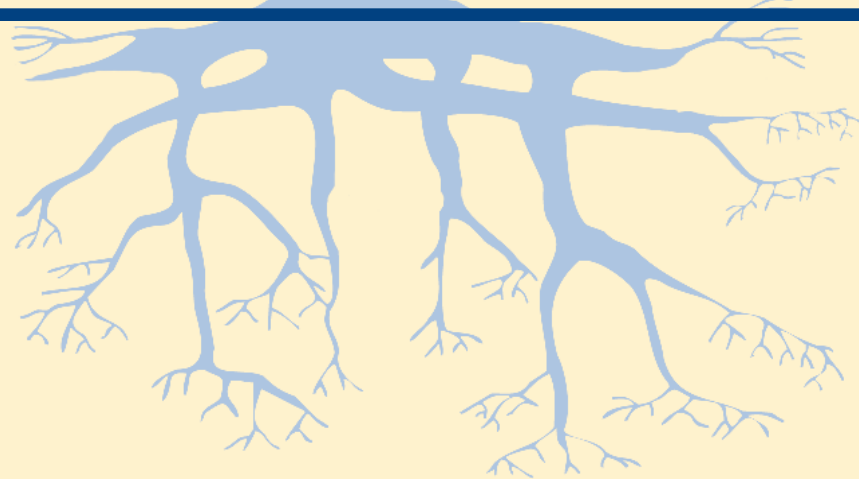




UNDERSTANDING GENETICS



A NEW YORK – MID-ATLANTIC GUIDE FOR PATIENTS AND HEALTH PROFESSIONALS

THE NEW YORK – MID-ATLANTIC CONSORTIUM FOR GENETIC AND NEWBORN SCREENING SERVICES

The New York – Mid-Atlantic Guide for Patients and Health Professionals was produced thanks to a partnership between Genetic Alliance and NYMAC, the New York – Mid-Atlantic Consortium for Genetic and Newborn Screening Services.

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TABLE OF CONTENTS

PREFACE		3
CHAPTER 1	GENETICS 101	5
1.1	Cells, Genomes, DNA, and Genes	6
1.2	Types of Genetic Disease	6
1.3	Laws of Inheritance	7
1.4	Genetic Variation	9
CHAPTER 2	DIAGNOSIS OF A GENETIC DISEASE	11
2.1	History and Physical Examination	12
2.2	Red Flags for Genetic Disease	12
2.3	Uses of Genetic Testing	13
2.4	Types of Genetic Testing	13
2.4.1	Cytogenetic Testing	13
2.4.2	Biochemical Testing	14
2.4.3	Molecular Testing	14
CHAPTER 3	PEDIGREE AND FAMILY HISTORY-TAKING	15
3.1	Importance of Family History	16
3.2	How to Take a Family Medical History	17
3.3	Pedigrees	17
CHAPTER 4	NEWBORN SCREENING	19
4.1	Overview of Newborn Screening	20
4.1.1	Screening Procedure and Follow-up	20
4.1.2	Retesting	20
4.1.3	Clinical Evaluation and Diagnostic Testing	20
4.1.4	Treatment	20
4.1.5	Tests Performed	21
4.2	Newborn Screening Programs	21
4.3	Newborn Hearing Screening	22
4.3.1	Screening Procedure	22
4.3.2	Retesting	22
4.3.3	Treatment	22
4.4	Newborn Hearing Screening Programs	23
CHAPTER 5	GENETIC COUNSELING	25
5.1	Role of Genetic Counseling	26
5.2	Process of Genetic Counseling	26
5.3	Patient Education	27
CHAPTER 6	INDICATIONS FOR A GENETIC REFERRAL	29
6.1	When to Refer to a Genetic Specialist	30
6.1.1	Family History	30
6.1.2	Delayed Growth and Development	30
6.1.3	Reproductive Issues	30
CHAPTER 7	PSYCHOLOGICAL AND SOCIAL IMPLICATIONS	33
7.1	Genetic Information and Other Medical Information	34
7.2	A Lifetime of Affected Relationships	34

7.3	Impact of a Genetic Diagnosis	35
7.3.1	Patients	35
7.3.2	Parents	35
7.3.3	Family	35
7.3.4	Communities	36
7.4	Coping Mechanisms	36
CHAPTER 8	ETHICAL, LEGAL, AND SOCIAL ISSUES	39
8.1	Description of Ethical, Legal, and Social Issues	40
8.1.1	Communicating Test Results	40
8.1.2	Direct-to-consumer Tests	40
8.1.3	Duty to Disclose	40
8.1.4	Genetic Discrimination	40
8.1.5	Informed Consent	41
8.1.6	Privacy	41
8.1.7	Psychosocial Impact	41
8.1.8	Reproductive Issues	41
8.1.9	Societal Values	42
8.1.10	Test Utility	42
8.1.11	Test Validity	42
CHAPTER 9	PATIENT STORIES AND CONSUMER PROFILES	43
9.1	Inherited Breast & Ovarian Cancer	44
9.2	The Value of Newborn Screening	44
9.3	Hereditary Hemochromatosis	45
9.4	Type II Diabetes	46
CHAPTER 10	GENETICS RESOURCES AND SERVICES	47
APPENDICES		61
A.	Basic Genetics Information	62
B.	Family History is Important for Your Health	64
C.	Family Health History Questionnaire	66
D.	Healthcare Provider Card	68
E.	Inheritance Patterns	70
F.	Chromosomal Abnormalities	72
G.	Genetic Testing	73
H.	Prenatal Screening and Testing	75
I.	Genetic Testing Methodologies	78
J.	Newborn Screening	80
K.	Birth Defects	81
L.	Genetics and the Environment	82
M.	Pharmacogenomics and Pharmacogenetics	84
N.	Integrated Health Data Systems	86
O.	Making Sense of Your Genes: A Guide to Genetic Counseling	87
P.	Cultural Competency in Genetics	90
Q.	National Coalition for Health Professional Education in Genetics (NCHPEG)—Principles of Genetics for Health Professionals	91
R.	Centers for Disease Control and Prevention (CDC)—Genomic Competencies for All Public Health Professionals and Clinicians	98

PREFACE

Over the past few decades, advances in genetics and genomics have revolutionized the way we think about health. Although genetics has traditionally been associated with pregnancy, birth defects, and newborn screening, almost every disease is influenced in part by an individual's genetic makeup. Therefore, it is important to consider the impact of genetics in health and disease throughout an individual's lifetime.

The purpose of this manual is to provide an educational genetics resource for individuals, families, and health professionals in the New York – Mid-Atlantic region and increase awareness of specialty care in genetics. The manual begins with a basic introduction to genetics concepts, followed by a description of the different types and applications of genetic tests. It also provides information about diagnosis of genetic disease, family history, newborn screening, and genetic counseling. Resources are included to assist in patient care, patient and professional education, and identification of specialty genetics services within the New York – Mid-Atlantic region. At the end of each section, a list of references is provided for additional information. Appendices can be copied for reference and offered to patients. These take-home resources are critical to helping both providers and patients understand some of the basic concepts and applications of genetics and genomics.

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 (HHS) Health Resource and Services Administration (HRSA) Grant #5 H91 MC 00228-03.

Genetic Alliance transforms health through genetics. We promote an environment of openness centered on the health of individuals, families, and communities.

We bring together diverse stakeholders to create novel partnerships in advocacy. Genetic Alliance's network includes hundreds of disease-specific advocacy organizations, as well as universities, companies, government agencies, and policy organizations. The network is an open space for thousands of shared resources, creative tools, and dozens of focused programs.

We revolutionize access to information to enable translation of research into services and individualized decision-making. Genetic Alliance offers technical assistance to organizations, builds and sustains robust information systems, 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. In all we do, we integrate individual, family, and community perspectives to improve health systems.

Genetic Alliance is supported by a HRSA Collaborative Agreement.

NYMAC, the New York – Mid-Atlantic Consortium for Genetic and Newborn Screening Services, is one of seven federally-funded regions in the U.S., created to ensure that individuals with heritable disorders and their families have access to quality care and appropriate genetic expertise and information. It is funded by HRSA Collaborative Agreement #U22 MC 03956.

This manual is available on the Genetic Alliance website, www.geneticalliance.org/publications, and on the NYMAC website, www.wadsworth.org/newborn/nymac/resources.html.

GENETIC ALLIANCE MANDATE FOR QUALITY GENETIC SERVICES

Access to quality genetics services is critical to healthcare.

1. Individuals and families partner with their healthcare providers to identify needs, develop and monitor treatment plans, and manage their genetic condition.
2. Healthcare providers refer individuals to appropriate specialists, as needed, including those outside of their health insurance plans.
3. Providers and payers consider the psychosocial, as well as the medical, effects of a genetic condition—on both the individual and the individual’s family—at each stage of life.
4. Healthcare insurance plans reimburse genetic testing, diagnosis, and treatment for genetic conditions.
5. Quality resources are available to assist individuals and their families in understanding family health history, signs/symptoms, screening/testing options and their implications, diagnosis, treatment, and long-term follow-up, as needed.
6. A healthcare provider with experience in genetic services is available to all individuals.
7. Providers, payers, and employers create and use policies, guidelines, and procedures to ensure the appropriate use of genetic information.
8. Information about genetic conditions is provided to individuals and families in a culturally-appropriate manner, which may include primary language, appropriate educational level, and various media.
9. Information about genetic research and clinical trials is available to the affected individuals and integrated into clinical practice when appropriate.
10. Referrals to support groups and resources are offered at regular office visits.
11. Outpatient, home, and hospital care for individuals with genetic conditions is available and integrated.





CHAPTER 1 : GENETICS 101

Almost every human trait and disease has a genetic component, whether inherited or influenced by behavioral factors such as exercise. Genetic components can also modify the body's response to environmental factors such as toxins. Understanding the underlying concepts of human genetics and the role of genes, behavior, and the environment is important for appropriately collecting and applying genetic and genomic information and technologies during clinical care. It is important in improving disease diagnosis and treatment as well. This chapter provides fundamental information about basic genetics 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.

