhs/mch.htm)





**Rhode Island**

Rhode Island Hearing Assessment Program  
Women and Infants Hospital  
Dudley Street  
Providence, RI 02905  
(401) 274-1122 x1844  
[www.health.state.ri.us/family/hearing/universal.php](http://www.health.state.ri.us/family/hearing/universal.php)

**Vermont**

Vermont Universal Newborn Hearing  
Screening Program  
108 Cherry Street, P.O. Box 70  
Burlington, VT 05402  
(800) 660-4427 x1330  
[www.healthvermont.gov/family/hearing/newborn.aspx](http://www.healthvermont.gov/family/hearing/newborn.aspx)

**SELECTED REFERENCES****Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children**

[www.mchb.hrsa.gov/programs/genetics/committee/](http://www.mchb.hrsa.gov/programs/genetics/committee/)

**American Academy of Pediatrics: Metabolic/Genetic Screening**

[www.medicalhomeinfo.org/screening/newborn.html](http://www.medicalhomeinfo.org/screening/newborn.html)

**Center for Disease Control's Early Hearing Detection and Intervention Program**

[www.cdc.gov/ncbddd/ehdi/](http://www.cdc.gov/ncbddd/ehdi/)

**National Newborn Screening and Genetics Resource Center**

<http://genes-r-us.uthscsa.edu/>







## CHAPTER 5 : GENETIC COUNSELING

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As members of a health care team, genetic counselors provide information and support to families affected by or at risk of a genetic disorder. They serve as a central resource of information about genetic disorders for other health care professionals, patients, and the general public. This chapter provides an overview of the role of genetic counselors, and their approach to educating patients and identifying individuals/families at risk of a genetic disorder. In addition, some useful patient resources are provided.

Genetic counselors play an important role in providing expert genetic services. They are trained to present often complex and difficult-to-comprehend information to families and patients about genetic risks, testing, and diagnosis. They also discuss available options, and provide counseling services and referrals to educational and support services.

## 5.1 ROLE OF GENETIC COUNSELING

Genetic counselors work as part of a health care team, providing information and support to families affected by or at risk of a genetic disorder. They help to identify families at possible risk of a genetic disorder, gather and analyze family history and inheritance patterns, calculate risks of recurrence and provide information about genetic testing and related procedures. In particular, genetic counselors can help families to understand the significance of genetic disorders in the context of cultural, personal, and familial situations. Genetic counselors also provide supportive counseling services, serve as patient advocates, and refer individuals and families to other health professionals and community or state support services. They serve as a central resource of information about genetic disorders for other health care professionals, patients, and the general public.

The most common indications for genetic counseling include advanced maternal age, family history of a genetic condition, and suspected diagnosis of a genetic condition. **For more information about genetic counseling or to find a genetic counselor in your area, please see the National Society of Genetic Counselors' website at <http://www.nsgc.org>.**

## 5.2 PROCESS OF GENETIC COUNSELING

In general, a genetic counseling session aims to:

- Increase the family's understanding about a genetic disease, discuss options regarding disease management, and the risk/benefits of possible testing.
- Identify with the individual and family the psychosocial tools required to adjust to potential outcomes.
- Reduce the family's anxiety.

It is not unusual for multiple genetic counseling sessions to occur and, at a minimum, to include a pre-testing and post-testing session. During the initial genetic counseling visit, the genetic counselor will determine why the patient/family is seeking genetic counseling, identify what information they wish to obtain from the session, collect and record a family history, and assess and record the psychosocial history of the patient.

Among the topics discussed during a pre-test session are the clinical presentation of the condition(s) the patient may be at risk for, the pattern of genetic inheritance of the condition, risk of recurrence, available testing procedures and test limitations, reproductive options, and follow-up procedures if needed. General questions relating to suggested treatment or therapy are also addressed. Referrals may be made to specialists regarding specific issues which fall outside the scope of genetic counseling practice.





If the patient decides to have genetic testing performed, the genetic counselor often acts as the point person to communicate the results. However, the post-test session involves more than the provision of medical information and often focuses on helping families cope with the emotional, psychological, medical, social and economic consequences of the test results. In particular, psychological issues such as denial, anxiety, anger, grief, guilt, or blame are addressed and when necessary, referrals for in-depth counseling are offered. Information about community resources and support groups are provided to the patient/family.

If the genetic test is positive, testing should be considered in additional relatives of this individual. Genetic counseling referrals for other family members for risk assessment are then discussed. It may be necessary to refer relatives to other genetic counselors due to geographical and other constraints.

At the conclusion of the genetic counseling sessions, the patient should be offered a written summary of the major topics discussed. The summary is often provided in the form of a letter which serves as a permanent record of the information discussed, as well as additional information that became available after the final counseling session. The patient may choose to share the letter with other family members.

### 5.3 PATIENT EDUCATION

Patients rely most upon their primary health care providers for information related to their condition. In general, though, your patients will require information you may not have. Before providing patients with any educational materials, please be sure to check that the information is produced by a credible source and is current.

Books and pamphlets are most widely distributed and appreciated by patients, even by patients who are web-savvy. Patient advocacy groups generally provide the best and most up-to-date information. The organizations listed below are excellent sources of information about genetic diseases that can be helpful to patients:

#### **Genetic Alliance**

4301 Connecticut Ave., NW

Suite 404

Washington, DC 20008

Ph: (202) 966-5557

Fax: (202) 966-8553

URL: <http://www.geneticalliance.org>

E-Mail: [info@geneticalliance.org](mailto:info@geneticalliance.org)

**Genetic and Rare Diseases Information Center (GARD)**

P.O. Box 8126

Gaithersburg, MD 20898-8126

Ph: (888) 205-2311

TTY: (888) 205-3223

Fax: (240) 632-9164

URL: <http://www.genome.gov/Health/GARD>

E-mail: GARDinfo@nih.gov

**National Organization of Rare Diseases (NORD)**

55 Kenosia Avenue

PO Box 1968

Danbury, CT 06813

Ph: (203) 744-0100

TTY: (203) 797-9590

Fax: (203) 798-2291

URL: <http://www.rarediseases.org/>

E-mail: orphan@rarediseases.org

**SELECTED REFERENCES****Genetic Alliance–Disease InfoSearch** [http://www.geneticalliance.org/ws\\_display.asp?filter=diseases](http://www.geneticalliance.org/ws_display.asp?filter=diseases)

Provides accurate and reliable information developed by the advocacy organizations which form the Genetic Alliance. Users can search for information about advocacy support groups related to specific genetic conditions, the clinical features of a wide number of genetic conditions, and updates on management, treatment and other related topics.

**International Society of Nurses in Genetics** <http://www.ISONG.org>**March of Dimes** [www.marchofdimes.com](http://www.marchofdimes.com) (Spanish <http://www.nacersano.org/>)

Provides information about improving the health of babies by preventing birth defects, premature birth, and infant mortality.

**MedlinePlus** <http://www.nlm.nih.gov/medlineplus/>

MedlinePlus has extensive information from the National Institutes of Health and other trusted sources on over 700 diseases and conditions. There are also lists of hospitals and physicians, a medical encyclopedia and a medical dictionary, health information in Spanish, extensive information on prescription and nonprescription drugs, health information from the media, and links to ongoing clinical trials.

**National Human Genome Research Institute–Health** <http://genome.gov/Health/>

The site provides useful information about basic genetics concepts, genetic conditions, current research, and valuable tools to help make genetics an important tool in determining health.

**National Society of Genetic Counselors (NSGC)** <http://www.nsgc.org>



## CHAPTER 6 : INDICATIONS FOR A GENETIC REFERRAL

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Referrals to genetic specialists should be considered if a physician suspects a patient is at risk of or is affected with a genetic disorder. Genetic specialists can help identify the appropriate tests to order (genetic or additional laboratory tests), consider the family history, and provide information about the treatment and long-term outcomes for patients diagnosed with a genetic disorder, including recommendations to other medical specialists. This chapter provides a brief overview of points to consider when deciding if a referral to a genetic specialist is appropriate.

A referral to or consultation with a genetic specialist may be indicated for several reasons. In general, a consultation with a genetic specialist should be considered if a hereditary condition is suspected. Symptoms that may suggest a genetic disorder are listed in Chapter 3 (“Red flags for genetic disease”). For conditions such as cancer and diabetes, specific clinical guidelines are available.

## 6.1 WHEN TO REFER TO A GENETIC SPECIALIST

Patients meeting any of the following criteria should be considered for referral to a genetic specialist.

### *6.1.1 Family History*

- One or more members with mental retardation, an inherited disorder or a birth defect
- One or more members with early deaths due to known or unknown medical conditions
- One or more members with adult onset health conditions such as cardiovascular disease, dementia and cancer, particularly if onset is at an early age
- Couples who would like testing or more information about genetic conditions that occur with higher frequency in their ethnic group

### *6.1.2 Developmental Delay/Growth*

- Those who have or are concerned that their child has developmental delays that may be due to an inherited disorder or birth defect
- Parents whose infant has a genetic disease diagnosed by routine newborn screening

### *6.1.3 Reproductive Issues*

- Women who are or are planning to be pregnant after age 35
- Women who have experienced multiple pregnancy losses, including babies who died in infancy
- People concerned that their jobs, lifestyles or medical history may pose a risk to outcome of pregnancy. Common causes of concern include exposure to radiation, medications, illegal drugs, chemicals or infections
- Couples who are first cousins or other close blood relatives
- Pregnant women whose ultrasound examinations or blood testing indicates that their pregnancy may be at increased risk for certain complications or birth defects







A genetic specialist can provide assistance through a variety of ways—a formal or informal consultation, a genetic counseling session, or a genetic evaluation. A genetic specialist can provide a more accurate assessment of the risk or confirm the diagnosis of a genetic disease. A diagnosis may be made primarily through genetic testing, or a combination of testing, clinical examination, and family history. Genetic specialists are able to provide management options or referrals to specialists as needed; provide advice to primary care practitioners about a genetic condition, prognosis, treatment and long-term outcome; and recommend educational materials to patients and families.

The primary genetic specialists to be considered for referral are clinical geneticists and genetic counselors. While these specialists can play a major role in the diagnosis and education of family members with a genetic disorder, other medical specialists may be required for

appropriate treatment or intervention such as surgeons, nutritionists, social workers, psychologists, and occupational therapists. The requirements for a referral will vary from system to system. In general, though, a genetic referral requires the following information:

- Patient information
- Name and address of the referrer
- Reason for the referral
- Information about the suspected diagnosis, if known
- Family history

## SELECTED REFERENCES

**Cancer Genetics Service Directory** [http://www.cancer.gov/search/genetics\\_services/](http://www.cancer.gov/search/genetics_services/)

**March of Dimes—Genetics and Your Practice** <http://www.marchofdimes.com/gyponline/index.bm2>

**National Society of Genetic Counselors** <http://www.nsgc.org/resourcelink.cfm>





## CHAPTER 7 : PSYCHOLOGICAL & SOCIAL IMPLICATIONS

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Genetic disorders impact not only the physical health, but also the psychological and social well-being of patients and their families. Understanding the unique aspects of genetic information and anticipating reactions to genetic tests and diagnoses can help guide a course of action to minimize distress and maximize benefit for both the patient and family. Referrals to specialists or support groups can also help address the psychological well-being of the patient and family.

An increased genetic risk or a genetic diagnosis can substantially impact medical management as well as the psychological and social well-being of the patient and family. The personal and permanent nature of genetic information raises a range of emotions including guilt, fear, and helplessness. Specialists such as genetic counselors, social workers, and psychologists, as well as support groups, can be extremely helpful to patients and families as they deal with these difficult issues.

## 7.1 GENETIC INFORMATION VS. OTHER MEDICAL INFORMATION

Genetic information, like other medical information:

- Has the potential to help or harm patients and must be considered in making patient care decisions.
- Is complex, demanding thoughtful, critical communication of risks and uncertainties.
- Will arise in your practice. It is helpful to think through how you will respond in the face of inevitable questions, some of them involving difficult judgments.

In addition, genetic information, unlike much of medicine:

- Provides information about family members and relatives. Disclosure of genetic information can often be helpful to family members.
- Can lead to breaches of confidentiality that must be considered and addressed proactively.

## 7.2 A LIFETIME OF AFFECTED RELATIONSHIPS

Genetic disorders have powerful effects on families. Like many chronic conditions, they may require continual attention and lack cures or treatments. They have implications for the health of relatives, so a genetic diagnosis for one family member may mean other blood relatives are also at risk, even if they currently show no symptoms. In addition to the medical implications, genetic disorders present emotional challenges and special reproductive implications. Families may be concerned about the risk that additional offspring will inherit the condition, prenatal and newborn testing decisions, and difficult treatment options.



### 7.3 IMPACT OF A GENETIC DIAGNOSIS

The psychosocial effect of a genetic disorder varies by the nature of the condition and the relationship of a person to the affected individual. Every family is different and it is difficult to predict how people will react to a genetic diagnosis. It's helpful to think in advance about some of the possible reactions, though, so you can react quickly and minimize distress.

**7.3.1 Patients.** A genetic diagnosis generally provides great benefit to patients. It helps patients understand their disorder, especially when the condition is rare and the patient has struggled to find a diagnosis. Oftentimes, patients spend years living with a condition without knowing its name or cause. Diagnoses usually lead to improved treatment options and access to support services. They can also help other family members make decisions about their own lives.

A genetic diagnosis may lead to negative reactions, too. The science of genetics can be confusing, and patients are often frustrated until they understand the nature of their condition. Patients identified with a mutation may consider themselves at fault or “broken” or interpret their diagnoses as leading to something they cannot fight. A genetic diagnosis can lead to fears about insurance and employment discrimination.

The reaction to a diagnosis varies from individual to individual and is affected by many factors including gender, education, and religious and cultural beliefs. By being aware of these differences and understanding your patients' backgrounds, you will be able to communicate with your patients effectively.

**7.3.2 Parents.** Understandably, the diagnosis of a genetic condition may put stress on a relationship. For adult-onset diseases, unaffected spouses may view their partners differently, and the diagnosis can lead to a breakdown in communication. Couples with an affected child often face difficult family planning decisions because future children may be at higher risk. Depending on the condition, parents may also be faced with hard choices regarding prenatal testing and termination of pregnancy. The magnitude of these decisions and their outcomes has an impact on the individuals involved and on their relationship.

**7.3.3 Family.** Given the shared nature of genetic information, it is important to consider the family unit. Unaffected family members should not be forgotten in the case of a genetic disorder. When one family member is diagnosed with a mutation, family members who do not have the mutation often feel guilt that loved ones are affected when they are not. Siblings of children with special needs sometimes feel neglected because parents need to focus more time and effort on their siblings. Including unaffected family members in the planning of care for individuals with special needs can help them come to grips with their own emotional issues. Adults who are diagnosed with a genetic condition and are considering having a child will need to consider the risk of having an affected child as well as their ability to care for the child.

In cases in which a genetic test is predictive, other family members may misinterpret the results as a diagnosis rather than an indicator of risk for a condition. It is important to keep in mind that genetic test results are often complex and may be difficult for patients and their families to understand. In some cases, a genetic test may reveal the risk status of other family members who may not wish to know this information, potentially encroaching upon their autonomy or privacy.

The financial burden of a chronic genetic condition can also lead to stress among family members. A family already struggling financially may be intimidated by the costs associated with caring for a child with special needs. Referrals to appropriate support services are crucial to help ease the stress caused by a genetic diagnosis.

In general, support or advocacy groups and community resources can provide ongoing support to patients and their families with genetic conditions. Support groups provide a forum for sharing experiences about caring for a family member affected with a genetic condition, coping with a new diagnosis, obtaining healthcare or other services, and healing. Members of support groups know first-hand what it means to be faced with a diagnosis and to need accurate, up-to-date information. Staying connected with their community helps individuals fight the feelings of isolation that often surround families living with a genetic condition.

**7.3.4 Communities.** Genetic testing can also affect the community at large. Genetics has been used in the past to stigmatize and discriminate along ethnic or racial lines, and underserved or underrepresented communities often view genetic research and services with distrust. They may feel that the results of a genetic test or newborn screening will be used to segregate their communities. These fears often work in combination with other difficulties with the medical establishment, including communication and cultural barriers.

Members of the deaf community, for example, may oppose hearing tests for fear that deafness will be considered a disability rather than a lifestyle. In general, it is a good idea to understand the communities in which your patients belong so you can present information and options in ways that promote trust.

## 7.4 COPING MECHANISMS



When a newborn is diagnosed with a genetic condition, parents are overcome with concern for their child. Some common reactions include fear, confusion, and grief that their child is not “normal,” guilt that they did something to cause the condition, and anger at the lack of a solution, or the belief that the other parent is to blame. The fact that a medical cure or treatment may not exist often comes as a great surprise to parents. This further adds to the parents’ concerns about their ability to care for the child. How care providers react makes a big impact on how parents cope with negative feelings and can help them focus on the challenges and blessings of the newborn child.



The following suggestions can help parents cope with the birth of a child with an inherited condition:

- For routine visits, focus on the child's well-being and not solely on the child's genetic condition. Talk about the newborn's personality, feeding patterns, and other personal traits and always remember that the newborn is an infant first and an infant with special needs second.
- Provide realistic expectations for the future and models for coping. The parents are likely to be asked many well-intentioned questions by relatives and friends, and parents will be better able to respond if they've asked the questions themselves already.
- Explain the genetics of the condition in an understandable manner and consider referring the parents to a genetics specialist, either a clinical geneticist, a genetic counselor, or genetics nurse.
- Emphasize that you are aware of the difficulty of the situation and acknowledge that each parent has his or her own way of coping with the stress of caring for an infant with medical needs. It may be helpful for families to share their feelings with others, and referrals to a social worker, psychologist, or support group may facilitate these discussions.
- Identify resources such as support groups that focus on the condition in question. Support groups can help families overcome feelings of isolation often associated with a rare genetic condition, provide first-hand experience about caring for an infant with the condition, provide information about expectations for the affected infant, and suggest coping mechanisms for both parents and siblings to adjust to new challenges.

## SELECTED REFERENCES

**Genetic Alliance** <http://www.geneticalliance.org>

**National Organization for Rare Diseases** <http://www.nord.org>

**Organizations for Support Groups & Information** (Genetic/Rare Conditions)  
<http://www.kumc.edu/gecl/support/grouporg.html#specific>

**Burke W, Fryer-Edwards K, and Pinsky L E** (eds). *Genetics in Primary Care (GPC): A Faculty Development Initiative*. 2001. <http://genes-r-us.uthscsa.edu/resources/genetics/pdfs/gpc-completedoc.pdf>







## CHAPTER 8 : ETHICAL, LEGAL, AND SOCIAL ISSUES

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Over the past decade, many ethical, legal, and social implications (ELSI) associated with genetic testing and research have been raised. In order for genetic testing to be used safely and appropriately, these issues should be discussed with patients so that they are aware of risks and benefits. This chapter provides a brief overview of some of the major ELSI concerns related to genetic testing.

Several concerns have arisen regarding the use and potential misuse of genetic information. Genetic information may differ from other health information because of its long-term implications for an individual and his or her family. Concerns range from the analytical and clinical validity of a genetic test, to potential discrimination by health insurers or employers, to the duty to disclose genetic information to potentially affected family members.

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## 8.1 DESCRIPTION OF ELSI ISSUES

To protect patients from additional distress, health care providers should be aware of the relevant ethical, legal, and social issues related to genetics in health care. Genetic specialists may be better able to address patient concerns and questions regarding these issues. A brief discussion of the major ELSI issues related to genetic testing is provided below.

*8.1.1 Communicating Test Results.* It is critical that genetic test results are discussed with patients in an understandable manner. As many genetic tests will not provide simple positive/negative results, but potentially inconclusive results or risk estimates, it is important that patients understand the extent of the information actually provided from a genetic test. Results should be released only to those individuals for whom the test recipient has given consent. The method of communication should be chosen in advance (for example by phone, or in person) to minimize the likelihood that results will be shared with unauthorized persons or organizations. Under no circumstances should results with identifiers be provided to any outside parties, including employers, insurers, or government agencies, without the test recipient's written consent.

*8.1.2 Direct-to-consumer Tests.* A number of companies market genetic tests directly to consumers without requiring physician involvement. Patients should be cautious when considering direct-to-consumer genetic testing and encouraged to discuss this option with their healthcare professional. Some of these companies may play off consumer fears and offer invalidated or bogus tests, or their laboratories may not be properly certified.

*8.1.3 Duty to Disclose.* The results of a genetic test may have implications for a patient's family members. However, health care providers have an obligation to the person being tested not to inform other family members without the permission of the person tested, except in extreme circumstances. If a health professional believes family members may be at risk, the patient may be encouraged to discuss test results with other family members. In general, families are opposed to doctors informing at-risk members without their consent, even in cases where the disease is easily preventable. The duty to inform varies by state, and courts have ruled on differing sides in different cases.



The American Society of Human Genetics suggests that disclosure to at-risk individuals is permissible when the following criteria are met:

- Attempts to encourage disclosure on the part of the patient have failed
- Harm is highly likely, serious, imminent, and foreseeable
- At-risk relatives are identifiable
- Disease is preventable, or medically accepted standards for treatment or screening are available
- The harm from failing to disclose outweighs the harm from disclosure

*8.1.4 Genetic Discrimination.* When considering genetic testing, a major concern often raised is the potential of discrimination based on genetic information. Since genetic test results are typically included in a patient's medical record, patients should be aware that the results may be accessible to others. As a result, genetic test results could affect a person's insurance coverage or employment. More than 30 states have legislation prohibiting genetic discrimination. However, the scope of these protections differs slightly from state to state. As this publication goes to print, no federal legislation has been passed despite several attempts over the last decade.

In addition, members of minority communities often fear that genetic information will be used to stigmatize them. Health providers should be sensitive to the fact that some groups may mistrust the use of genetics as a health tool.

*8.1.5 Informed Consent.* To help ensure that patients understand the risks and benefits of health care choices, informed consent is an important part of the medical decision-making process. For patients considering genetic testing, the following items should be carefully discussed and understood before consent is obtained:

- Testing is voluntary
- Risks, limitations, and benefits of testing or not testing
- Alternatives to genetic testing
- Details of the testing process (for example, what type of sample is required, accuracy of test, turn-around time, etc.)
- Privacy/confidentiality of test results
- Potential consequences related to results including
  - > Impact on health
  - > Possible emotional and psychological reactions
  - > Treatment/prevention options
  - > Ramifications for family

*8.1.6 Privacy.* Genetic information has enormous implications to an individual and his or her family. The privacy of that information is a major concern to patients: in particular, who should have or needs access to that information. In order to protect personal genetic information and to avoid its inclusion in a patient's medical record, some patients may wish to pay for genetic testing out-of-pocket if possible.

*8.1.7 Psychosocial Impact.* Every individual will respond differently to news of his or her genetic test results whether negative or positive. As there is no right or wrong response, health professionals should refrain from judgment and help the patient understand what the test results mean with respect to their own health, available interventions or follow-up, and risks to their family. An individual may respond to genetic information on several levels, the individual level, family level, or on a community and society level. Referrals to genetic counselors, psychologists, or social workers should be made as needed.

**8.1.8 Reproductive Issues.** Genetic information is routinely used to inform reproductive decisions and medical care. Risk factors for genetic conditions for which preconception or prenatal genetic testing may be considered include advanced maternal age, family history, multiple miscarriages, or drug and alcohol exposure. As these procedures carry risks and benefits, parents should carefully consider and discuss these options with a physician or genetic counselor. Providers should take a non-directive stance, especially when the only management option is termination of pregnancy.

**8.1.9 Societal Values.** Genetic information can raise questions about personal responsibility, personal choice versus genetic determinism/fate, and concepts of health and disease. Personal factors, family values, and community and cultural beliefs will influence responses to these issues. While genetic information may influence one individual to change his or her lifestyle or behavior in order to reduce risk or disease severity, others may choose to respond differently. Health professionals should be respectful and sensitive to cultural and societal values and work with the patient to define the appropriate course of action for them with respect to genetic testing and follow-up care.

**8.1.10 Test Utility.** The useful application of genetic tests will depend on the correct interpretation of test results and their utility in guiding medical care and treatment. However, for some genetic conditions, the utility of genetic test results may be limited if no treatment is available or if the results are inconclusive. These issues should be discussed with patients or parents of patients when a genetic test is being considered. Even if a test is not considered to be medically useful, a patient or the family may still gain benefit from testing. Clinical guidelines should be consulted for recommended follow-up care and treatment.

**8.1.11 Test Validity.** Several issues regarding test validity should be considered prior to ordering a genetic test. The analytical and clinical validity of a test are generally measured as test specificity, sensitivity, and predictive value. This information should be shared with the patient as they consider whether or not testing is appropriate for them. Because most genetic tests are offered as services, they are not approved by the Food and Drug Administration. However, genetic tests (or any other clinical laboratory test) should only be ordered from laboratories certified by Clinical Laboratory Improvement Amendments (CLIA).

## SELECTED REFERENCES

**American Medical Association.** Why Physicians Should Know the Legal and Ethical Issues Raised by Genetic Information and Technology. *Genethics* 2000

<http://www.ama-assn.org/ama/pub/category/3719.html>

**American Society of Human Genetics** Professional Disclosure of Familial Genetic Information (*Am J Hum Genet*, 62:474-483, 1998)

<http://www.ashg.org/genetics/ashg/pibs/policy/pol-29.htm>

**Lehmann LS, Weeks JC, Klar N, et al.** Disclosure of familial genetic information: perceptions of the duty to inform. (*Am J Med Genet* 2000; 109(9): 705-11.)