1.1 CELLS, GENOMES, DNA, AND GENES

Cells are the fundamental structural and functional units of every known living organism. Instructions needed to direct activities are contained within a DNA (deoxyribonucleic acid) sequence. DNA from all organisms is made up of the same chemical units (bases) called adenine, thymine, guanine, and cytosine, abbreviated as A, T, G, and C. In complementary DNA strands, A matches with T, and C with G, to form base pairs. 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 to 250 million base pairs. Human cells contain two sets of chromosomes, one set inherited from each parent. Each cell normally contains 23 pairs of chromosomes, which consist of 22 autosomes (numbered 1 through 22) and one pair of sex chromosomes (XX or XY). However, sperm and ova normally contain half as much genetic material: 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 for 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 to 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 the genes active in a brain cell because 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 TYPES OF GENETIC DISEASE

Many, if not most, diseases are caused or influenced by genetics. 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.

Changes in the DNA sequence of single genes, also known as mutations, cause thousands of diseases. A gene can mutate in many ways, resulting in an altered protein product that is unable to perform its normal 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 base(s). The altered protein product may still retain some normal 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. Other mutations, called polymorphisms, are natural variations in DNA sequence that have no adverse effects and are simply differences among individuals.

In addition to mutations in single genes, genetic diseases can be caused by larger mutations in chromosomes. Chromosomal abnormalities may result from either the total number of chromosomes differing from the usual amount or the physical structure of a chromosome differing from the usual structure. The most common type of chromosomal abnormality is



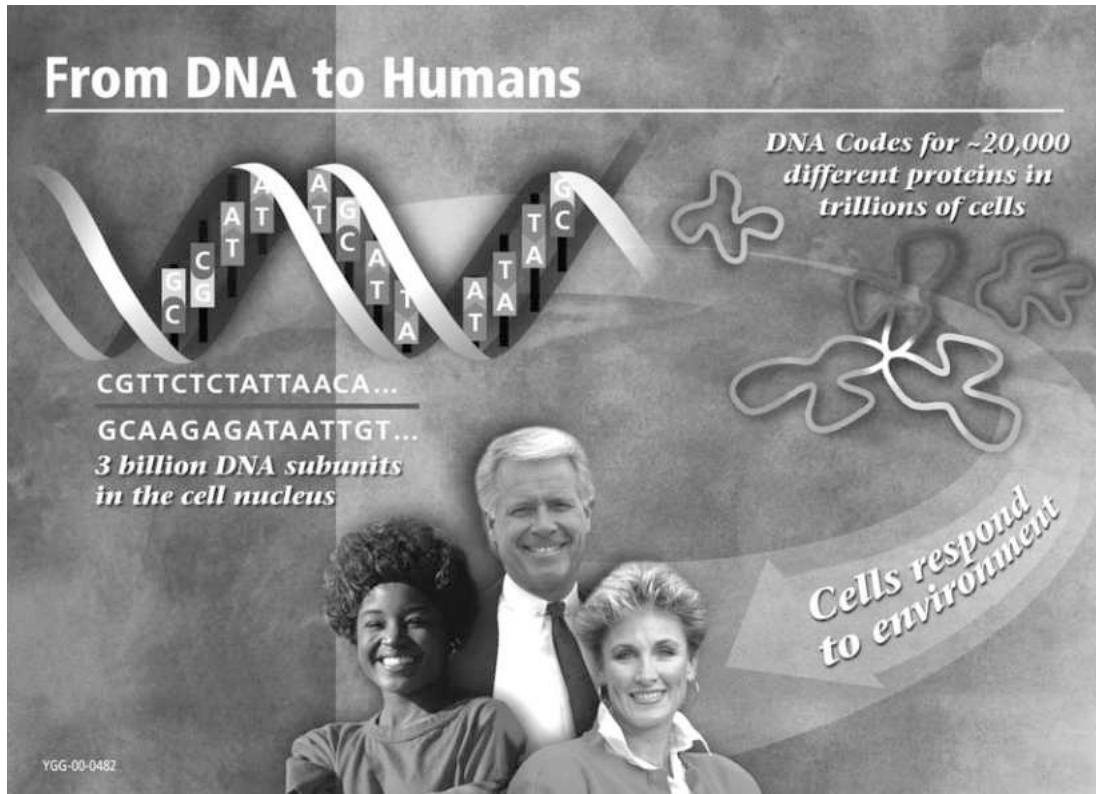


IMAGE CREDIT: U.S. Department of Energy Human Genome Program, <http://www.ornl.gov/hgmis>.

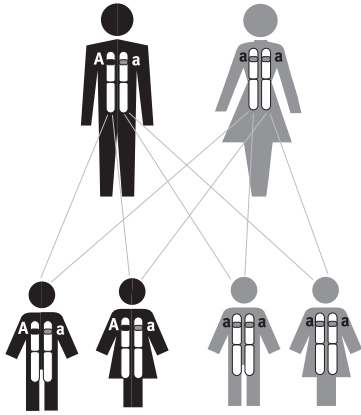
known as aneuploidy, an abnormal number of chromosomes due to an extra or missing chromosome. A usual karyotype (complete chromosome set) contains 46 chromosomes including an XX (female) or an XY (male) sex chromosome pair. Structural chromosomal abnormalities include deletions, duplications, insertions, inversions, or translocations of a chromosome segment. (See *Appendix F* for more information about chromosomal abnormalities.)

Multifactorial diseases are caused by a complex combination of genetic, behavioral, and environmental factors. Examples of these conditions include spina bifida, diabetes, and heart disease. Although multifactorial diseases can recur in families, some mutations such as cancer can be acquired throughout an individual's lifetime. 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 influence genetic traits.

1.3 LAWS OF INHERITANCE

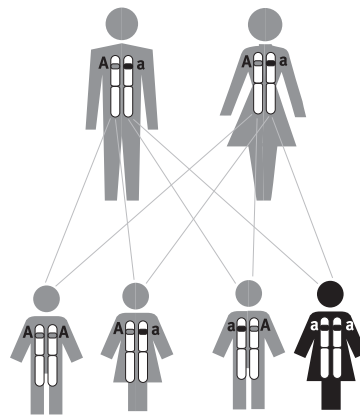
The basic laws of inheritance are useful in understanding patterns of disease transmission. Single-gene diseases are usually inherited in one of several patterns, depending on the location of the gene (e.g., chromosomes 1-22 or X and Y) and whether one or two normal copies of the gene are needed for normal protein activity. Five basic modes of inheritance for single-gene diseases exist: autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive, and mitochondria. (See diagram on following page.)

■ Affected ■ Unaffected



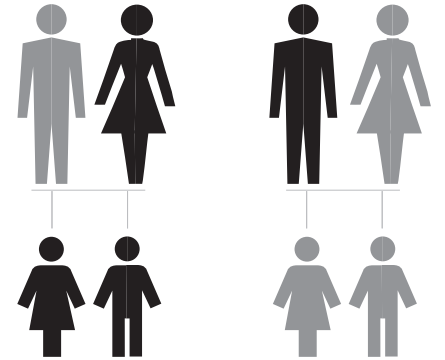
AUTOSOMAL DOMINANT

- 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



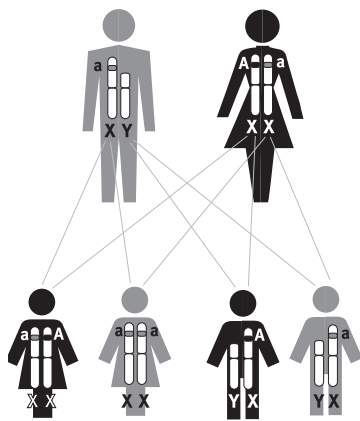
AUTOSOMAL RECESSIVE

- 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



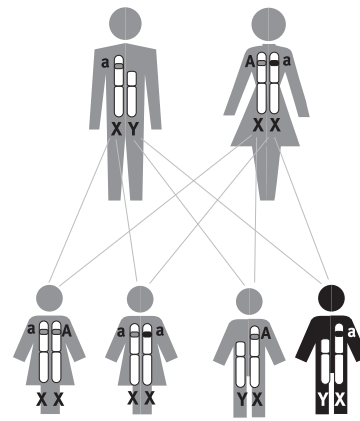
MITOCHONDRIAL

- 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 genetically. The differences in the sequence of DNA among individuals, or genetic variation, explain some of the differences among people such as physical traits and higher or lower risk for certain diseases. Mutations and polymorphisms are forms of genetic variation. While mutations are generally associated with disease and are relatively rare, polymorphisms are more frequent and their clinical significance is not as straightforward. Single nucleotide polymorphisms (SNPs, pronounced “snips”) 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.



Although some genetic variations may cause or modify disease risk, other changes 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 process.

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www.ornl.gov/sci/techresources/Human_Genome/education/education.shtml

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National Human Genome Research Institute

www.genome.gov/health

Online Mendelian Inheritance in Man

www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=omim



CHAPTER 2 : DIAGNOSIS OF A GENETIC DISEASE

Advances in understanding the genetic mechanisms behind disease 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 that may be suggestive of a genetic disease, family history, the different uses of genetic testing, and the different types of genetic diseases.

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

2.1 HISTORY AND PHYSICAL EXAMINATION

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

1. Physical examination
2. Detailed medical family history
3. Clinical and laboratory testing, if appropriate and available

Although 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

Several factors indicate 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, *Pedigree and Family History-taking*). The occurrence of the same condition such as multiple miscarriages, stillbirths, or childhood deaths in more than one family member (particularly first-degree relatives) is suggestive of a genetic disease. Additionally, family history of common adult conditions (e.g., heart disease, cancer, and dementia) that occur in two or more family members at relatively young ages may also suggest a genetic predisposition.