**March of Dimes** Genetics and Your Practice (Financial, Ethical, Legal and Social Issues (FELSI)

<http://www.marchofdimes.com/gyponline/index.bm2>

**U.S. Department of Energy** Ethical, Legal, and Social Issues

[http://www.ornl.gov/sci/techresources/Human\\_Genome/elsi.shtml](http://www.ornl.gov/sci/techresources/Human_Genome/elsi.shtml)





## CHAPTER 9 : PATIENT STORIES & CONSUMER PROFILES

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This chapter contains four stories about inherited cancer, newborn screening, late-onset disease and family history told from the perspective of a patient or consumer. For some patients, diagnosing a genetic condition can be a challenging and lengthy process involving many doctors and office visits, examinations, testing, and months or years of stress and uncertainty. For other patients, the lack of treatment or effective interventions can prove to be extremely frustrating and difficult to comprehend. These stories can help both health professionals and patients understand the issues faced by patients and families affected with a genetic condition and how they overcame and dealt with these issues.

## 9.1 INHERITED BREAST AND OVARIAN CANCER

At a holiday dinner, my family and I were talking about my sister's recent diagnosis. Just 38 years old, Rachael had detected a lump in her left breast and was diagnosed with breast cancer. She was recovering from the mastectomy she had chosen to have in order to increase her chances of survival. It was still too painful to talk about our mother's death, years ago, of breast cancer at the age of 48, but from the silence in the room, it was obviously on everyone's mind. It was also believed that a great-aunt had died of some form of cancer, although no one was really certain.

The high incidence of cancer deaths in our family was cause for concern. My husband and I were considering having another child. We had two healthy sons but wished for a little girl. I was only 34 years old, but what if I developed breast cancer in 10 years? Would I be able to care for my children? Could I pass on the risk of breast cancer to my children?

I met with my family doctor to discuss my family history of breast cancer. I asked if there was any way to find out if I was at risk for the disease and if there was anything that could be done to prevent the disease from occurring. My doctor referred me to a genetic counselor who specialized in inherited cancer to discuss my risk for cancer and the types of genetic testing available. The genetic counselor told me that a small percentage of all breast cancers are inherited and that two genes, called BRCA1 and BRCA2, have been discovered to cause inherited breast cancer in some families. The genetic counselor also told me that genetic testing is available to some women with a family history of breast and/or ovarian cancer. A positive result would indicate that I have a much higher risk of cancer, but not a 100 percent certainty.

My husband and I were overwhelmed by this information and felt that we needed to talk to someone who had experienced this situation. We found a support group in our community and spoke with the director, who also had a family history of early-onset breast cancer and had decided to undergo genetic testing herself. After several weeks, and with my family's support, I decided to undergo genetic testing. My sister Rachael was tested first for specific mutations in BRCA1 and BRCA2, and once we knew that she has a particular mutation in BRCA1, my blood was tested. I found out that I have the same mutation in the BRCA1 gene.

## 9.2 THE VALUE OF NEWBORN SCREENING

We brought our 7lb. 5oz. baby boy home on April 14th. After a tiring but blissfully happy first week of 4 a.m. feedings and little sleep, our pediatrician called to say that one of the newborn screening tests done on the blood spot collected from our son at birth had come back positive. My husband and I both thought that it had to be a mistake; our son Miguel was a completely healthy and happy baby boy.

The positive result was for a disease called homocystinuria. The following week, we took Miguel back to the hospital to have him re-tested. The second test also came back positive. There was no doubt that Miguel had this disorder although he still seemed completely healthy. The doctor told us that children with this rare genetic disorder are unable to break down excessive protein and that in order for Miguel to have a normal life, he would have to be put on a special low protein diet. I had so many questions about would happen to Miguel. How different would he be from other children? Would his development be delayed? Would he be able to walk and talk and go to school with other kids?

After talking with other parents of children with homocystinuria, several pediatricians, a geneticist at a medical center located two hours away, and nutritionists, we gained some confidence that we could take care of Miguel and provide him with a normal childhood. Miguel



has been on a low protein diet for almost 10 years now, and his disease is under control. He is in the 5th grade and is a very active and bright child. He is doing well in school, plays soccer and baseball, and does all of the things any 10-year old would do: birthday parties, Little League, Boy Scouts. Because Miguel's condition was detected at such an early age, we were able to adjust his diet and prevent symptoms from developing.

### 9.3 HEREDITARY HEMACHROMATOSIS

Growing up, I was busy and energetic like everyone else. I rarely visited the doctor, and there was no hint of any chronic medical problem.

Soon after I turned 40, I started to notice my joints were achy, but I figured I was just getting old. About a year later, I just wasn't feeling as well as I thought I should. I was always tired, and I had occasional abdominal pain. I saw my doctor for a routine physical. After a long series of tests and visits with specialists, a blood test revealed that I had unusually high levels of iron. A liver biopsy confirmed that I have hereditary hemochromatosis.

To understand my own health risks and the chances of my relatives developing this condition, I met with a genetic counselor and had a genetic test performed.

After meeting with the genetic counselor and doing my own research, I am beginning to understand what it means to have hereditary hemochromatosis. I now know that hereditary hemochromatosis is a fairly common adult-onset condition that can be associated with many serious complications, including heart problems, diabetes, liver cirrhosis and arthritis. I consider myself lucky to have been diagnosed at a relatively young age, before any of the major complications developed. I now have periodic phlebotomies (like donating blood) to keep the iron from accumulating in my body and damaging my organs, and this treatment should allow me to live a long, normal life.

### 9.4 TYPE II DIABETES

I was 42 years old when I was diagnosed with Type II diabetes. I had had a recurrent skin infection for almost a year, but it seemed minor at first and I had no health insurance, so I put off seeing a doctor. Eventually I noticed that I always felt thirsty, although I was drinking plenty of water and other beverages. In spite of my increased drinking habits and normal appetite, I somehow lost 40 pounds. Finally, the discomfort from the skin condition became so severe that I went to the emergency room, where I was diagnosed with Type II diabetes. It appears I had actually had this condition for some time.

Since my diagnosis, I have learned a lot about my family and about Type II diabetes. I now understand that Type II diabetes appears to be caused by a combination of genetic and environmental factors. My increased risk for diabetes should have been noted many years earlier. If my doctor and I had been aware that my grandfather, mother and two cousins have diabetes, we could have recognized that my risk was greater than that of someone without a family history.

In addition, it would have been helpful to know that my love of sweets and fatty foods and my tendency to be overweight further increased my risk. Being aware of my risk factors might have prompted me to monitor my health more carefully. I could have exercised more and modified my diet, which might have prevented or delayed the onset of my condition or perhaps made it less severe, and I might have acted more quickly when I recognized the symptoms of diabetes. Knowing about your family history can help you to recognize your risk for a condition and possibly enable you to take action to avoid or delay its development.







## CHAPTER 10 : NEW ENGLAND GENETICS RESOURCES AND SERVICES

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This chapter contains contact information for genetics resources and services in New England, including health centers that provide genetic counseling and testing services. Selected genetic resources located outside of New England are also provided.

## CONNECTICUT RESOURCES

### Connecticut Department of Public Health

410 Capitol Avenue, P.O. Box 340308  
Hartford, CT 06134-0308  
(860) 509-8000

TDD: (860) 509-7191

<http://www.dph.state.ct.us/>

### Connecticut Newborn Screening Program

410 Capitol Avenue, P.O. Box 340308  
Hartford, CT 06134-0308  
(860) 509-8081

<http://www.dph.state.ct.us/bch/nbs/nbs.htm>

### Connecticut Pregnancy Exposure Information Service

University of Connecticut  
Health Partners Building  
65 Kane Street

West Hartford, CT 06119

(860) 523-6419

or (800) 325-5391 (in CT Only)

<http://www.docdb.uhc.edu/genetics/PregnancyExposure.htm>

### March of Dimes: Connecticut Chapter

867 Main Street  
Manchester, CT 06040  
(860) 812-0080

<http://www.marchofdimes.com/connecticut/>

## CONNECTICUT GENETICS PROVIDERS/REFERRALS

### Bridgeport Hospital, Antenatal Testing Unit

267 Grant Street, 5th floor  
Bridgeport, CT 06610  
(203) 384-3049

<http://www.bridgeporthospital.org/ATU>

### Greenwich Hospital, Prenatal Diagnostic Testing and Genetic Counseling

5 Perryridge Road  
Greenwich, CT 06830  
(203) 863-3917

[http://www.greenhosp.org/medicalservices\\_genetics.asp](http://www.greenhosp.org/medicalservices_genetics.asp)

### The Stamford Hospital

30 Shelburne Road  
Stamford, CT 06904-9317  
Division of Maternal-Fetal Medicine:  
(203) 325-7060

- **Bennett Cancer Center**

(203) 276-7199

<http://www.stamfordhospital.org/Services/Cancer/default.aspx>

### University of Connecticut Health Center, Division of Human Genetics

65 Kane Street, MC-7120  
West Hartford, CT 06119  
(860) 523-6464

<http://www.docdb.uhc.edu/genetics/>

### Yale University School of Medicine

333 Cedar Street  
New Haven, CT 06510

<http://info.med.yale.edu/genetics/>

- **Cancer Genetics**

(203) 764-8400

- **General Clinical Genetics**

(203) 785-2660

- **Prenatal Diagnosis**

(203) 785-2661

## MAINE RESOURCES

### Maine Department of Health and Human Services/Genetics Program

11 Statehouse Station, 286 Water Street  
Augusta, ME 04333  
(207) 287-5357

TTY: (800) 606-0215

<http://www.maine.gov/dhhs/boh/cshn/cshn>

### Maine Newborn Screening Program

11 Statehouse Station  
286 Water Street  
Augusta ME 04333  
(207) 287-5357

### March of Dimes: Maine Chapter

60 Gray Rd. Unit #8  
Falmouth, ME 04105  
(207) 878-1199

<http://www.marchofdimes.com/maine>



**Pregnancy Environmental Hotline**

(serves ME, MA, RI and NH)  
 40 Second Avenue, Ste 520  
 Waltham, MA 02451  
 (781) 466-8474  
<http://www.thegenesisfund.org/pehquestion.htm>

**MAINE GENETICS PROVIDERS/REFERRALS****Eastern Maine Medical Center**

**Genetics Program**  
 Webber East, Suite 305  
 417 State Street  
 Bangor, ME 04401  
 (877) 366-3662 x7559  
<http://www.emmc.org/Patient+Services/Pediatrics/Pediatric+Specialty+Clinics>

**Maine Medical Center**

887 Congress Street  
 Portland, ME 04102  
<http://www.mmc.org/>

- **Barbara Bush Children's Hospital, Division of Genetics**  
 (800) 860-6277
- **Division of Maternal-Fetal Medicine**  
 (800) 499-8344  
[http://www.mainehealth.org/mmc\\_body.cfm?id=1951](http://www.mainehealth.org/mmc_body.cfm?id=1951)
- **Maine Center for Cancer Medicine and Blood Disorders**  
 (207) 885-7630  
<http://www.mccm.org/>

**MASSACHUSETTS RESOURCES****March of Dimes: Massachusetts Chapter**

114 Turnpike Rd., Suite 202  
 Westborough, MA 01581  
 (508) 366-9066  
<http://www.marchofdimes.com/massachusetts>

**Massachusetts Department of Public Health**

250 Washington Street  
 Boston, MA 02108-4619  
 (617) 624-6000  
 TTY: (617) 624-6001  
<http://www.mass.gov/dph>

**Massachusetts Newborn Screening Program  
University of Massachusetts Medical School**

305 South Street  
 Jamaica Plain, MA 02130-3515  
 (617) 983-6300  
<http://www.umassmed.edu/nbs>

**Pregnancy Environmental Hotline**

(serves ME, MA, RI and NH)  
 40 Second Avenue, Ste 520  
 Waltham, MA 02451  
 (781) 466-8474  
 or (800) 322-5014 (in MA only)  
<http://www.thegenesisfund.org/pehquestion.htm>

**MASSACHUSETTS GENETICS PROVIDERS/REFERRALS****Baystate Medical Center**

759 Chestnut Street  
 Springfield, MA 01199  
 (413) 794-8890  
<http://www.baystatehealth.com>

**Beth Israel Deaconess Medical Center, Clinical Genetics Program**

330 Brookline Avenue  
 Boston, MA 02215  
 (617) 667-7110  
[http://www.bidmc.harvard.edu/display.asp?node\\_id=1489](http://www.bidmc.harvard.edu/display.asp?node_id=1489)

**Boston University School of Medicine, Center for Human Genetics**

715 Albany St., W-4th Floor  
 Boston, MA 02118  
 (617) 638-7083  
<http://www.bumc.bu.edu/Dept/Home.aspx?DepartmentID=118>

**Brigham and Women's Hospital**

75 Francis Street  
 Boston, MA 02115  
 Division of Genetics:  
 (617) 525-4744  
<http://www.brighamandwomens.org/genetics/>

- **Center for Fetal Medicine and Prenatal Genetics**  
 (617) 732-4840  
<http://www.brighamandwomens.org/mfml/Center4FetalGeneticsHome.aspx>

**Children's Hospital Boston**

300 Longwood Avenue, Fegan 10

Boston, MA 02115

(617) 355-6394

<http://www.childrenshospital.org/clinicalservices.cfm>**Dana Farber Cancer Institute**

44 Binney Street

Boston, Ma 02115

(617) 632-3000

<http://www.dfci.harvard.edu/pat/cancer/default.html>**Harvard Vanguard Medical Associates**

133 Brookline Avenue

Boston, MA 02215

(617) 421-3320

<http://www.harvardvanguard.org/locs/loc2.asp?dp t=Genetics&ofc=Kenmore>**Massachusetts General Hospital**

55 Fruit Street

Boston, MA 02114

- **Genetics and Teratology Unit**

(617) 726-1561

- **MGH Cancer Center**

(617) 726-5130

<http://www.massgeneral.org/cancer/>

- **Ultrasound and Prenatal Diagnostic Center**

(617) 724-2229

<http://www.massgeneral.org/vincent/prenatal.htm>**New England Medical Center**

750 Washington Street, NEMC Box #360

Boston, MA 02111

- **Prenatal Genetics**

(617) 636-4549

<http://www.tufts-nemc.org/obgyn/mat-fetl.htm>

- **Pediatric Genetics**

(617) 636-5461

<http://www.tufts-nemc.org/home/departments/pedil/pedgen.htm>**UMass Memorial Children's Medical Center****University Campus – Benedict Building**

55 Lake Avenue North

Worcester, MA 01655

(508) 856-5695

[http://www.umassmemorial.org/ummbhc/hospitals/med\\_center/services/CMC/genetics.cfm](http://www.umassmemorial.org/ummbhc/hospitals/med_center/services/CMC/genetics.cfm)**NEW HAMPSHIRE RESOURCES****March of Dimes: New Hampshire Chapter**

22 Bridge Street

Concord, NH 03301

(603) 228-0317

<http://www.marchofdimes.com/newhampshire>**New Hampshire Department of Public Health**

105 Pleasant Street

Concord, NH 03301

(603) 271-8140 or (800) 852-3345

TDD: (800) 735-2964

<http://www.dhhs.state.nh.us/>**New Hampshire Newborn Screening Program**

29 Hazen Drive

Concord, NH 03301-6504

(603) 271-4225

<http://www.dhhs.state.nh.us/dhhs/mch.htm>**Pregnancy Environmental Hotline**

(serves ME, MA, RI and NH)

40 Second Avenue, Ste 520

Waltham, MA 02451

(781) 466-8474

<http://www.thegenesisfund.org/pehquestion.htm>**NEW HAMPSHIRE GENETICS PROVIDERS/REFERRALS****Dartmouth Hitchcock Medical Center**

1 Medical Center Drive

Lebanon, NH 03756

<http://www.dhmc.org>

- **Division of Maternal Fetal Medicine & Prenatal Diagnosis**

(603) 653-9306



- **Familial Cancer Program at Norris Cotton Cancer Center**

(800) 251-0097

<http://www.cancer.dartmouth.edu/>

- **Medical Genetics Clinic**

(603) 653-6044

**Elliot Hospital/Health System**

275 Mammoth Road

Suite 1

Manchester, NH 03109

(603) 663-8611

[www.elliophospital.org/services/genetic\\_counseling.html](http://www.elliophospital.org/services/genetic_counseling.html)

**RHODE ISLAND RESOURCES**

**March of Dimes: Rhode Island Chapter**

260 West Exchange Street, Suite 002

Providence, RI 02903

(401) 454-1911

<http://www.marchofdimes.com/rhodeisland>

**Pregnancy Environmental Hotline**

(serves ME, MA, RI and NH)

40 Second Avenue, Ste 520

Waltham, MA 02451

(781) 466-8474

<http://www.thegenesisfund.org/pehquestion.htm>

**Rhode Island Department of Health**

3 Capitol Hill, Room 302

Providence, RI 02908-5097

(800) 942-7434

<http://www.health.ri.gov/genetics/newborn.php>

**Rhode Island Newborn Screening Program**

3 Capitol Hill, Room 302

Providence, RI 02908-5097

(800) 942-7434

<http://www.health.ri.gov/genetics/newborn.php>

**RHODE ISLAND GENETICS PROVIDERS/REFERRALS**

**Rhode Island Hospital, Genetic Counseling Center**

593 Eddy Street

Providence, RI 02903

(401) 444-8361

<http://www.lifespan.org/rih/>

**Women and Infants' Hospital**

101 Dudley Street

Providence, RI 02905

<http://www.womenandinfants.org>

- **Cancer Risk Assessment and Prevention Program**

(401) 453-7540

- **Prenatal Diagnosis Center**

(401) 453-7510

**VERMONT RESOURCES**

**March of Dimes: Vermont Chapter**

107 North Main Street

Barre, VT 05641

(802) 479-3265

<http://www.marchofdimes.com/vermont>

**Vermont Department of Public Health**

108 Cherry Street

Burlington, VT 05402

(802) 863-7200

In Vermont: (800) 464-4343

TTY/TDD: Dial 711 first

<http://www.healthvermont.gov>

**Vermont Newborn Screening Program**

108 Cherry Street, P.O. Box 70

Burlington, VT 05402

(802) 951-5180

**Vermont Pregnancy Risk Information**

112 Colchester Ave

Burlington, VT 05401

(800) 932-4609 (press option 4)

## VERMONT GENETICS PROVIDERS/REFERRALS

### Vermont Regional Genetics Center

112 Colchester Avenue  
Burlington, VT 05401  
(802) 847-4310

## REGIONAL RESOURCES

### New England Regional Genetics Group (NERGG)

P.O. Box 920288  
Needham, MA 02492  
(781) 444-0126  
<http://www.nergg.org>

## NATIONAL RESOURCES

### PRENATAL/PREGNANCY RESOURCES

#### March of Dimes

1275 Mamaroneck Avenue  
White Plains, NY 10605  
(914) 997-4488  
<http://www.marchofdimes.com>

#### National Healthy Mothers, Healthy Babies Coalition

2000 N. Beauregard Street, 6th Floor  
Alexandria, VA 22311  
(703) 836-6110  
<http://www.hmhb.org>

#### National SIDS/Infant Death Resource Center

8280 Greensboro Drive, Suite 300  
McLean, VA 22102  
(866) 866-7437  
<http://www.sidscenter.org>

#### Resolve: The National Infertility Association

1310 Broadway  
Somerville, MA 02144  
(888) 623-0744  
<http://www.resolve.org>

### Share Pregnancy and Infant Loss Support, Inc.

St. Joseph Health Center  
300 First Capitol Drive  
St. Charles, MO 63301  
(800) 821-6819  
<http://www.nationalshareoffice.com>

## RESOURCES FOR SPECIFIC GENETIC CONDITIONS

### GeneTests

9725 Third Avenue NE, Suite 602  
Seattle, WA 98115  
(206) 616-4033  
<http://www.genetests.org>

Funded by the NIH, the GeneTests web site offers expert-authored reviews of genetic conditions as well as searchable directories of genetic testing laboratories and genetics clinics.

### Genetic Alliance

4301 Connecticut Avenue, NW, Suite 404  
Washington, DC 20008  
(202) 966-5557  
<http://www.geneticalliance.org>

Genetic Alliance is an international coalition comprised of more than 600 advocacy, research, and healthcare organizations. The Alliance maintains a searchable directory of support groups and other information for hundreds of genetic conditions.

### National Organization for Rare Disorders (NORD)

55 Kenosia Avenue, P.O. Box 1968  
Danbury, CT 06813  
(800) 999-6673  
<http://www.rarediseases.org>

NORD offers written summaries of genetic conditions as well as a searchable directory of support organizations for more than 2000 rare diseases, including genetic diseases.



GENETICS PROFESSIONAL  
ORGANIZATIONS

**American College of Medical Genetics  
(ACMG)**

9650 Rockville Pike  
Bethesda, MD 20814  
(314) 634-7127  
*<http://www.acmg.net>*

**American Society of Human Genetics  
(ASHG)**

9650 Rockville Pike  
Bethesda, MD 20814  
(866) HUM-GENE  
*<http://www.ashg.org>*

**National Coalition for Health Professional  
Education in Genetics (NCHPEG)**

2360 W. Joppa Rd., Suite 320  
Lutherville, MD 21093  
(410) 583-0600  
*<http://www.nchpeg.org>*

**National Society of Genetic Counselors  
(NSGC)**

401 N. Michigan Avenue  
Chicago, IL 60611  
(312) 321-6834  
*<http://www.nsgc.org>*







## CHAPTER 11 : CONSUMER FACT SHEETS

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Family History (Fact Sheet from CDC) \* Basic Genetic Information \* Dominant and Recessive Genetic Diseases \* X-linked Genetic Diseases \* What is a Chromosome Abnormality? \* Understanding Genetic Testing \* Prenatal Diagnosis \* Birth Defects & Congenital Abnormalities \* Newborn Screening \* Genetic Counseling

## Family History Is Important for Your Health

adopted from CDC's Family History Fact sheet

<http://www.cdc.gov/genomics/public/famhix/fs.htm>

Most of us know that we can reduce our risk of disease by eating a healthy diet, getting enough exercise, and not smoking. But did you know that your family history might be one of the strongest influences on your risk of developing heart disease, stroke, diabetes, or cancer? Even though you cannot change your genetic makeup, knowing your family history can help you reduce your risk of developing health problems.



Family members share their genes, as well as their environment, lifestyles and habits. Everyone can recognize traits that run in their family, such as curly hair, dimples, leanness or athletic ability. Risks for diseases such as asthma, diabetes, cancer, and heart disease also run in families. Everyone's family history of disease is different. The key features of a family history that may increase risk are:

- Diseases that occur at an earlier age than expected (10 to 20 years before most people get the disease);
- Disease in more than one close relative;
- Disease that does not usually affect a certain gender (for example, breast cancer in a male);
- Certain combinations of diseases within a family (for example, breast and ovarian cancer, or heart disease and diabetes).

If your family has one or more of these features, your family history may hold important clues about your risk for disease. People with a family history of disease may have the most to gain from lifestyle changes and screening tests. You can't change your genes, but you can change unhealthy behaviors, such as smoking, inactivity, and poor eating habits. In many cases, adopting a healthier lifestyle can reduce your risk for diseases that run in your family. Screening tests (such as mammograms and colorectal cancer screening) can detect diseases like cancers at an early stage when they are most treatable. Screening tests can also detect disease risk factors like high cholesterol and high blood pressure, which can be treated to reduce the chances of getting disease.



## LEARNING ABOUT YOUR FAMILY HISTORY

To learn about your family history:

- Ask questions,
- Talk at family gatherings, and
- Look at death certificates and family medical records, if possible.

Collect information about your grandparents, parents, aunts and uncles, nieces and nephews, siblings, and children. The type of information to collect includes:

- Major medical conditions and causes of death,
- Age of disease onset and age at death, and
- Ethnic background.

Write down the information and share it with your doctor. Your doctor will:

- Assess your disease risk based on your family history and other risk factors,
- Recommend lifestyle changes to help prevent disease, and
- Prescribe screening tests to detect disease early.

If your doctor notices a pattern of disease in your family, it may be a sign of an inherited form of disease that is passed on from generation to generation. Your doctor may refer you to a specialist who can help determine whether you have an inherited form of disease. Genetic testing may also help determine if you or your family members are at risk. Even with inherited forms of disease, steps can be taken to reduce your risk.

## WHAT IF YOU HAVE NO FAMILY HISTORY?

Even if you don't have a history of a particular health problem in your family, you could still be at risk. This is because

- Your lifestyle, personal medical history, and other factors influence your chances of getting a disease;
- You may be unaware of disease in some family members;
- You could have family members who died young, before they had a chance to develop chronic conditions such as heart disease, stroke, diabetes, or cancer.

Being aware of your family health history is an important part of a lifelong wellness plan.

## WHERE YOU CAN FIND MORE INFORMATION

For more information on CDC's Office of Genomics and Disease Prevention, visit <http://www.cdc.gov/genomics>.