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

Other clinical symptoms suggestive of a genetic disease include developmental delay, mental retardation, and congenital abnormalities. Dysmorphologies (unusual physical features), as well as growth problems, can be suggestive of a genetic disorder. Although these clinical features may be caused by a number of factors, genetic conditions should be considered as part of the differential diagnosis, particularly if the patient expresses several clinical features together that might be indicative of a syndrome (e.g., mental retardation, distinct facial features, and a heart defect or heart defects). Some physical features such as wide-set or droopy eyes, flat face, short fingers, and tall stature may appear unique or slightly different than the average. Even though 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 identifying the presence of a genetic disease.

Genetic conditions should not be ruled out in adolescents or adults, though many genetic conditions appear during childhood. Genetic diseases 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 results in disease later in life.



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 United States is screened for a number of 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 learn if they carry—and thus risk passing to their children—an allele (variant form of the same gene) for a recessive condition such as cystic fibrosis, sickle cell anemia, or Tay-Sachs disease. This type of testing is typically offered to individuals who have a family history of a genetic disorder or 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 chance of having a child with a specific genetic condition.
- **Prenatal diagnostic testing** is used to detect changes in a fetus' 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 H*).
- 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 (see *Appendix G*).
- **Predictive or predispositional 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 conditions 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 being measured. In general, three major types of genetic testing are available: cytogenetic, biochemical, and molecular.

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

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 such as enzymes, transporters, structural proteins, regulatory proteins, receptors, and hormones exist to fulfill multiple functions. A mutation in any type of protein can result in disease if the mutation results in failure of the protein to function correctly. (See Table 2.2 for types of protein alterations that may result in disease.)

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 (buildup of protein)
- Incorrectly assembled protein

Clinical testing for a biochemical disease uses techniques that examine the protein instead of the gene. Tests can be developed to measure directly 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. Since proteins are less stable 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 unknown 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 examine the entire sequence of the CFTR gene routinely to identify the causative mutation because the gene is quite large. However, since the majority of CF cases are caused by approximately 30 mutations, this smaller group of mutations is tested before more comprehensive testing is performed. (See *Appendix I* for more information on genetic testing methodologies.)

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CHAPTER 3 : PEDIGREE AND FAMILY HISTORY-TAKING

Healthcare professionals have long known that common diseases (e.g., heart disease, cancer, and diabetes) and rare diseases (e.g., hemophilia, cystic fibrosis, and sickle cell anemia) can run in families. For example, if one generation of a family has high blood pressure, it is not unusual for the next generation to have similarly high blood pressure. Family history can be a powerful screening tool and has often been referred to as the best “genetic test.” Family history should be updated on each visit, and patients should be made aware of its significance to their health. (See *Appendix D* for the Healthcare Provider Card.)

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. A family history can also identify potential health problems such as heart disease, diabetes, or cancer that an individual may be at increased risk for in the future. Early identification of increased risk may allow the individual and health professional to take steps to reduce risk by implementing lifestyle changes, introducing medical interventions, and/or increasing disease surveillance.



Although providers may be familiar with childhood-onset genetic conditions, 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. The U.S. Preventive Services Task Force (USPSTF) recommends that doctors and patients be aware of family history patterns associated with an increased risk for BRCA mutations.

Another example of an adult-onset disease that can be inherited is Alzheimer's disease. Although most Alzheimer's disease cases are not seen in many consecutive generations, a small number of cases 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 to-date.

Despite the importance of family history in helping define occurrence of a genetic disorder within a family, it should be noted that some genetic diseases—such as single-gene disorders like Duchenne muscular dystrophy and hemophilia A, as well as most cases of Down syndrome, chromosomal deletion syndromes, and other chromosomal disorders—are caused by spontaneous mutations. 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, healthcare professionals start by asking the patient about his/her health history and then ask about siblings and parents.

Questions should include:







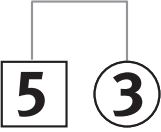


1. General information such as names and birthdates
2. Family's origin or racial/ethnic background
3. Health status, including medical conditions and ages at diagnoses
4. Age at death and cause of death of each deceased family member
5. Pregnancy outcomes of the patient and genetically-related relatives

It may be easier to list all the members of the nuclear family first, 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

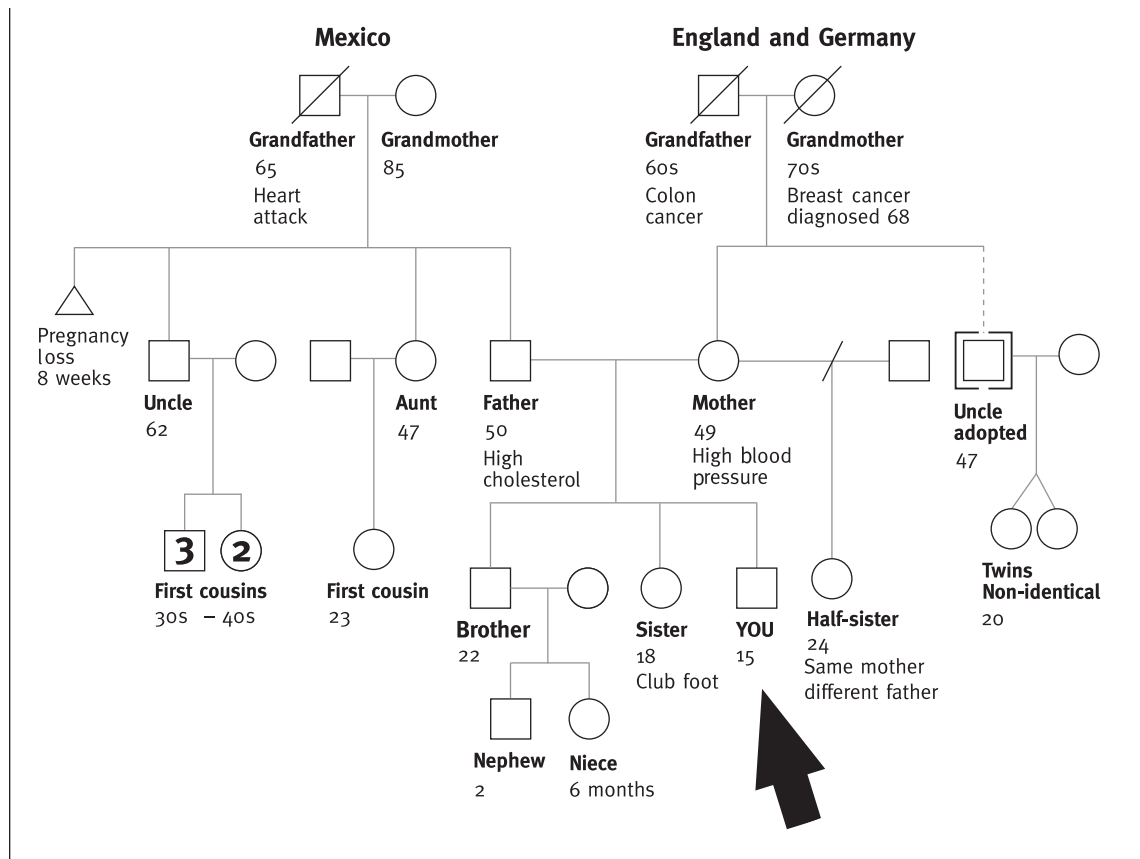
One can record a family history in several ways, including charts, checklists, forms, and drawings of a family tree or "pedigree." Pedigrees are sometimes the preferred method of collecting family history information because a pedigree can be drawn more quickly than the information can be written and allows patterns of disease to emerge as it is drawn. A pedigree represents family members and relationships using standardized symbols (see Pedigree Symbols below). Because the family history continually changes, the pedigree can be updated easily on future visits. Patients should be encouraged to record information and update their family histories regularly.

PEDIGREE SYMBOLS

		WHAT IF INFORMATION ABOUT FAMILY MEMBERS IS LIMITED?
Male	Female	
		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:
Adopted	Deceased Diagonal line used to show that a person has died	
		 Example: This shows that there are 5 boys and 3 girls.
Pregnancy loss Include the number of weeks if known	Stillbirth Include the number of weeks if known	
		2. If you do not know the number of boys and the number of girls, use a diamond with number inside it (if total is known) or a "?."
Divorced/not together Diagonal line used to show parents are divorced or not together		 Example: This shows that there are 8 children.

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

SAMPLE PEDIGREE



SELECTED REFERENCES

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*. www.cdc.gov/genomics/public/famhist.htm

Genetic Alliance. *Taking a Family History*; 2004. www.geneticalliance.org/ws_display.asp?filter=fhh

March of Dimes—Genetics and Your Practice. www.marchofdimmes.com/gyponline/index.bm2

My Family Health Portrait
familyhistory.hhs.gov

U.S. Department of Health and Human Services. U.S. Surgeon General's Family Health Initiative; 2004. www.hhs.gov/familyhistory/





CHAPTER 4 : NEWBORN SCREENING

Almost every child born in the United States undergoes state-mandated newborn screening. In each state, a small blood sample (“heel stick”) is collected within 48 hours of birth. The sample is sent to a laboratory and tested for a panel of medical conditions. State newborn screening panels include testing for an ever-increasing number of conditions. Every year, over 100,000 newborns have an abnormal screen for one of these conditions. In the event that a newborn is affected by one of the diseases screened for, 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 the New York – Mid-Atlantic region. In the U.S., newborn screening programs are state-mandated, and each state’s list of screened conditions varies. Efforts are underway to develop a consistent panel to be used throughout the U.S. New technologies have enabled substantial expansion of newborn screening programs.

4.1 OVERVIEW OF NEWBORN SCREENING

By state law, all newborns are screened for various serious medical conditions. Babies with any of these conditions may look healthy at birth; but, if left untreated, these conditions can cause health problems such as mental retardation, slow growth, and even death. These outcomes may be prevented with treatment and long-term follow-up.

Newborn screening programs began in the U.S. in the 1960s with the work of Dr. Robert Guthrie, who developed a screening test for phenylketonuria (PKU). PKU is an inherited metabolic disease caused by a mutation of the gene for 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 would otherwise lead to brain damage and mental retardation. When Dr. Guthrie introduced a system for collecting and transporting blood samples on filter paper, cost-effective, wide-scale genetic screening became possible.



4.1.1 Screening Procedure and Follow-up. A nurse or other medical professional takes a few drops of blood from the baby's heel. The blood should be drawn after the baby is 24 hours old, but before the baby leaves the hospital. This blood sample is sent to a newborn screening laboratory. The baby's doctor contacts the parent(s) if the results are not in normal range for any of the screened conditions. If this scenario occurs, follow-up testing may be required.

4.1.2 Retesting. Sometimes a baby must be screened 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
- A problem occurred with the way the blood sample was taken
- The first test showed risk of 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.

4.1.3 Clinical Evaluation and Diagnostic Testing. Occasionally, the results of the newborn screen strongly suggest that the infant has one of the conditions. The newborn screening program notifies one of four specialty-care centers, depending on which test was abnormal. The specialties are metabolic, cystic fibrosis, endocrine, and hematology. The parents will be notified by the newborn screening program, the primary physician, the hospital of birth, or the specialty-care center, depending on the newborn screening program's protocol. If this happens, it is extremely important that the parents bring their child to the specialist as soon as possible, sometimes that very day, for further evaluation and laboratory testing.

4.1.4 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.



4.1.5 Tests Performed. Completed tests vary from state to state. Typically, each state has an advisory committee that reviews and selects which conditions are screened for based on current scientific and clinical data. Social and ethical issues are also included in the decision-making process. Increasingly, tandem mass spectrometry is being used for newborn screening. This technology is capable of screening for over 50 metabolic conditions from dried blood-spot specimens. In 1999, the American College of Medical Genetics released a report commissioned by the U.S. Health Resources and Services Administration recommending a uniform screening panel of 29 genetic conditions. Efforts are under way to examine the feasibility of instituting a uniform newborn screening policy so that every infant is screened for the same conditions, regardless of the state in which he or she is born. In general, the conditions on newborn screening panels fall into one of the following groups: metabolic conditions, endocrine conditions, hemoglobin conditions, and pulmonary conditions.

For information on the diseases tested for in a particular state, contact that state's newborn screening program or the National Newborn Screening and Genetics Resource Center (*genes-r-us.uthscsa.edu*). Screening for more conditions may be available at other laboratories for a fee.

4.2 NEWBORN SCREENING PROGRAMS

Delaware

Delaware Health and Social Services,
Division of Public Health
Delaware Public Health Laboratory
30 Sunnyside Road
P.O. Box 1047
Smyrna, DE 19977
Ph: 302.223.1520
www.dhss.delaware.gov/dhss/dph/chca/dphnsp1.html

District of Columbia

District of Columbia Department of Health
Newborn Screening Program
825 North Capital Street, NE
Washington, DC 20002
Ph: 202.650.5000
www.dchealth.dc.gov/doh/site/default.asp

Maryland

Maryland Department of Health and
Mental Hygiene
Division of Newborn and
Childhood Screening
201 West Preston Street, Room 1A6
Baltimore, MD 21201
Ph: 410.767.6099
www.fha.state.md.us/genetics/newprog.cfm

New Jersey

New Jersey Department of Health and
Senior Services
Public Health and Environmental Laboratories
Newborn Genetic and Biochemical
Screening Program
Health and Agriculture Building
Market & Warren Streets, P.O. Box 371
Trenton, NJ 08625
Ph: 609.292.4811
www.state.nj.us/health/fhs/nbs/index.shtml

New York

New York State Department of Health
Wadsworth Center
Newborn Screening Program
Empire State Plaza, P.O. Box 509
Albany, NY 12201
Ph: 518.473.7552
www.wadsworth.org/newborn

Pennsylvania

Pennsylvania Department of Health
Bureau of Family Health
Division of Newborn Screening
Health and Welfare Building
7th and Forster Streets
7th Floor, East Wing
Harrisburg, PA 17120
Ph: 717.783.8143
www.dsf.health.state.pa.us/health/cwp/view.asp?a=179&q=232592

Virginia

Virginia Department of Health
 Division of Child and Adolescent Health
 Pediatric Screening and Genetic Services
 109 Governor Street, 8th Floor
 Richmond, VA 23219
 Ph: 804.864.7712
www.vahealth.org/genetics

West Virginia

West Virginia Department of Health and
 Human Resources
 Office of Maternal, Child, and Family Health
 Newborn Metabolic Screening Program
 350 Capitol Street, Room 427
 Charleston, WV 25301
 Ph: 304.558.5388
www.wvdhhr.org/nbms

4.3 NEWBORN HEARING SCREENING



Hearing loss is a common condition present in as many as one 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.

4.3.1 Screening Procedure. Babies are usually screened in the first few days of life, before they are discharged from the hospital. The screen, 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. The OAE test measures how the baby's inner ear responds to sound, and the ABR test measures how the brain responds to sound. Typically, testing is done when the baby is asleep and unaware of the testing. Passing the hearing screening indicates that the baby's hearing is within the normal range at the time of the test. However, some babies with a family history of hearing loss, repeated ear infections, or serious illness may develop hearing loss later. The child's hearing and speech should be monitored as he or she grows.

4.3.2 Retesting. Babies who do not pass the first screening are retested and may be referred to an audiologist (hearing specialist). The second screening should occur while the baby is still in the hospital or within two weeks after leaving the hospital. If the baby does not pass the initial hearing screening, it does not mean that the baby has permanent hearing loss since most babies who do not pass the first hearing screening pass the second screening. Often, babies can have fluid, blockage, or debris in the ear that clears naturally. If further testing shows that a baby has hearing loss, an audiologist along with an ear, nose, and throat specialist can best determine the next steps.

4.3.3 Treatment. Treatment will depend on the type and degree of hearing loss. If hearing loss is permanent, treatment options include hearing aids, cochlear implants, or early intervention services.



4.4 NEWBORN HEARING SCREENING PROGRAMS

Delaware

Delaware Health and Social Services,
 Division of Public Health
 Delaware Newborn Hearing
 Screening Program
 655 Bay Road, Suite 216
 Dover, DE 19903
 Ph: 302.741.2975
www.dhss.delaware.gov/dhss/dph/chcal/dphnhsp1.html

District of Columbia

District of Columbia Department of Health
 Newborn Hearing Screening Program
 825 North Capital Street NE, 3rd Floor
 Washington, DC 20002
 Ph: 202.671.5000

Maryland

Maryland Department of Health and
 Mental Hygiene
 Office of Genetics and Children with
 Special Health Care Needs
 Infant Hearing
 201 West Preston Street, Room 423A
 Baltimore, MD 21201
 Ph: 410.767.6432
www.fha.state.md.us/genetics/inf_hrg.cfm

New Jersey

New Jersey Department of Health and
 Senior Services
 Early Hearing Detection and
 Intervention Program
 50 East State Street, P.O. Box 364
 Trenton, NJ 08625
 Ph: 609.292.5676
www.nj.gov/health/fhs/ehdi/index.shtml

New York

New York State Department of Health
 Division of Family Health
 Early Intervention Program
 Empire State Plaza
 Corning Tower, Room 287
 Albany, NY 12237
 Ph: 518.473.7016
www.health.state.ny.us/community/infants_children/early_intervention/newborn_hearing_screening

Pennsylvania

Pennsylvania Department of Health
 Pennsylvania Newborn Hearing Screening and
 Intervention Program
 Health and Welfare Building
 7th and Forster Streets
 7th Floor, East Wing
 Harrisburg, PA 17108
 Ph: 717.783.8143
www.dsf.health.state.pa.us/health/CWP/view.asp?A=179&QUESTION_ID=232585

Virginia

Virginia Department of Health
 Virginia Early Hearing, Detection, and
 Intervention Program
 109 Governor Street, 8th Floor
 Richmond, VA 23219
 Ph: 804.864.7713
www.vahealth.org/hearing

West Virginia

West Virginia Department of Health and
 Human Resources
 Office of Maternal, Child, and Family Health
 Right From The Start Project
 Department of Health
 350 Capitol Street, Room 427
 Charleston, WV 25301
 Ph: 304.558.5388
www.wvdhhr.org/rfts/newbornhearing.asp

SELECTED REFERENCES

Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children

www.hrsa.gov/heritabledisorderscommittee/

American Academy of Pediatrics, Newborn Screening Overview

www.medicalhomeinfo.org/screening/newborn.html

Centers for Disease Control and Prevention, Early Hearing Detection and Intervention Program

www.cdc.gov/ncbddd/ehdi

March of Dimes

www.marchofdimes.com

National Newborn Screening and Genetics Resource Center

genes-r-us.uthscsa.edu





CHAPTER 5 : GENETIC COUNSELING

As members of a healthcare team, genetic counselors provide information and support to families affected by or at risk for a genetic disorder. They serve as a central resource of information about genetic disorders for other healthcare 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. Patient resources are also provided.

5.1 ROLE OF GENETIC COUNSELING

Genetic counselors help identify families at possible risk of a genetic condition by gathering and analyzing family history and inheritance patterns and calculating chances of recurrence. They provide information about genetic testing and related procedures. They are trained to present complex and difficult-to-comprehend information about genetic risks, testing, and diagnosis to families and patients. Genetic counselors can help families understand the significance of genetic conditions in relation to cultural, personal, and familial contexts. They also discuss available options and can provide referrals to educational services, advocacy and support groups, other health professionals, and community or state services. Genetic counselors can serve as a central resource of information about genetic conditions for other healthcare professionals, patients, and the general public. (See *Appendix O* for *Making Sense of Your Genes: A Guide to Genetic Counseling*.)

5.2 PROCESS OF GENETIC COUNSELING

In general, a genetic counseling session aims to:

- Increase the family's understanding of a genetic condition
- Discuss options regarding disease management and the risks and benefits of further testing and other options
- Help the individual and family identify the psychosocial tools required to cope with 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 medical history, and assess and record the medical and psychosocial history of the patient.