The following websites provide additional information on family history:

**CDC's Family History Web site for the Public**, <http://www.cdc.gov/genomics/public/fambhist.htm>

**U.S. Surgeon General's Family History Initiative**, <http://www.hhs.gov/familyhistory/>

**National Society of Genetic Counselors**, <http://www.nsgc.org/consumer/familytree/>

## Basic Genetic Information

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- Cells are the body's building blocks. Inside most cells is a nucleus—the center of the cell. The nucleus contains threadlike structures called chromosomes made up of smaller structures called genes.
- Genes direct the structure and function of your cells which make up all of your body's organs and tissues.
- Genes are inherited from your parents and determine how you will look.
- Genes come in pairs. One gene comes from your father and one from your mother. This is why you look like your parents.
- Genes also contain instructions for how you age, what diseases you are at risk for or may get as you grow older, or what diseases you might pass down to your children.
- Some genes are stronger, or dominant, and they take over directing your body for that function.
- Some genes are weaker, or recessive, and need the presence of a like partner to become active and make a difference.
- Changes (also called mutations) can sometimes happen in a gene. Changes in a gene may cause cells or organs not to work correctly, leading to a disease. Changes in a gene may also lead to improvement in your body's ability to cope with disease. Changes in the genes can be inherited from your parents or happen due to the environment you live in—the chemicals you are exposed to, through the air you breathe, the food you eat, or the water you drink.
- Whether the specific set of genes you inherited from your parents—or any changes that occur to them during your lifetime—promote health or produce disease may depend on both environmental and behavioral factors. Proper exercise and nutrition can help delay or prevent disease, while smoking and lack of exercise can increase your chances of disease.
- You can take special tests—genetic tests—to see what specific genes are present in your body. These tests can sometimes tell you what diseases you might have or might develop later, and what diseases you might pass along to your children.
- Newborn babies also take genetic tests to look for diseases that might harm the baby or cause mental retardation if they are not treated immediately. These tests are done just after the baby is born so that treatment can be started immediately to protect the baby from these diseases. If a disease is found, a doctor will help you understand what treatment your baby needs. Sometimes you may be asked to see a genetic counselor.



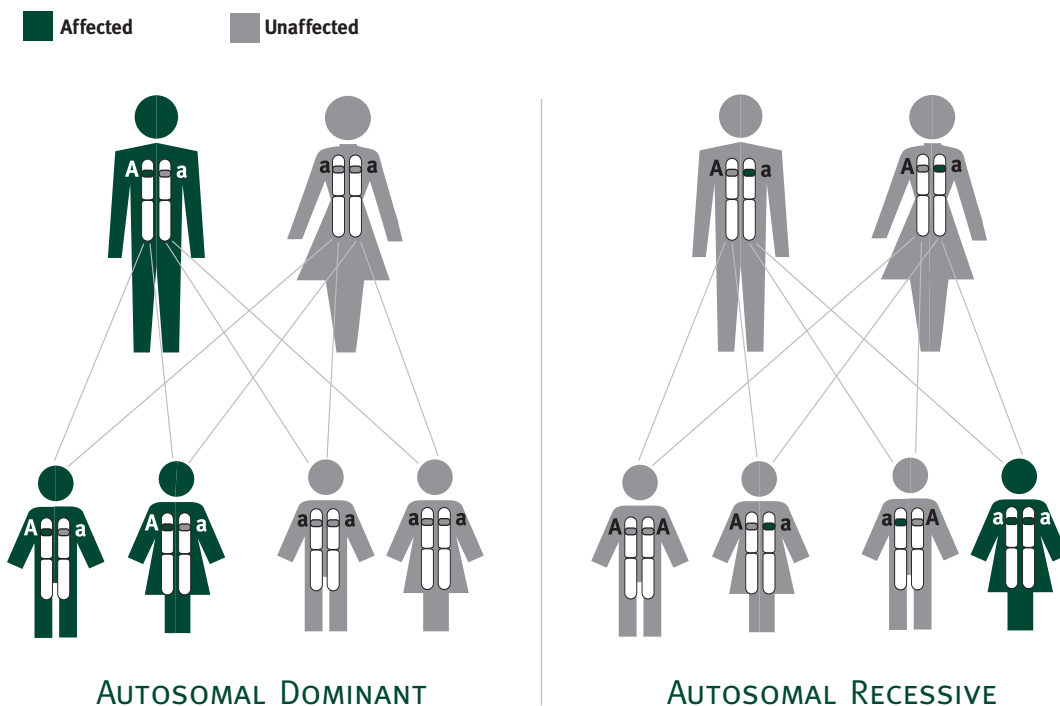
## Dominant and Recessive Genetic Diseases

The basic laws of inheritance are important in order to understand how diseases are passed on in a family. For almost every gene, a person has two copies of each gene—one copy from your father and one copy from your mother. Changes to either copy of the gene or both copies of the gene can result in a wide range of effects. Some changes result in relatively minor or undetectable changes; these types of changes are often called single nucleotide polymorphisms (“snips”) or gene variations.

Other changes in a gene can result in changes to the corresponding protein which can lead to disease. These changes are often known as mutations. Diseases caused by mutations in a single gene are usually inherited in a simple pattern, depending on the location of the gene and whether one or two normal copies of the gene are needed. For certain functions in the body, you need two copies of a gene to work normally. For other functions, only one copy is necessary.

There are two major modes of inheritance for single-gene diseases: recessive and dominant. When a person inherits a mutation in one of the two copies of a gene, disease may develop if both copies are required for normal function. In this case, the mutated gene is dominant and the person develops a genetic disease. Dominantly inherited genetic diseases tend to occur in every generation of a family. Each affected person usually has one affected parent.

If a person inherits a mutation in one copy of a gene, but does not develop a disease, the mutated gene is recessive. For a recessively inherited disease to develop, both copies of the gene must be mutated. This can happen when both the mother and father carry a copy of the mutated gene and pass each copy onto the child, who will then have two copies of the mutated gene. Recessive genetic diseases are typically not seen in every generation of an affected family. The parents of an affected person are generally not affected.



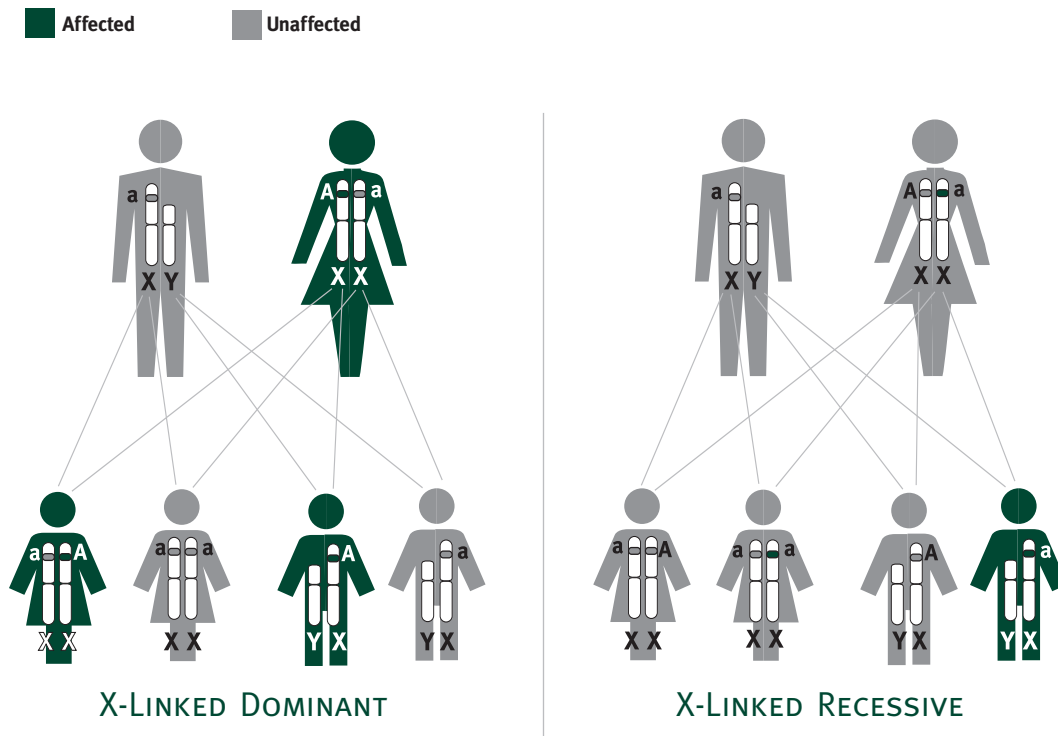
## X-linked Genetic Diseases

For genes located on the sex chromosomes (X or Y), the inheritance patterns are slightly different than for genes located on the other chromosomes (1-22). This is due to the fact that females carry two X chromosomes (XX) and males carry a single X and Y chromosome each (XY). Therefore, females carry two copies of each X-linked gene similar to all other genes, but males carry only one copy of X-linked and Y-linked genes.

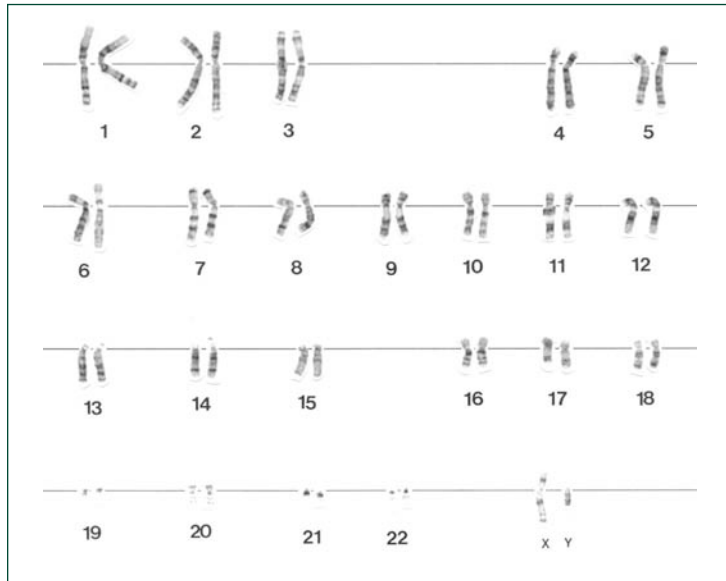
Since males only have one X chromosome, any mutated gene on the X chromosome will result in disease. But because females have two copies of X-linked genes, diseases caused by mutated genes located on the X chromosome can be inherited in either a dominant or recessive manner. For X-linked dominant diseases, a mutation in one copy of an X-linked gene will result in disease. Families with an X-linked dominant disorder often have both affected males and affected females in each generation.

For X-linked recessive diseases to occur, both copies of the gene must be mutated in order for disease to occur in females. Families with an X-linked recessive disorder often have affected males, but rarely affected females, in each generation.

A striking characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons since they only pass on the Y chromosome. In contrast, affected mothers can pass the mutated X-linked gene to either their son or daughter.



## What is a Chromosome Abnormality?



A normal male karyotype

Almost every cell in our body contains 23 pairs of chromosomes for a total of 46 chromosomes. Half of the chromosomes come from our mother and the other half come from our father. The first 22 pairs (called autosomes) are numbered according to size—the largest chromosome is chromosome 1. The 23rd pair are the sex chromosomes X and Y—females have two X chromosomes and males have an X and Y chromosome each. All of the information that the body needs to work comes

from the chromosomes. Each chromosome contains thousands of genes which direct the body's development, growth, and chemical reactions.

Although almost everyone has a complete set of chromosomes, sometimes pieces of chromosomes can be switched or moved. In general, as long as all of the material is present, the majority of people with rearranged chromosomes do not develop any health problems. However, when sections of or entire chromosomes are missing or duplicated, miscarriage, infant death, or disease usually occurs. For example, an extra copy of chromosome 21 results in Down syndrome (trisomy 21).

Chromosome abnormalities usually happen as a result of an error when cells grow and divide. Errors can occur when eggs or sperm are formed, resulting in either too many chromosomes or not enough chromosomes. Or, errors can occur during the early developmental stages of the fetus, also resulting in an abnormal number of chromosomes. The age of the mother and certain environmental factors can increase the risk of a fetal chromosomal abnormality.

Testing can be performed to examine the chromosomes of the fetus. The two types of testing available are amniocentesis and chorionic villus sampling. In both cases, some cells from the fetus are grown and processed in the laboratory so that the chromosomes can be studied. Pictures of the chromosomes viewed under a microscope are taken and the chromosomes are then arranged by size and paired together. The picture of the arranged chromosomes is known as a karyotype, as seen above. The karyotype is evaluated for size and structure of the chromosomes.