Among the topics that may be discussed during a pre-testing session are the clinical presentation of the condition(s) the patient may be at risk for, pattern of genetic inheritance of the condition, chance 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 that 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 psychosocial counseling are offered. Information about community resources and support groups can be provided to the patient/family.

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





At the conclusion of the final genetic counseling session, the patient may receive 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 and can include additional information that became available after the final counseling session. The patient may choose to share the letter with other family members or healthcare providers.

5.3 PATIENT EDUCATION

Many patients rely heavily on their primary healthcare providers for information related to their condition. In general, though, patients will require information providers may not have. Before providing patients with any educational materials, providers should be sure to check that the information is current and produced by a credible source.

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

Genetic Alliance

4301 Connecticut Avenue, NW, Suite 404
 Washington, DC 20008
 Ph: 202.966.5557
 Fax: 202.966.8553
 Email: info@geneticalliance.org
www.geneticalliance.org

Genetic and Rare Diseases Information Center (GARD)

P.O. Box 8126
 Gaithersburg, MD 20898
 Ph: 888.205.2311
 TTY: 888.205.3223
 Fax: 240.632.9164
 Email: GARDinfo@nih.gov
www.genome.gov/health/gard

Genetics Home Reference

Reference and Web Services
 National Library of Medicine
 8600 Rockville Pike
 Bethesda, MD 20894
 Ph: 888.346.3656
 Fax: 301.496.2809
 Email: custserv@nlm.nih.gov
www.ghr.nlm.nih.gov

National Organization of Rare Diseases (NORD)

55 Kenosia Avenue, P.O. Box 1968
 Danbury, CT 06813
 Ph: 203.744.0100
 TTY: 203.797.9590
 Fax: 203.798.2291
 Email: orphan@rarediseases.org
www.rarediseases.org

SELECTED REFERENCES**American College of Medical Genetics, Newborn Screening Act Sheets and Confirmatory Algorithms**

www.acmg.net/resources/policies/act/condition-analyte-links.htm

Genetic Alliance Disease InfoSearch

www.geneticalliance.org/dis

International Society of Nurses in Genetics

www.isong.org

March of Dimes

www.marchofdimes.com (Spanish at www.nacersano.org)

MedlinePlus

www.nlm.nih.gov/medlineplus

National Human Genome Research Institute–Health

www.genome.gov/health

National Society of Genetic Counselors (NSGC)

www.nsgc.org





CHAPTER 6 : INDICATIONS FOR A GENETIC REFERRAL

Referrals to genetic specialists should be considered if a healthcare provider suspects a patient is at risk for or affected with a genetic disorder. Genetic specialists can help identify the appropriate tests to order, consider the family history, and provide information about the treatment and long-term outcomes for patients diagnosed with a genetic disorder. They may recommend a referral or referrals 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 *Section 2.2: Red Flags for Genetic Disease*. Specific clinical guidelines are available for some conditions such as cancer and diabetes.

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, developmental disability, 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, or cancer, particularly if onset is early in adulthood
- Couples who would like testing or more information about genetic conditions that occur with higher frequency in their ethnic group

6.1.2 Delayed Growth and Development

- 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 newborn screening

6.1.3 Reproductive Issues

- Women who are interested in genetic testing or screening
- Women who have experienced multiple pregnancy losses or babies who died in infancy
- People concerned that their jobs, lifestyles, or medical history may pose a risk to the outcome of a 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 indicate that their pregnancy may be at increased risk for certain complications or birth defects

A genetic specialist can provide assistance in several ways: a formal or informal consultation, genetic counseling session, or genetic evaluation. A genetic specialist can provide an accurate assessment 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 considered for referral are clinical geneticists and genetic counselors. Although these specialists can play a major role in the diagnosis and education of family members with a genetic disorder, other medical specialists such as surgeons, cardiologists, or ophthalmologists may be required for appropriate treatment or intervention. The services of other allied health professionals such as nutritionists, social workers, psychologists, and occupational and physical therapists may also be necessary. 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

GeneTests

www.genetests.org

March of Dimes, Genetics and Your Practice

www.marchofdimes.com/gyponline/index.bm2

National Cancer Institute, Cancer Genetics Service Directory

www.cancer.gov/search/genetics_services

National Society of Genetic Counselors

www.nsgc.org/resourcelink.cfm



CHAPTER 7 : PSYCHOLOGICAL AND SOCIAL IMPLICATIONS

Genetic disorders impact not only the physical condition, but also the psychological and social health 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 services can also help address the psychological health of the patient and family.

The personal and permanent nature of genetic disease can raise a range of emotions including guilt, fear, and helplessness. Specialists such as genetic counselors, social workers, and psychologists, as well as members of support groups, can be extremely helpful to patients and families as they deal with these difficult issues.

7.1 GENETIC INFORMATION AND OTHER MEDICAL INFORMATION

Genetic information is often perceived as different from other medical information. Some people believe that genetic information is uniquely sensitive because of its predictive nature and potential implications for other family members; therefore, it raises unique social issues. This belief has translated to specific policy positions to protect genetic information and prevent it from becoming part of a patient's medical record. Others believe that genetic information is like other medical information, and the same protections and high standards of privacy and confidentiality should apply to all personal medical information. In fact, they believe that treating genetic information differently from other medical information may result in unintended disparities.

Regardless, both genetic and non-genetic medical information:

- Have the potential to help or harm patients and must be considered in making patient care decisions
- Are complex and demands 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 decisions

Concerns that may be specific to genetic information:

- Provides information about family members and relatives; disclosure of genetic information often directly impacts other family members
- Can lead to breaches of confidentiality that must be considered and addressed proactively

7.2 A LIFETIME OF AFFECTED RELATIONSHIPS

Genetic conditions have powerful effects on families. Like many chronic conditions, they may require continuous attention and lack cures. They have implications for the health of relatives. So a genetic diagnosis for one family member may mean other biological relatives are 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 difficult treatment options, the chance that additional offspring will inherit the condition, and prenatal and newborn testing decisions.



7.3 IMPACT OF A GENETIC DIAGNOSIS

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

7.3.1 Patients. A genetic diagnosis can provide a great benefit to patients. When the condition is rare and patients and families spend years without knowing its name or cause, a diagnosis can help make sense of the situation. Diagnoses can 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. A common response is that the science of genetics is confusing and frustrating. Patients identified with a genetic diagnosis may consider themselves at fault or “broken” or interpret their diagnosis as leading to something they cannot handle. A genetic diagnosis can lead to concerns about stigmatization.

The reaction to a diagnosis varies from individual to individual and is affected by many factors including age, gender, education, religion, and culture. Providers should be aware of these differences and understand the patient’s background in order to communicate effectively.

7.3.2 Parents. Understandably, diagnosis of a genetic condition may put stress on a relationship. Couples with an affected child often face difficult family-planning decisions because future children may have a chance of inheriting the condition. Depending on the condition, parents may also be faced with hard choices regarding prenatal testing and termination of a pregnancy. The magnitude of these decisions and their outcomes impacts both individuals and relationships. Parents may experience guilt due to the hereditary nature of genetic conditions.

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 disease, family members who do not have the disease often feel guilt that loved ones are affected when they are not. For adult-onset diseases, unaffected spouses may view their partners differently. The diagnosis can lead to a breakdown in communication. Siblings of children with special needs sometimes feel neglected because parents may focus more time and effort on the siblings affected by a genetic condition. Including unaffected family members in the care of individuals with special needs can help them examine their own emotional issues. Adults who are diagnosed with a genetic condition and are considering having a child may need to consider the chance of having an affected child, as well as their ability to care for the child.

In cases where 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. Advocacy groups, state health departments, and The Patient Advocate Foundation are all organizations that may provide a starting point for support services.

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 firsthand what it means to be faced with a diagnosis and 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, including newborn screening, will be used to segregate their communities. These fears often work in combination with other difficulties, including availability of services and health insurance, communication, and cultural barriers, when navigating the medical system.

Some communities do not see their condition as a disability, but rather as one aspect of their lifestyle. For example, members of the deaf community may oppose hearing tests for this reason. In general, it is a good idea to understand the communities to 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 may be 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, 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. The manner in which healthcare providers react has a large 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 healthcare providers help parents cope with the birth of a child with an inherited condition:

- Focus on the child's overall well-being, not solely on the child's genetic condition at routine visits. Talk about the newborn's personality, feeding patterns, and other personal traits. 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 have thought about the questions themselves.
- Explain the genetics of the condition in an understandable manner. Consider referring the parents to a genetic specialist.
- Emphasize that you are aware of the difficulty of the situation and acknowledge that each parent has his/her own way of coping with the stress of caring for an infant with special needs. It may be helpful for families to share their feelings with others. 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 firsthand experience about caring for an infant with the condition, provide information about expectations for the affected infant, and suggest coping mechanisms that will help both parents and siblings adjust to new challenges.

SELECTED REFERENCES

Burke W, Fryer-Edwards K, and Pinsky LE (eds). 2001. Genetics in Primary Care (GPC): Training Program Curriculum Materials.
genes-r-us.uthscsa.edu/resources/genetics/primary_care.htm

Genetic Alliance

www.geneticalliance.org

National Organization for Rare Diseases

www.rarediseases.org

Organizations for Support Groups & Information (Genetic/Rare Conditions)

www.kumc.edu/gec/support/grouporg.html#specific

The Patient Advocate Foundation

www.patientadvocate.org



CHAPTER 8 : ETHICAL, LEGAL, AND SOCIAL ISSUES

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

Concerns have arisen regarding the use and potential misuse of genetic information. The unease relates to a range of misuse: from the analytical and clinical validity of a genetic test, to the possible stigma of carrying a genetic difference, to the duty of disclosing genetic information to potentially affected family members.

8.1 DESCRIPTION OF ETHICAL, LEGAL, AND SOCIAL ISSUES

To protect patients from additional distress, healthcare providers should be aware of the relevant ethical, legal, and social issues related to genetics in healthcare. Genetic specialists may be able to address specific patient concerns and questions regarding these issues.

8.1.1 Communicating Test Results. It is critical that genetic test results are discussed with patients in an understandable and compassionate 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 personal 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 offer genetic tests directly to consumers without requiring physician involvement. Patients should be cautious when considering direct-to-consumer genetic testing and are encouraged to discuss this option with their healthcare professional. Some of these companies may play off consumer fears, offer tests with little clinical utility, or not be properly certified or licensed.

8.1.3 Duty to Disclose. The results of a genetic test may have implications for a patient's family members. However, healthcare 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 differently in response to distinct 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
- Harm from failing to disclose outweighs the harm from disclosure

8.1.4 Genetic Discrimination. When considering genetic testing, the potential for discrimination based on genetic information is a major concern often raised. This fear can impact an individual's decision to utilize genetic testing services. Since genetic test results are typically included in an individual's medical record, people should be aware that the results could be accessible to others.

On May 21, 2008, President Bush signed the Genetic Information Nondiscrimination Act (GINA) into law. As the first major new civil rights bill of the new century, GINA protects individuals from discrimination on the basis of genetic information in health insurance and



employment. The health insurance provisions of the law take effect 12 months after the date of signing, in May 2009, and the employment protections take effect 18 months after the date of signing, in November 2009.

In summary, GINA prevents health insurers from denying coverage or adjusting premiums on the basis of genetic information or requesting that an individual undergo a genetic test. Similarly, employers are prohibited from using genetic information to make hiring, firing, or promotion decisions. The law also limits an employer's right to request, require, or purchase an employee's genetic information. GINA does not apply to life, disability, or long-term care insurance. Before the federal protections of GINA, more than 40 states established legislation prohibiting genetic discrimination. However, the scope of these protections differs from state to state. GINA does not overturn broader protections provided in some state regulations.

In addition to fears of discrimination in employment and health insurance, members of some communities often fear that genetic information will be used to stigmatize them. Healthcare providers should be sensitive to the fact that some groups may distrust the use of genetics as a health tool.

8.1.5 Informed Consent. To help ensure that patients understand the risks and benefits of healthcare 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:

- Risks, limitations, and benefits of testing or not testing
- Alternatives to genetic testing
- Details of the testing process (e.g., what type of sample is required, accuracy of test, and turn-around time)
- Privacy/confidentiality of test results
- The voluntary nature of testing
- Potential consequences related to results, including: (1) impact on health; (2) emotional and psychological reactions; (3) treatment/prevention options; and (4) ramifications for the family

8.1.6 Privacy. Genetic information has enormous implications for the individual and the family. The privacy of that information is a major concern to patients—in particular, who should have or needs access to that information. To protect personal genetic information and avoid its inclusion in a patient's medical record, some patients pay for genetic testing out-of-pocket.

8.1.7 Psychosocial Impact. Every individual will respond differently to news of his/her genetic test results, whether negative or positive. As there is no right or wrong response, healthcare professionals should refrain from judgment and help the patient understand the test results with respect to his/her own health, available interventions or follow-up, and risks to his/her family. An individual may respond to genetic information on several levels: individual, family, or community and society. 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, and 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 nondirective stance and support the patients' decisions.

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. Genetic information may influence one individual to change his or her lifestyle or behavior to reduce risk or disease severity; whereas, 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 him/her 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 treatment is unavailable or 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 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 he or she considers whether or not testing is appropriate for him/her. 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) or another governmental certifying entity.

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American Medical Association. "Why physicians should know the legal and ethical issues raised by genetic information and technology." *Genethics*. 2000.

American Society of Human Genetics. **Professional disclosure of familial genetic information.** *American Journal of Human Genetics*. 1998; 62: 474-483.
www.ashg.org/pdf/pol-29%20.pdf

Coalition for Genetic Fairness

www.geneticfairness.org

Lehmann LS, Weeks JC, Klar N, et al. **Disclosure of familial genetic information: perceptions of the duty to inform.** *American Journal of Medical Genetics*. 2000; 109(9): 705-711.

March of Dimes, **Genetics and Your Practice**

www.marchofdimes.com/gyponline/index.bm2

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

www.ornl.gov/sci/techresources/human_genome/research/elsi.shtml





CHAPTER 9 : PATIENT STORIES AND CONSUMER PROFILES

This chapter contains four true stories about inherited cancer, newborn screening, late-onset disease, and family history told from the perspective of a patient or consumer. Diagnosing a genetic condition can be a challenging and lengthy process involving multiple doctors and office visits, examinations, testing, and months or years of stress and uncertainty. The lack of treatment or effective interventions can be extremely frustrating and difficult to comprehend. However, genetic diagnosis can enhance educated decision-making and alleviate the stress of the unknown. It can also encourage healthy lifestyle choices and inform family planning. These stories can help both health professionals and patients understand the issues faced by patients and families affected by a genetic condition and learn how to deal with these issues.

9.1 INHERITED BREAST AND OVARIAN CANCER

My grandmother, my dad, and I have all had breast cancer, and our stories are inextricably linked.

My grandmother was diagnosed with breast cancer when she was in her late 30s, had a mastectomy, and lived until age 95! What an inspiration she was!

Most people don't know that men can get breast cancer too. Dad discovered his breast cancer in 2001. While showering, he felt a lump in his left breast/chest area. His doctor confirmed it was suspicious. Dad had a mammogram and then a mastectomy to get rid of the cancer. Shortly after, he was diagnosed with prostate cancer and underwent 40 radiation treatments over eight weeks. His cancers of the breast and prostate were genetically linked. Within a few years, he was diagnosed with bladder cancer. Fortunately, this was caught early and removed, and from that point on he has been cancer free. My dad is now 78 years old and going strong.

After my dad's cancers, his oncologist tested him for the BRCA2 gene mutation and discovered he was positive as a carrier. My siblings and I were tested to see if we were carriers too. I was positive for BRCA2, which carries up to an 85 percent lifetime risk of breast cancer for women.

The oncologist gave me valuable suggestions. He directed me to support groups, where I found good answers to the many questions I had about my risks and options. I researched my options and, based on my BRCA risk, decided to have a bilateral mastectomy with immediate reconstruction. I selected two amazing plastic surgeons to perform DIEP, an advanced reconstruction procedure that, without implants, leaves a woman's breasts whole, made of my own soft, warm, living tissue. I do not feel as if I lost my breasts...only my risk of breast cancer.

My breast surgeon said to consider myself cured. I still have regular breast exams, although my chance of having breast cancer is now 1 to 2 percent, which is lower than the general population's 8 to 12 percent risk. I am satisfied that I have now done all I can to prevent cancer.

Looking back over my family's history, I am reminded that we are a tough bunch—survivors and co-survivors all. Thanks to medical research advances, the future of my children, and all BRCA mutation carriers is bright.

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 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 retested. The second test also came back positive. Without a doubt, Miguel had this disorder; though he still seemed completely healthy. The doctor told us that children with this rare genetic disorder are unable to break down excessive protein and 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 what 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 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, 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, and Boy Scouts. Since 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 had 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 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, cirrhosis of the liver, 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 (a procedure similar to donating blood) to keep the iron from accumulating in my body and damaging my organs. 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 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, despite drinking plenty of water and other beverages. In spite of my increased drinking habits and normal appetite, I somehow lost 40 pounds. Finally, my discomfort from the skin condition became so severe that I went to the emergency room, where I was diagnosed with Type II diabetes. Apparently, I had actually had this condition for some time.

Since my diagnosis, I have learned a lot about my family and 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 realized my risk was greater than that of someone without a family history.

Additionally, 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. Also, 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 : GENETICS RESOURCES AND SERVICES

This chapter contains contact information specifically for genetics resources and service providers in the states that comprise the New York – Mid-Atlantic region. Also, contact information is listed for the Genetics and Newborn Screening Regional Collaborative Groups, as well as for selected national resources.

DELAWARE RESOURCES**Children with Special Healthcare Needs**

Delaware Health and Social Services
655 Bay Road, Suite 216
Dover, DE 19903
Ph: 302.741.2980
www.dhss.delaware.gov/dph/chcal/dphschcn.html

Maternal and Child Health (Title V)

Delaware Health and Social Services
655 Bay Road, Suite 216
Dover, DE 19903
Ph: 302.741.2980
www.dhss.delaware.gov/dhss

Newborn Screening Laboratory

Delaware Health and Social Services, Division
of Public Health
Delaware Public Health Laboratory
30 Sunnyside Road
P.O. Box 1047
Smyrna, DE 19977
Ph: 302.223.1520
www.dhss.delaware.gov/dhss/dph/chcal/dphnsp1.html

Newborn Screening Follow-up

Delaware Health and Social Services
655 Bay Road, Suite 216
Dover, DE 19903
Ph: 302.744.4544

Newborn Hearing Screening

Delaware Health and Social Services
655 Bay Road, Suite 216
Dover, DE 19903
Ph: 302.744.4544
www.dhss.delaware.gov/dhss/dph/chcal/dphnhsp1.html

State Genetic Services Program

Delaware Health and Social Services
655 Bay Road, Suite 216
Dover, DE 19903
Ph: 302.741.2990

Family Voices of Delaware

Ph: 888.835.5669
www.familyvoices.org/states.php?state=DE

March of Dimes: Delaware Chapter

236C North James Street, Tower Office Park
Newport, DE 19804
Ph: 302.225.1020
www.marchofdimes.com/delaware

DELAWARE GENETICS PROVIDERS/REFERRALS**Alfred I. duPont Hospital for Children**

Division of Medical Genetics
1600 Rockland Road
Wilmington, DE 19899
Ph: 302.651.5916
www.nemours.org/service/genetics.html

DISTRICT OF COLUMBIA RESOURCES**Children with Special Health Care Needs**

Community Health Administration
825 North Capitol Street, NE, 3rd Floor
Washington, DC 20002
Ph: 202.671.5000