## Understanding Genetic Testing

Genetic testing involves examining a person's DNA, found in blood or other tissues, for some abnormality linked to a disease or condition. DNA is actually a chemical alphabet composed of four units that make up all of the genes, or genetic material, found inside our cells. Genes are important for the body's normal development and functioning. Each gene is unique due to the order of the four DNA units.

When a mistake happens affecting part or all of the gene, this can result in an abnormal function or change in the body, leading to disease. The mistake can be fairly large or very small, and different types of genetic tests are used to identify the specific gene abnormality.

The most common type of genetic testing is newborn screening. Almost every baby born in the United States has a blood sample tested for abnormal or missing genes or proteins. Early detection can allow the doctor to prescribe drugs or to place the baby on a specific diet in order to prevent or reduce the severity of a disease. Another type of testing, known as carrier testing, can help determine the risk of parents passing on a mutation to their child. Predictive or predispositional genetic testing can determine the risk of a healthy person developing a disease in the future. Finally, genetic tests can be used to look for gene abnormalities in persons suspected of having a genetic disease based on symptoms or family history.

Genetic testing is not always 100 percent accurate. Even when a genetic test positively detects a mutation, the test usually cannot determine when or what symptoms of the disease may show, which symptoms will occur first, how severe the disease will be, or how the disease will progress over time. If a test is negative, an individual may still be at risk for a disease. Therefore, it is important to speak to a health professional such as a genetic counselor to help you understand the benefits and risks of genetic testing and to answer any questions you may have before and after testing.

Genetic counselors are health professionals trained in the areas of medical genetics and counseling. Genetic counselors are trained to help persons as they consider testing, when they receive the results, and in the weeks and months afterward.

When deciding whether or not to have a genetic test for you or your child, several issues should be considered. In addition to the medical issues, genetic testing also raises some social, ethical, and legal issues you should be aware of. Below is a list of some of the issues you should discuss with your physician or genetic counselor:

- What treatments are available for this genetic disease?
- What impact would the genetic test results have on my family?
- What happens if the results are uncertain or inconclusive?
- What are the risks for future pregnancies?
- What is the cost of the test and will my insurance cover it?
- Who will have access to the test results?
- What emotional support services are available?
- Do other family members have a right to know the test results?
- What is the risk of discrimination by my employer or insurer?





## Prenatal Diagnosis

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Prenatal diagnosis refers to testing performed during a pregnancy. Prenatal diagnosis is helpful for determining the outcome of the pregnancy, planning for possible complications during delivery, planning for problems that may occur in the newborn, deciding whether to continue the pregnancy, and finding conditions that may affect future pregnancies.

A common reason for prenatal diagnosis is the mother's age. According to professional guidelines, prenatal diagnosis should be offered to women who will be over the age of 35 years at the time of delivery because of an increased risk of having a child with a chromosome abnormality such as Down syndrome. Children with Down syndrome have a distinct facial appearance and mental retardation; however, the severity of the disease can vary greatly from child to child. The disease is caused by an extra copy of chromosome 21 (trisomy 21).

Other possible reasons for prenatal diagnosis include: a previous child with a genetic condition, a fetus known to be at risk for a genetic condition because both parents are mutation carriers, a family history of a genetic condition, a positive prenatal screening test (triple/quadruple/first trimester screen), or abnormal ultrasound findings.

Several types of prenatal diagnosis are available depending how far along the pregnancy is and what type of disorder is being tested. Chorionic villus sampling (CVS) and amniocentesis are two common procedures used to obtain a sample for further testing.

Amniocentesis and chorionic villus sampling are both invasive procedures that carry a risk of miscarriage (less than 0.5% for amniocentesis and about 1% for CVS). Amniocentesis involves removing a sample of amniotic fluid that surrounds the fetus by inserting a syringe through the abdomen. The technique is generally performed at 15 to 20 weeks gestation. In



CVS, the fetal cells are removed from an area around the fetus known as the chorion with a syringe inserted through the cervix or abdomen. CVS can be performed as early as nine week's gestation, but based on safety data, it is typically performed at 10 to 13 weeks' gestation. This allows the results to be available at an earlier stage of pregnancy. Both amniocentesis and CVS samples contain fetal cells that can be grown in the laboratory for genetic testing.

## Birth Defects/Congenital Abnormalities

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A birth defect is a problem that happens while a fetus is developing prior to birth. Congenital abnormalities refer to features or conditions that a baby is born with, as opposed to conditions that develop later in life. About 1 in 33 babies is born with a birth defect in the U.S.

A birth defect may cause physical or mental disabilities. It can affect almost any part of the body and can range from mild to severe. Some birth defects can be corrected by surgery or other medical treatments and children can lead normal lives. But some birth defects are very severe and can cause death. Some birth defects are easily detected, such as a club foot or cleft lip, but others such as heart defects or hearing loss may require x-rays and special tests. Not all birth defects can be detected prenatally.

Some of the most common birth defects affect the heart. About 1 in every 200-300 babies is born with a heart defect. Depending on the type and severity of the heart defect, it may be correctable by surgery. Other common birth defects are called “neural tube” defects. These are due to abnormal development of the baby’s spine or brain and affect about 1 in 1,000 babies. These defects are sometimes very severe, causing early death. Birth defects of the lip and the roof of the mouth are also common. They are referred to as cleft lip and cleft palate and affect about 1 in 700-1,000 babies.

Many birth defects are caused by multiple factors—both genetic and environmental. For example, the risk of neural tube defects is increased in families with a history of neural tube defects, but the risk can be reduced with folic acid supplementation during early pregnancy. Uncontrolled medical conditions of the mother, such as diabetes, can also lead to birth defects such as heart defects. Some medicines such as Accutane are also known to cause birth defects.

To learn more about your risk of having a baby with a birth defect, please talk with your doctor or a genetic counselor. In particular, women should consult their doctor before becoming pregnant to begin multi-vitamin supplements containing folic acid, to get help with managing their medical conditions, to decide which medications are safe to take, and to avoid exposure to alcohol, drugs, and smoking.



## Newborn Screening

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Each year, approximately 98% of all children born in the United States (at least 4 million babies) are tested for a panel of diseases that, when detected and treated early, can lead to significant reduction in disease severity and possibly even prevention of the disease. Between 2,700 and 3,000 newborns test positive for one of these severe disorders each year.

Within 48 hours of a child's birth, a sample of blood is obtained from a "heel stick." The blood can be analyzed for more than 50 life-threatening diseases, including phenylketonuria (PKU), sickle cell disease, and hypothyroidism. The sample, called a "blood spot," is tested at a state public health or other participating laboratory. Each state has its own panel of tests.

Newborn screening programs began in the U.S. in the 1960's with the work of Dr. Robert Guthrie, who developed a screening test for PKU. PKU is an inherited metabolic disease that is caused by a mutation in an enzyme responsible for metabolism of the amino acid phenylalanine. Children who are identified early can avoid foods with phenylalanine, thereby avoiding buildup of the amino acid which can lead to brain damage and mental retardation. When Dr. Guthrie also introduced a system for collection and transportation of blood samples on filter paper, cost effective wide scale genetic screening became possible.

In general, newborn screening is performed for conditions that, when detected and treated early, can lead to significant reduction in disease severity and possibly even prevention of the disease. The panel of newborn diseases screened for varies from state to state, and decisions for adding or deleting tests involve many complex social, ethical, and political issues. Usually, newborn population screening disorders are selected based on disease prevalence, detectability, treatment availability, outcome, and overall cost effectiveness. It is possible to screen for many disorders at birth and soon more will be possible. The American College of Medical Genetics and the March of Dimes recommend that all babies be screened for a core panel of 29 disorders. About half of the state newborn screening programs have adopted this recommendation.

For specific information on newborn screening in New England, including contact information for each state, see the printable brochure, *Newborn Screening Tests: They Could Save Your Baby's Life*, available at [www.nerhg.org/nbsbrochures.php](http://www.nerhg.org/nbsbrochures.php)

## Genetic Counseling

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Genetic counselors work as part of a health care team, providing information and support to individuals and families affected by or at risk for a genetic disorder. Genetic counselors are trained not only to present complex information about genetic risks, testing, and diagnosis, but also to provide supportive counseling as well as referrals to other sources of information and support.

Common reasons for seeing a genetic counselor include: pregnancy in a woman age 35 or older; family history of a genetic condition; or suspected diagnosis of a genetic condition in a fetus, child, or adult.

A genetic counselor may do any or all of the following during your appointment:

- Ask you questions about your medical/pregnancy history
- Create a picture of your family health history (a pedigree)
- Assess your genetic health risks
- Provide information about the genetic condition(s) affecting you or your family
- Discuss screening and/or preventive measures to address your genetic health risks
- Help you process the significance of your genetic risks or diagnosis
- Assess whether you might benefit from genetic testing
- Help you evaluate the pros and cons of undergoing genetic testing
- Explain genetic test results
- Refer you to relevant resources for further education and support

It is not uncommon for multiple genetic counseling appointments to occur, especially if genetic testing is performed and/or a diagnosis has been made. Depending on the reason for the visit(s), you may also see a geneticist, a physician specializing in genetics.

For more information on genetic counseling, or to find a genetic counselor near you, contact: The National Society of Genetic Counselors, (312) 321-6834, [www.nsgc.org](http://www.nsgc.org)





## APPENDIX

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Teratogens/Prenatal Substance Abuse \* Single-Gene Disorders \* Chromosomal Abnormalities \* Pharmacogenomics \* Cultural Competencies in Genetics  
NCHPEG Principles of Genetics for Health Professionals \* CDC Genomic Competencies for the Public Health Workforce

## APPENDIX A. TERATOGENS/PRENATAL SUBSTANCE ABUSE

A teratogen is any agent that causes an abnormality following fetal exposure during pregnancy. Teratogens are usually discovered after an increased prevalence of a particular birth defect. For example, in the early 1960's, a drug known as thalidomide was used to treat morning sickness. Exposure of the fetus during this early stage of development resulted in cases of phocomelia, a congenital malformation in which the hands and feet are attached to abbreviated arms and legs. Teratogens can also be found at home or the workplace. The effect is related to type of agent, dose and duration, and time of exposure. The first half of pregnancy is the most vulnerable.

Teratogenic agents include infectious agents (rubella, cytomegalovirus, varicella, herpes simplex, toxoplasma, syphilis, etc.); physical agents (ionizing agents, hyperthermia); maternal health factors (diabetes, maternal PKU); environmental chemicals (organic mercury compounds, polychlorinated biphenyl or PCB, herbicides and industrial solvents); and drugs (prescription, over-the-counter, or recreational). In general, if medication is required, the lowest dose possible should be used and combination drug therapies and first trimester exposures should be avoided, if possible.

The types or severity of abnormalities caused by a teratogenic agent is also dependent on the genetic susceptibilities carried by the mother and fetus. For example, variation in maternal metabolism of a particular drug will determine what metabolites the fetus is exposed to and the duration of exposure. The genetic susceptibility of the fetus to a particular teratogenic agent will also have an effect on the final outcome.



Two of the leading preventable causes of birth defects and developmental disabilities are alcohol and smoking. Alcohol use in pregnancy has significant effects on the fetus and the baby. Alcohol can pass from the mother's blood stream through the placenta to the fetus. Since alcohol is broken down more slowly in a fetus than in an adult, alcohol levels tend to remain high and stay in the baby's body longer. Birth defects associated with prenatal exposure to alcohol can occur in the first 3 to 8 weeks of pregnancy, before a woman even knows that she is pregnant.

Fetal alcohol syndrome is a group of abnormalities in babies born to mothers who consume alcohol during pregnancy. It is the most common known non-genetic (non-inherited) cause of mental retardation in the U.S. Several educational materials in English and Spanish are available from the CDC at <http://www.cdc.gov/ncbddd/fas/faspub.htm>.



In 2001, the estimated prevalence of smoking during pregnancy for all U.S. women was 11.4 percent, ranging from 3.9 percent in DC to 26.2 percent in West Virginia. Smoking nearly doubles a woman's risk of having a low birth-weight baby as a result of poor growth before birth, preterm delivery or a combination of both. Premature and low birth-weight babies face an increased risk of serious health problems during the newborn period, chronic lifelong disabilities (e.g., cerebral palsy, mental retardation) and possibly death. More recent studies have suggested a possible link between prenatal smoking exposure and behavioral problems in later childhood and adolescence.

In addition, almost 3 percent of pregnant women use illicit drugs such as marijuana, cocaine, Ecstasy and other amphetamines, and heroin. These drugs can cause low birth-weight, withdrawal symptoms, birth defects, or learning or behavioral problems.