Maternal and Child Health (Title V)

District of Columbia Department of Health
Community Health Administration
825 North Capitol Street, NE, 3rd Floor
Washington, DC 20002
Ph: 202.442.9333

Newborn Screening Testing and Follow-up

District of Columbia Department of Health
Newborn Screening Program
825 North Capitol Street, NE, 3rd Floor
Washington, DC 20002
Ph: 202.650.5000

Newborn Hearing Screening

District of Columbia Department of Health
Newborn Hearing Screening Program
825 North Capitol Street, NE, 3rd Floor
Washington, DC 20002
Ph: 202.671.5000

Genetic Services Program

District of Columbia Department of Health
Genetics Program/Maternal and Child Health
825 North Capitol Street, NE, 3rd Floor
Washington, DC 20002
Ph: 202.727.7667



Family Voices of DC

Ph: 202.230.8201

*www.familyvoices.org/states.php?state=DC***March of Dimes: District of
Columbia Chapter**

2700 South Quincy Street, Suite 220

Arlington, VA 22206

Ph: 703.824.0111

*www.marchofdimes.com/marylandmetrodc***DISTRICT OF COLUMBIA GENETICS
PROVIDERS/REFERRALS****Children's National Medical Center**

111 Michigan Avenue, NW

Washington, DC 20010

Ph: 202.476.2187

*www.childrensnational.org/Departmentsand
Programs/default.aspx?Id=378&Type=Dept&
Name=Genetics%20and%20Metabolism***Georgetown University Hospital**

3800 Reservoir Road, NW, 2 PHC

Washington, DC 20007

Ph: 202.444.8518

*www.georgetownuniversityhospital.org/body.
cfm?id=601***MARYLAND RESOURCES****Children with Special Healthcare Needs**Maryland Department of Health and
Mental HygieneOffice for Genetics and Children with Special
Healthcare Needs

201 West Preston Street, Room 319

Baltimore, MD 21201

Ph: 410.767.6730

Maternal and Child Health (Title V)Maryland Department of Health and
Mental Hygiene

201 West Preston Street, Room 317

Baltimore, MD 21201

Ph: 410.767.6713

*www.dhmb.state.md.us***Newborn Screening Laboratory**Maryland Department of Health and
Mental HygieneDivision of Newborn and
Childhood Screening

201 West Preston Street, Room 1A6

Baltimore, MD 21201

Ph: 410.767.6099

*www.fha.state.md.us/genetics/newprog.cfm***Newborn Screening Follow-up**Maryland Department of Health and
Mental HygieneOffice for Genetics and Children with Special
Healthcare Needs

201 West Preston Street, Room 319

Baltimore, MD 21201

Ph: 410.767.6730

*www.fha.state.md.us/genetics/newprog.cfm***Newborn Hearing Screening**Maryland Department of Health and
Mental HygieneOffice for Genetics and Children With Special
Healthcare Needs

Infant Hearing Program

201 West Preston Street, Room 423A

Baltimore, Maryland 21201

Ph: 410.767.6432

*www.fha.state.md.us/genetics/inf_brg.cfm***State Genetic Services Program**Maryland Department of Health and
Mental HygieneOffice for Genetics and Children with Special
Healthcare Needs

201 West Preston Street, Room 319

Baltimore, MD 21201

Ph: 410.767.6730

*www.fha.state.md.us/genetics***Family Voices of Maryland**

Ph: 800.394.5694

Ph: 410.768.9100

www.familyvoices.org/states.php?state=MD

March of Dimes: Maryland Chapter

175 West Ostend Street, Suite C
 Baltimore, MD 21230
 Ph: 410.752.7990
www.marchofdimes.com/marylandmetrodc

MARYLAND GENETICS PROVIDERS/REFERRALS**The Johns Hopkins Children's Center**

600 North Wolfe Street
 Baltimore, MD 21287
 Ph: 410.614.6112
www.hopkinschildrens.org

University of Maryland Hospital for Children

22 South Greene Street
 Baltimore, MD 21201
 Ph: 800.492.5538
www.umm.edu/pediatrics/ped-genetics.htm

NEW JERSEY RESOURCES**Children with Special Healthcare Needs**

New Jersey Department of Health and Senior Services
 Special Child Health Services
 50 East State Street, P.O. Box 364
 Trenton, NJ 08625
 Ph: 609.984.0755
www.state.nj.us/health/fhs/schl/index.shtml

Maternal and Child Health (Title V)

New Jersey Department of Health and Senior Services
 Division of Family Health Services
 50 East State Street, P.O. Box 364
 Trenton, NJ 08625
 Ph: 609.292.4043
www.state.nj.us/health/fhs/index.shtml

Newborn Screening Laboratory

New Jersey Department of Health and Senior Services
 Public Health and Environmental Laboratories
 Newborn Genetic and Biochemical Screening Program
 Health and Agriculture Building
 Market & Warren Streets, P.O. Box 371
 Trenton, NJ 08625
 Ph: 609.292.4811
www.state.nj.us/health/fhs/nbs/index.shtml

Newborn Screening Follow-up

New Jersey Department of Health and Senior Services
 Division of Family Health Services
 50 East State Street, P.O. Box 364
 Trenton, NJ 08625
 Ph: 609.943.4792
www.state.nj.us/health/fhs/nbs/index.shtml

Newborn Hearing Screening

New Jersey Department of Health and Senior Services
 Early Identification and Monitoring Program
 50 East State Street, P.O. Box 364
 Trenton, NJ 08625
 Ph: 609.292.5676
www.nj.gov/health/fhs/ehdil/index.shtml

State Genetic Services Program

New Jersey Department of Health and Senior Services
 Newborn Screening and Genetic Services Program
 50 East State Street, P.O. Box 364
 Trenton, NJ 08625
 Ph: 609.292.1582
www.state.nj.us/health/fhs/nbs/genetic.shtml

Family Voices of New Jersey

Statewide Parent Advocacy Network
 35 Halsey Street, 4th Floor
 Newark, NJ 07102
 Ph: 973.642.8100
www.spannj.org/familywrap/familyvoices.htm

March of Dimes: New Jersey Chapter

5 Cedar Brook Drive
 Cranbury, NJ 08512
 Ph: 609.655.7400
www.marchofdimes.com/newjersey

Pregnancy Healthline (Teratogen Services)

Southern New Jersey Perinatal Cooperative
 2500 McClellan Avenue, Suite 110
 Pennsauken, NJ 08109
 Ph: 856.665.6000
 Ph: 888.722.2903
www.snjpc.org/programs/healthline.html



NEW JERSEY GENETICS PROVIDERS/REFERRALS

Bristol Myers-Squibb Children's Hospital at Robert Wood Johnson University Hospital

1 Robert Wood Johnson Place
New Brunswick, NJ 08903
Ph: 732.235.9386
www.bmsch.org

Children's Hospital at St. Peter's University Hospital

254 Easton Avenue
New Brunswick, NJ 08901
Ph: 732.745.6659
www.saintpetersuh.com

Children's Regional Hospital at Cooper

3 Cooper Plaza
Camden, NJ 08103
Ph: 856.968.7255
www.cooperhealth.org/content/childrens_Genetics.htm

The Joseph M. Sanzari Children's Hospital at Hackensack University Medical Center

30 Prospect Avenue
Hackensack, NJ 07601
Ph: 201.996.2000
www.thechildrenshospitalhumc.net/s123/index.asp?lob=123

St. Joseph's Children's Hospital

703 Main Street
Paterson, NJ 07503
Ph: 973.754.2500
www.stjosephshealth.org

University of Medicine and Dentistry of New Jersey/University Hospital

150 Bergen Street
Newark, NJ 07103
Ph: 973.972.3300
www.theuniversityhospital.com

NEW YORK RESOURCES

Children with Special Healthcare Needs

New York State Department of Health
Division of Family Health
Corning Tower, Room 890
Albany, NY 12237
Ph: 518.474.2001
www.health.state.ny.us/community/special_needs

Maternal and Child Health (Title V)

New York State Department of Health
Family and Community Health
Division of Family Health
Corning Tower, Room 890
Albany, NY 12237
Ph: 518.473.7922
www.health.state.ny.us/community

Newborn Screening Laboratory

New York State Department of Health
Wadsworth Center
Newborn Screening Program
P.O. Box 509
Albany, NY 12201
Ph: 518.473.7552
www.wadsworth.org/newborn

Newborn Screening Follow-up

New York State Department of Health
Wadsworth Center
P.O. Box 509
Albany, NY 12201
Ph: 518.486.4949
www.wadsworth.org/newborn

Newborn Hearing Screening

New York State Department of Health
Early Intervention Program
Corning Tower, Room 287
Albany, NY 12237
Ph: 518.473.7016
www.health.state.ny.us/community/infants_children/early_intervention/newborn_hearing_screening

State Genetic Services Program

New York State Department of Health
Wadsworth Center
P.O. Box 509
Albany, NY 12201
Ph: 518.474.7148
www.wadsworth.org/newborn/genes/index.htm

Family Voices of New York

Ph: 518.474.0570
www.familyvoices.org/states.php?state=NY

March of Dimes: New York Chapter

515 Madison Avenue, 20th Floor
New York, NY 10022
Ph: 212.353.8353
www.marchofdimes.com/newyork

PEDECS (Teratogen)

University of Rochester Medical Center
Department of Obstetrics and Gynecology
601 Elmwood Avenue
Rochester, NY 14642
Ph: 585.275.3638

Pregnancy Risk Network (Teratogen)

124 Front Street
Binghamton, NY 13905
Ph: 800.724.2454 (NY only)
www.pregnancyrisknetwork.org

NEW YORK GENETICS PROVIDERS/REFERRALS**Albany Medical Center**

47 New Scotland Avenue
Albany, NY 12208
Ph: 518.262.5120
www.amc.edu/Patient/services/childrens/services/genetics.html

Beth Israel Medical Center

First Avenue at 16th Street
New York, NY 10003
Ph: 212.420.4179
www.wehealny.org/services/bi_genetics/index.html