**More information about specific teratogens can be found the following web-sites:**

- Organization of Teratogen Information Services *[http://otispregnancy.org/otis\\_about\\_us.asp](http://otispregnancy.org/otis_about_us.asp)*
- Reprotox—an online Information System on Environmental Hazards to Human Reproduction and Development *<http://reprotox.org/>*
- Teratogen Information System (TERIS —online version Shepard's Catalog of Teratogenic Agents) *<http://depts.washington.edu/~terisweb/teris/>*
- March of Dimes *<http://www.marchofdimes.com>*

## APPENDIX B. SINGLE-GENE DISORDERS

Single gene disorders are among the most well-understood genetic disorders due to their straightforward inheritance patterns (recessive or dominant) and relatively simple genetic etiology. Although the majority of these diseases are rare, in total, they affect millions of Americans. Some of the more common single-gene disorders include cystic fibrosis, hemochromatosis, Tay-Sachs, and sickle cell anemia.

Even though these diseases are primarily caused by a single gene, several different mutations can result in the same disease but with varying degrees of severity and phenotype. But even the same mutation can result in slightly different phenotypes. This may be caused by differences in the patient's environment and/or other genetic variations that may influence the disease phenotype or outcome. For example, other genes have been shown to modify the cystic fibrosis phenotype in children who carry the same CFTR mutation. In addition, for some disorders such as galactosemia, mutations in different genes can result in similar phenotypes.

Genetic testing is available for many single-gene disorders, however, the clinical examination is extremely important in the differential diagnosis particularly in patients with no family history. For some genetic conditions, patients can often be treated for their symptoms or modify their diets to prevent the onset of symptoms if diagnosed at an early age (newborn screening). However, despite advancements in the understanding of genetic etiology and improved diagnostic capabilities, no treatments are available to prevent disease onset or slow disease progression for a number of these disorders.

Some useful resources to bookmark include GeneTests and OMIM. GeneTests (<http://www.genetests.org>) is an online genetic testing laboratory database providing information about conditions and laboratory testing services. The Online Mendelian Inheritance in Man (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>) database is a comprehensive resource that provides information about the genetic etiology, clinical symptoms, and a bibliography. Of over 5,000 known genetic conditions, the molecular basis is known in almost 2,000.

| CONDITION                          | GENE (CHR. LOCATION)     | INHERITANCE PATTERN |
|------------------------------------|--------------------------|---------------------|
| Congenital Deafness (nonsyndromic) | Connexin 26 (13q11)      | Recessive           |
| Tay-Sachs                          | hexosaminidase A (15q23) | Recessive           |
| Familial hypercholesterolemia      | LDL receptor (19p13)     | Dominant            |
| Sickle cell anemia                 | Beta-globin (11p15)      | Recessive           |
| Duchenne muscular dystrophy        | Dystrophin (Xq21)        | X-linked Recessive  |
| Cystic Fibrosis                    | CFTR (7q31)              | Recessive           |
| Hemochromatosis                    | HFE (6p21)               | Recessive           |
| Huntington disease                 | Huntington (4p16)        | Dominant            |





## APPENDIX C. CHROMOSOMAL ABNORMALITIES

Chromosomal abnormalities may be either numerical or structural. The most common type of chromosomal abnormality is known as aneuploidy, an abnormal chromosome number due to an extra or missing chromosome. Most aneuploid patients have trisomy (three copies of a chromosome) instead of monosomy (single copy of a chromosome). Down Syndrome is probably the most well-known example of a chromosomal aneuploidy, caused by an extra copy of chromosome 21 known as trisomy 21. While a trisomy can occur with any chromosome, the condition is rarely viable. Besides trisomy 21, the major chromosomal aneuploidies seen in liveborn babies are: trisomy 18; trisomy 13; 45, X (Turner syndrome); 47, XXY (Klinefelter syndrome); 47, XYY; and 47, XXX.

Structural chromosomal abnormalities result from breakage and incorrect rejoining of chromosome segments. There is a range of structural chromosomal abnormalities that results in disease. Structural rearrangements are defined as balanced if the complete chromosome set is still present though rearranged, and unbalanced if there is additional or missing information. Unbalanced rearrangements include deletions, duplications, or insertions of a chromosome segment. Ring chromosomes can result when a chromosome undergoes two breaks and the broken ends fuse into a circular chromosome. An isochromosome can form when an arm of the chromosome is missing and the remaining arm duplicated.

Balanced rearrangements included inverted or translocated chromosomal regions. Since the full complement of DNA material is still present, balanced chromosomal rearrangements may go undetected since they may not result in disease. A disease can arise as a result of a balanced rearrangement if the breaks in the chromosomes occur in a gene, resulting in an absent or non-functional protein, or if the fusion of chromosomal segments results in a hybrid of two genes producing a new protein product whose function is damaging to the cell. For example, a chimeric gene is observed in many cases of chronic myelogenous leukemia as a result of a translocation between chromosomes 9 and 22. Part of the chimeric gene is made up of a proto-oncogene, a gene that normally regulates cell proliferation and differentiation. The disruption of the normal function of this gene results in uncontrolled cell growth leading to leukemia.

## APPENDIX D. PHARMACOGENOMICS

Pharmacogenomics is the study of how an individual's genetic make-up affects the body's response to drugs. Pharmacogenomics holds the potential for drugs to be tailored to an individual's genetic make-up, sometimes referred to as "personalized medicine." While environment, diet, age, lifestyle, and health status can all influence a person's response to medicines, understanding an individual's genetic makeup is thought to be the key to creating personalized drugs with greater efficacy and safety.

The impact of an individual's genetic make-up on drug response and outcome has actually been known since the 1950's but interest has been reignited by the sequencing of the human genome. Genetic variation in drug targets or genes involved in drug disposition can result in different drug responses and outcomes for a given group of patients treated with the same drug. At this early stage of pharmacogenomics research, the development of clinical tests and targeted drugs is slow due to the limited knowledge of which genes are involved with each drug response. Since many genes are likely to influence responses, obtaining the big picture on the impact of gene variations is highly time-consuming and complicated.



The cytochrome (CYP) P450 family of liver enzymes is responsible for breaking down more than 30 different classes of drugs. DNA variations in genes that code for these enzymes can influence their ability to metabolize certain drugs. Less active or inactive forms of CYP enzymes that are unable to break down and efficiently eliminate drugs from the body can lead to drug toxicity.

It is hoped that new findings from genetic studies will facilitate drug discovery and allow drug makers to produce treatments better targeted to the cause of specific diseases. This accuracy not only will maximize therapeutic effects but also decrease damage to nearby healthy cells. In addition, physicians will be able to analyze a patient's genetic profile and prescribe the best available drug therapy from the beginning rather than relying on the traditional trial-and-error method of matching patients with the right drugs. Pharmacogenomics aims to improve the likelihood of an improved outcome and reduce risk of serious adverse responses. Pharmacogenomics has the potential to dramatically reduce health care costs associated with the more than 2 million hospitalizations each year in the U.S. as a result of adverse drug response and multiple drug prescriptions and patient visits.



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## APPENDIX E. CULTURAL COMPETENCY IN GENETICS

Cultural competency involves attitudes, policies and structures that enable health professionals to work effectively cross-culturally. The term “cultural competence” represents a process of working towards a greater understanding and respect for different beliefs. It does not imply that anyone can truly achieve full “competence” in any particular culture. Health professionals should have the capacity to value diversity, manage dynamics of difference and adapt to the cultural contexts of the communities they serve. Health organizations and services should acquire and institute cultural knowledge across all aspects of policy making, administration, practice, service delivery and systematically involve consumers, key stakeholders and communities.

In genetics, cross-cultural genetic services focus on the health beliefs and cultural customs of the patient and family. Culturally and linguistically appropriate health care services may include interpreter staff, translated written materials, culturally-sensitive discussions about treatment, and knowledgeable clinical and support staff. The provision of these kinds of services has the potential to improve patient outcomes and the efficiency and cost-effectiveness of health care delivery. In particular, reproductive issues and pediatric care may raise culturally-unique issues that require culturally sensitive discussions about treatment and care.

**In addition, the following links may be helpful for health professionals learning about different ethnocultural beliefs and diversity issues:**

National Center for Cultural Competencies at Georgetown University Center for Child and Human Development <http://gucchd.georgetown.edu/ncccl/index.html>

Assuring Cultural Competence in Health Care: Recommendations for National Standards and an Outcomes-Focused Research Agenda  
<http://www.pcusa.org/nationalhealth/advocacy/standard-hc.pdf>

Cross Cultural Health Care Program <http://www.xculture.org/>

Diversity Rx <http://www.diversityrx.org/>

EthnoMed <http://www.ethnomed.org/>

JAMARDA Resources <http://www.jamardaresources.com/>

The National Multicultural Institute <http://www.nmci.org/>

March of Dimes–GENE (Genetics Education Needs Evaluation) Project  
<http://www.marchofdimes.com/geneproject>



## APPENDIX F. NATIONAL COALITION FOR HEALTH PROFESSIONAL EDUCATION IN GENETICS (NCHPEG)—PRINCIPLES OF GENETICS FOR HEALTH PROFESSIONALS

NCHPEG's publication, *Core Competencies in Genetics Essential for All Health-Care Professionals* (Jan 2001), continues to provide basic guidance to a broad range of individuals and groups as they plan educational initiatives in genetics and genetically based health care. The current document, *Principles of Genetics for Health Professionals*, responds to requests for additional guidance about the content that should constitute basic instruction in genetics for those in health care. The principles focus on basic biology related to genetics.

### A. PRINCIPLES RELATED TO BIOLOGICAL VARIATION

1. Genetics is the study of heritable biological variation.
2. Genetics in the health-care setting concerns heritable variation that is related to health and disease.
3. Molecular biology is the study of the structures and functions of macromolecules such as nucleic acids and proteins.
4. Genomics is the study of the constitution of entire genomes, that is, all of the genetic material in an organism.
5. Proteomics is the study of the structures and functions of the protein products of the genes in the genome.
6. Individual genetic variation that leads to biochemical and molecular individuality results in part from the variable sequences of the four bases that are central components of the DNA molecule.
7. Mutations introduce additional variation, but not all mutations have biological significance. Some can be deleterious in varying degrees; others, fewer in number, may provide selective advantages that are useful to evolution. There would be no differential selection, and therefore no evolution, without mutation and variation. This principle helps to explain phenomena such as the emergence of bacterial strains that are resistant to antibiotics, as well as the obvious human differences we recognize in everyday life.
8. Human variation results from the interactions among variable gene products and environmental factors that vary from person to person in kind, duration, and intensity. Variation is expressed at the molecular level in differences in sequences of amino acids and therefore in the structure and function of proteins that maintain physiological systems. It also is expressed in disease, which is a result of some incompatibility between homeostatic variation and the individual's experience with the environment. Because that is the case, genetics and genomics are the most basic sciences for health care and for education of health professionals.
9. There is no fixed type—no archetypical individual—in a species, including *Homo sapiens*. A species comprises a population of unique individuals that may vary in each of their traits, including metabolism, immune responses, morphology, and behavior, and, therefore, in expression of disease.

10. There are no sharp genetic boundaries between populations of human beings around the globe, and there is more genetic variation within populations than between them. These facts make the designation of biological races scientifically untenable and make the grouping of people by phenotypes such as skin color a poor predictor of other traits.
11. The genotype for a given trait is the gene(s) associated with that trait. The phenotype is the expression of the genotype. That expression is mediated by protein gene products that work in the context of experiences with the environment, through development, maturation, and aging.
12. Some human traits, including diseases, result primarily from the action of the product of one gene. Other human traits, including most common diseases, result from the products of more than one gene acting in concert with the influence of environmental variables, which vary in kind, duration, and intensity through time.
13. The development of disease reflects three time frames: a) the evolutionary history—biological and cultural—of our species, which has produced the genome common to all of us; b) the individual developmental history of each person, which interacts with the products of his or her genes, and c) the more immediate factors that result in the expression of disease at a particular moment.
14. The phrase “the gene for,” as in “the gene for phenylketonuria,” can be misleading. It can imply erroneously that only genetic influences are responsible for a given trait or disease, discounting the influence of the environment. The phrase also can suggest that only one gene is associated with a given trait when there may be genetic heterogeneity, of alleles and modifiers, as well as multiple loci. The blood-group substances and hemoglobin variants demonstrate such heterogeneity.
15. Genetically based health care, which now embraces genomics, is uniquely positioned to provide insights into prevention because it acknowledges the individuality of each patient and the biological and environmental influences that produce that individuality. Genetically based care focuses primarily on the person who has the disease, not on the disease itself. It asks, “Why does this person have this disease at this point in his or her life?” and it recognizes that individual variation in genes, development, and experiences means that each person has his or her own version of each disease.

## B. PRINCIPLES RELATED TO CELL BIOLOGY

1. Classic cell theory holds that all life is made of cells and that all cells come from pre-existing cells.
2. Cells pass through a series of structural and functional stages known as the cell cycle. The cell cycle, which includes processes leading to cell division, is under genetic control. Cancer results from one or more disruptions in that cell cycle. Because most of these disruptions occur in somatic cells (as opposed to germ cells) all cancer is genetic, but not all of it is inherited.



3. Cell division produces new cells.
4. Mitosis, one aspect of cell division, helps to ensure genetic continuity from one generation of somatic cells to the next. Human somatic cells contain 46 chromosomes (the diploid number): 22 pairs of autosomes and one pair of sex chromosomes (X and Y).
5. Human germ cells, sperm and ova, contain 23 chromosomes (the haploid number). A special process of cell division—meiosis—occurs in the precursors to germ cells. Meiosis has two major biological effects: it reduces the number of chromosomes from 46 to 23 and it increases genetic variation through independent assortment and through the exchange of genetic material between maternal and paternal chromosomes (crossing over). Meiotic variations can result in abnormalities of chromosome number or structure.
6. In *Homo sapiens* and in other animals, the fungi, and plants, cells contain a nucleus that includes the chromosomes, the carriers of most of the genetic material (DNA).
7. Human cells also contain mitochondria. Because mitochondria were free-living organisms early in the evolution of life, they carry their own DNA, which now specifies proteins that are useful to us. Mutations in mitochondrial DNA can cause health problems.

### C. PRINCIPLES RELATED TO CLASSICAL (MENDELIAN) GENETICS

1. Our understanding of the behavior of chromosomes during meiosis allows us to make predictions about genotype from one generation to the next.
2. Some traits are inherited through an autosomal dominant pattern of inheritance, others through an autosomal recessive pattern. Still others, those traits associated with genes on the X chromosome, follow somewhat different patterns of transmission because the male has only one X chromosome.
3. Traits, not genes, are dominant or recessive. It is convenient, even traditional, to refer to genes as dominant or recessive, but today it is anachronistic, because of our new knowledge of how protein gene products influence phenotype.
4. Aberrations in the behavior of chromosomes during meiosis can result in structural or numerical alterations that have serious consequences for growth and development. Some of these aberrations occur more frequently in the offspring of older mothers. Others arise more frequently during the formation of sperm. We can detect many chromosomal aberrations prenatally. They account for a significant proportion of fetal death, and to a lesser extent, death in infancy.
5. Our understanding of genes in populations allows us to make predictions about the presence of genes in individuals and in given populations and, therefore, about the variable frequencies of disease phenotypes.

6. During the last two decades, research has uncovered genetic mechanisms that extend our understanding of non-mendelian inheritance and that provide biological explanations for heretofore-unexplained observations. These mechanisms, such as imprinting, trinucleotide repeats, and epigenesis, however, do not alter our fundamental understanding of the rules that govern genetic and molecular processes.

#### D. PRINCIPLES RELATED TO MOLECULAR GENETICS

1. DNA and RNA are information molecules; they store biological information in digital form in a well-defined code.
2. DNA is the primary information molecule for virtually all life on earth; this is but one piece of evidence for the relatedness of all life through evolution.
3. DNA does very little by itself. It is a stable storehouse of genetic information, but it takes proteins to put the information to use. DNA's transcription and the translation of its information into protein are accomplished by protein-mediated mechanisms. Similarly, the functions of the organs and body are carried out by sets of proteins whose properties and actions are not likely to be understood or predictable by our current knowledge of single genes or proteins.
4. The structure of DNA lends itself to replication. DNA replicates with great accuracy, which is critical to the proper transmission of genetic information from one generation of cells to the next and from one generation of organisms to the next.
5. Sometimes errors arise during DNA replication, and evolution has produced mechanisms that repair such mistakes. In fact, some of those mechanisms present in *Homo sapiens* are conserved evolutionarily all the way back to the bacterium *E. coli*. When repair mechanisms fail, mutations may remain. Some may become the basis for evolutionary change.
6. In most biological systems, the flow of information is: DNA to RNA to protein. The processes by which this occurs are replication of the DNA, transcription of the DNA into messenger RNA, and translation of the messenger RNA into protein.
7. DNA is susceptible to damage by environmental insults such as radiation and certain chemicals, and the damage that occurs to our DNA during the course of our lives can contribute to aging and the onset of cancer. Damage that occurs in the DNA of germ cells—sperm and ova—is not completely repaired. Evolution is a possible result of these new, heritable variations.
8. A gene is a segment of DNA. Some genes code for the production of structural proteins (collagen, for example) or enzymes (lactase, for example). Other genes are regulatory, helping to control such processes as prenatal development and ongoing cellular functions.
10. A gene occupies a particular place on a chromosome—a locus. A gene can have two or more alternative forms—alleles—but only one allele at a time can occupy a given locus on a given chromosome.





11. Because proteins direct the operations of cells, such statements as “gene-environment interaction” are inaccurate. The interaction is actually between the environment—for example, oxygen, food, drug, or antigen—and the protein products of the genes.

## E. PRINCIPLES RELATED TO DEVELOPMENT

1. The human life span comprises three major phases: development, including embryological development and growth after birth until maturation; maturation; and aging. Progression through the stages is continuous, however, and apart from birth it is difficult to tell where one ends and the next begins.
2. Although virtually all human beings proceed through the same developmental stages, there are individual differences in the rate of progression.
3. Embryological development begins with the fusion of sperm and ovum. This event restores the diploid number and initiates a complex series of events that involves an increase in the number of cells; differentiation of the zygote into the specialized cells, tissues, and organs that make up a new, individual organism; and growth of the organism itself.
4. Embryological development is under genetic control. That is, particular genes must be turned on and off at the correct time to ensure proper development.
5. Development is not, however, the simple unfolding of a genetic program resulting in a predictable end product. It involves the influence of maternal mitochondrial genes and gene products at the time of fertilization, as well as significant and variable non-genetic factors such as communication between cells, the migration of cells within the developing embryo, the proper spatial orientation of the embryo, and the effects of environmental influences. These factors render the precise outcome of development unpredictable and contribute to the uniqueness of each individual, the hallmark of life on earth.
6. Biologists have discovered a set of genes, called homeotic genes, that are central to embryological development of the body plan. These genes are highly conserved throughout evolution, and the genes even appear in the same order on the chromosomes of species as distantly related as round worms, fruit flies, mice, and human beings. Biologists therefore are able to study the genetic and molecular aspects of human development by studying those processes in other species.
7. The Human Genome Project has provided the complete DNA sequences of all human genes and will allow more detailed analysis of the genetic regulation of development. Likewise, the ability to analyze the protein products of genes involved in development will improve our understanding of the many and varied complex steps that produce a new individual.
8. The evolutionary changes that lead to the production of new species undoubtedly result from rare, beneficial changes during embryological development of individual organisms. Most embryological changes will be small, however, because the system will not tolerate major deviations from the basic developmental plan.

9. Environmental agents such as radiation or drugs can interfere with embryological development, resulting in birth defects and, more likely, fetal death. Various technologies allow detection of some of these abnormalities in utero.
10. Unlike development in species whose newborns are juveniles, development in *Homo sapiens* continues throughout infancy, and there is a long juvenile period. This requires prolonged parental investment and also exposes the still-developing organism to the possibility of environmental insults.
11. Change continues throughout the lifespan in the form of maturation and aging, always building upon, and constrained by, what has come before, and providing the substrate for subsequent events.
12. Some diseases that have their onset in middle age or old age may actually have had their origins much earlier in the individual's developmental history.

## F. PRINCIPLES RELATED TO NEW GENETIC TECHNOLOGY

1. Advances in technology allow us to analyze and manipulate the genetic material in ways that were not possible even a few years ago.
2. These technologies allow us to identify, isolate, and test for genes associated with disease, and in the future, perhaps for traits that have no clinical significance.
3. Like all technologies, genetic technologies are fallible, can have unintended consequences, and may serve the interests of entities apart from the patient.
4. The growth of information technology in concert with the expansion of genetic technology is a great boon to genetically based health care and to basic research, but it also raises concerns about the use of genetic information.

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## APPENDIX G. CDC–GENOMIC COMPETENCIES FOR ALL PUBLIC HEALTH PROFESSIONALS AND CLINICIANS

EXCERPTED FROM CDC'S GENOMICS COMPETENCIES FOR THE PUBLIC HEALTH WORKFORCE

### GENOMIC COMPETENCIES FOR ALL PUBLIC HEALTH PROFESSIONALS

A public health professional within his/her professional field and program is able to:

- Apply the basic public health sciences, (including behavioral and social sciences, biostatistics, epidemiology, informatics, environmental health) to genomic issues and studies and genetic testing, using the genomic vocabulary to attain the goal of disease prevention
- Identify ethical and medical limitations to genetic testing, including uses that don't benefit the individual
- Maintain up-to-date knowledge on the development of genetic advances and technologies relevant to his/her specialty or field of expertise and learn the uses of genomics as a tool for achieving public health goals related to his/her field or area of practice
- Identify the role of cultural, social, behavioral, environmental and genetic factors in development of disease, disease prevention, and health promoting behaviors; and their impact on medical service organization and delivery of services to maximize wellness and prevent disease
- Participate in strategic policy planning and development related to genetic testing or genomic programs
- Collaborate with existing and emerging health agencies and organizations, academic, research, private and commercial enterprises, including genomic-related businesses, agencies and organizations and community partnerships to identify and solve genomic-related problems
- Participate in the evaluation of program effectiveness, accessibility, cost benefit, cost effectiveness and quality of personal and population-based genomic services in public health
- Develop protocols to ensure informed consent and human subject protection in research and human subject protection in research

## GENOMIC COMPETENCIES FOR PUBLIC HEALTH PROFESSIONALS IN CLINICAL SERVICES EVALUATING INDIVIDUALS AND FAMILIES

The public health clinician, as appropriate to discipline, agency or program, is able to:

- Apply basic genomic concepts including patterns of inheritance, gene-environment interactions, role of genes in health and disease, and implications for health promotion programs to relevant clinical services
- Demonstrate understanding of the indications for, components of, and resources for genetic testing and/or genomic-based interventions
- Describe ethical, legal, social, and financial issues related to genetic testing and recording of genomic information
- Explain basic concepts of probability and risks and benefits of genomics in health and disease assessment in the context of the clinical practice
- Deliver genomic information, recommendations, and care without patient or family coercion within an appropriate informed-consent process

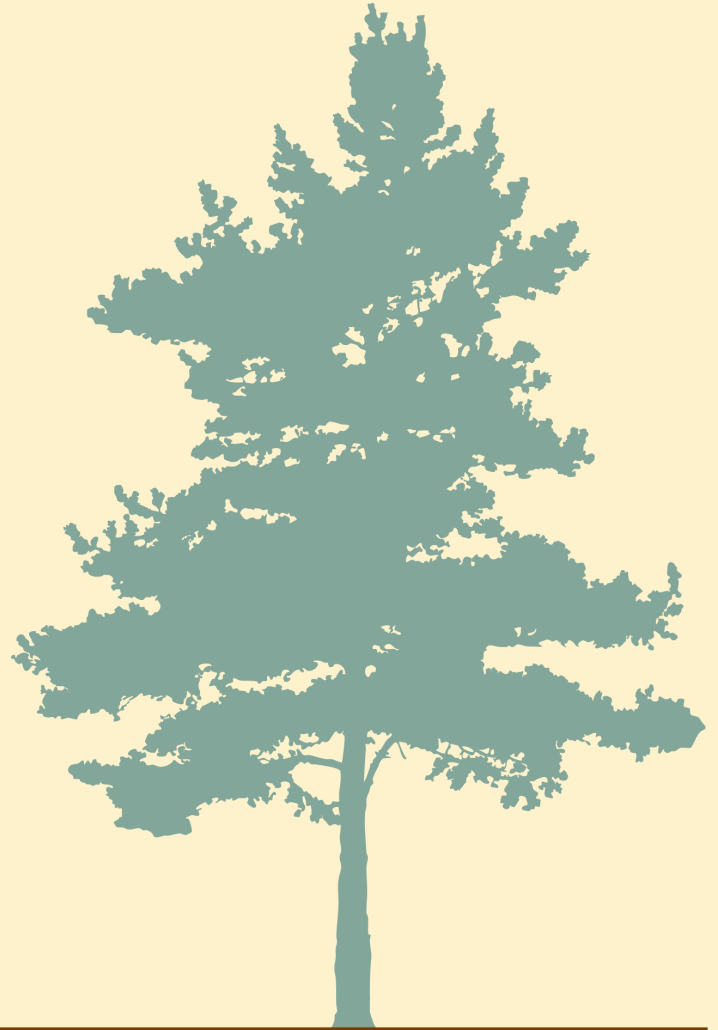
### SELECTED REFERENCE

**Centers for Disease Control and Prevention.** Office of Genomics and Disease Prevention. Genomics Competencies for the Public Health Workforce. Available at <http://www.cdc.gov/genomics/training/competencies/comps.htm>









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