Binghamton Genetic Counseling Program

Ferre Institute, Inc.
124 Front Street
Binghamton, NY 13905
Ph: 607.724.4308
www.ferre.org/communitygenetics.htm

The Brooklyn Hospital Center

121 Dekalb Avenue
Brooklyn, NY 11201
Ph: 718.250.8000
www.tbh.org/Departments/ReproductiveGenetics.htm

Children's Hospital at Downstate

450 Clarkson Avenue
Brooklyn, NY 11203
Ph: 718.270.1625
www.downstate.edu/peds

Children's Hospital at Montefiore Medical Center

3415 Bainbridge Avenue
Bronx, NY 10467
Ph: 718.741.2323
www.montekids.org/services/genetics

City Hospital Center at Elmhurst

79-01 Broadway
Elmhurst, NY 11373
Ph: 718.334.5510
www.nyc.gov/html/hhc/html/facilities/elmhurst.shtml

Golisano Children's Hospital at Strong

601 Elmwood Avenue
Rochester, NY 14642
Ph: 585.275.5857
www.stronghealth.com/services/childrens/patientcare/genetics

Golisano Children's Hospital at University Hospital, SUNY Upstate Medical Center

750 East Adams Street
Syracuse, NY 13210
Ph: 315.464.4458
www.upstate.edu/gch/services/programs/genetic.php



**Hagedorn Children's Pediatric Inpatient
Center at Winthrop University Hospital**

120 Mineola Boulevard
Mineola, NY 11501
Ph: 516.663.2657
www.winthrop.org

Harlem Hospital

135th Street at Lenox Avenue
New York, NY 10037
Ph: 212.939.1701
www.nyc.gov/html/hhc/html/facilities/harlem.shtml

Lincoln Medical and Mental Health Center

234 East 149th Street
Bronx, NY 10451
Ph: 718.579.5295
www.nyc.gov/html/hhc/html/facilities/lincoln.shtml

Long Island College Hospital

340 Henry Street
Brooklyn, NY 11201
Ph: 718.780.1772
www.wehealny.org/patients/lich_description.html

**Maimonides Infants' and Children's
Hospital of Brooklyn**

4802 10th Avenue
Brooklyn, NY 11219
Ph: 718.283.7229
www.maimonidesmed.org/clinical.cfm?id=120

**Maria Fareri Children's Hospital at
Westchester Medical Center**

95 Grasslands Road
Valhalla, NY 10595
Ph: 914.593.8900
www.worldclassmedicine.com/body_mfch.cfm?id=1085

Metropolitan Hospital Center

1901 First Avenue
New York, NY 10029
Ph: 212.423.6452
www.nyc.gov/html/hhc/html/facilities/metropolitan.shtml

**Morgan Stanley Children's Hospital of New
York-Presbyterian**

3959 Broadway
New York, NY 10032
Ph: 212.305.6731
www.childrensnyp.org/mschony/genetics-services.html

The Mount Sinai Hospital

1 Gustave L. Levy Place
New York, NY 10029
Ph: 212.241.6947
www.mssm.edu/genetics

Nassau University Medical Center

2201 Hempstead Turnpike
East Meadow, NY 11554
Ph: 516.572.5717
www.ncmc.edu

New York Methodist Hospital

506 Sixth Street
Brooklyn, NY 11215
Ph: 718.780.3000
www.nym.org

**New York-Presbyterian Hospital/Weill
Cornell Medical Center**

525 East 68th Street
New York, NY 10021
Ph: 212.746.1496
www.nyp.org

**New York State Institute for Basic Research
in Developmental Disabilities**

1050 Forest Hill Road
Staten Island, NY 10314
Ph: 718.494.0600
www.omr.state.ny.us/ws/ws_ibr_resources.jsp

New York University Medical Center

550 First Avenue
New York, NY 10016
Ph: 212.263.5746
www.med.nyu.edu/pediatrics/genetics

Northeast Health

35 Lower Hudson Avenue
Green Island, NY 12183
Ph: 518.270.2172
www.nehealth.com

North Shore University Hospital

300 Community Drive
Manhasset, NY 11030
Ph: 516.365.3996
www.northshorelij.com/body.cfm?id=51

Queens Hospital Center

82-68th 164th Street
Jamaica, NY 11432
Ph: 718.334.4000
www.nyc.gov/html/hhc/html/facilities/queens.shtml

St. Luke's-Roosevelt Hospital Center

1000 Tenth Avenue
New York, NY 10019
Ph: 212.305.7983
www.wehealny.org/patients/slr_description.html

Saint Vincent's Catholic Medical Centers of New York

Saint Vincent's-Manhattan
170 West 12th Street
New York, NY 10011
Ph: 212.604.7000
www.svcmc.org/body.cfm?id=32&oTopID=11

Schneider Children's Hospital, Long Island Jewish Medical Center

269-01 76th Avenue
New Hyde Park, NY 11040
Ph: 718.470.3010
www.northshorelij.com/body.cfm?ID=63

SUNY at Stony Brook University Hospital

Nicolls Road and Health Sciences Drive
Stony Brook, NY 11794
Ph: 631.444.5437
www.stonybrookmedicalcenter.org/pediatrics/genetic_home.cfm

Women and Children's Hospital of Buffalo

219 Bryant Street
Buffalo, NY 14222
Ph: 716.878.7760
www.wchob.org/services/services_display.asp?SID=499&CID=9

PENNSYLVANIA RESOURCES**Children with Special Healthcare Needs**

Pennsylvania Department of Health
Division of Children & Adult Health Services
P.O. Box 90, 7th Floor, East Wing
Harrisburg, PA 17108
Ph: 877.724.3258

Maternal and Child Health (Title V)

Pennsylvania Department of Health
Bureau of Family Health
P.O. Box 90, 7th Floor, East Wing (BFH)
Harrisburg, PA 17108
Ph: 877.724.3258
www.dsf.health.state.pa.us/health/site/default.asp

Pennsylvania Newborn Screening and Follow-up Program

Pennsylvania Department of Health
Bureau of Family Health
Division of Newborn Screening
Health and Welfare Building
7th and Forster Streets, 7th Floor, East Wing
Harrisburg, PA 17120
Ph: 717.783.8143
www.dsf.health.state.pa.us/health/cwp/view.asp?a=179&q=232592

Newborn Hearing Screening

Pennsylvania Department of Health
Newborn Hearing Screening and
Intervention Program
Health & Welfare Building
7th and Forster Streets, 7th Floor, East Wing
Harrisburg, PA 17108
Ph: 717.783.8143
www.dsf.health.state.pa.us/health/CWP/view.asp?A=179&QUESTION_ID=232585

State Genetic Services Program

Pennsylvania Department of Health
Division of Newborn Disease Prevention
and Identification
7th and Forster Streets, 7th Floor, East Wing
Harrisburg, PA 17120
Ph: 877.724.3258
www.dsf.health.state.pa.us/health/cwp/view.asp?a=179&q=232529



Family Voices of Pennsylvania

Ph: 215.844.6641

*www.familyvoices.org/states.php?state=PA***March of Dimes: Pennsylvania Chapter**1019 West 9th Avenue

King of Prussia, PA 19406

Ph: 610.945.6050

*www.marchofdimes.com/pennsylvania***Magee Women's Hospital (Teratogen)**

Women's Behavioral Health Care Program

University of Pittsburgh Medical Center

300 Halket Street

Pittsburgh, PA 15213

Ph: 412.246.6564

PENNSYLVANIA GENETICS**PROVIDERS/REFERRALS****Albert Einstein Medical Center**

5501 Old York Road

Philadelphia, PA 19141

Ph: 215.456.7890

*www.einstein.edu/facilities/aemc/index.html***Children's Hospital of Philadelphia**34th Street and Civic Center Boulevard

Philadelphia, PA 19104

Ph: 215.590.1000

*www.chop.edu/consumer/jsp/division/service.jsp?id=27693***Children's Hospital of Pittsburgh**

3705 Fifth Avenue

Pittsburgh, PA 15213

Ph: 412.692.5325

*www.chp.edu/CHP/genetic***Family Health Council of Central PA, Inc.**

3461 Market Street, Suite 200

Camp Hill, PA 17011

Ph: 717.761.7380

*www.fhccp.org/genetics.shtml***Family Planning Council**

260 South Broad Street, Suite 1000

Philadelphia, PA 19102

Ph: 215.985.2600

*www.familyplanning.org***Geisinger Medical Center**

100 North Academy Avenue

Danville, PA 17822

Ph: 800.275.6401

*www.geisinger.org/services/jwch/specialties/genetic_services/index.html***Magee Women's Hospital of the UPMC Health System**

300 Halket Street

Pittsburgh, PA 15213

Ph: 412.641.1000

*www.upmc.com/HospitalsFacilities/Hospitals/Magee/ObGynServices/MedicalGenetics/Pages/MedicalGenetics.aspx***Penn State Children's Hospital at the Milton S. Hershey Medical Center**

500 University Drive

Hershey, PA 17033

Ph: 800.243.1455

*www.hmc.psu.edu/childrens/medservices/genetics.htm***St. Christopher's Hospital for Children**

East Erie Avenue & North Front Street

Philadelphia, PA 19134

Ph: 215.427.5000

*www.stchristophershospital.com/CWSCContent/stchristophershospital/ourServices/medicalServices/ClinicalGenetics.htm***Shriners Hospitals for Children – Erie**1645 West 8th Street

Erie, PA 16505

Ph: 800.873.5437

*www.shrinershq.org/Hospitals/Erie***Thomas Jefferson University Hospital**

1015 Walnut Street

Philadelphia, PA 19107

Ph: 215.955.6000

*www.jeffersonhospital.org/article4240.html***Western Pennsylvania Hospital**

4900 Friendship Avenue

Pittsburgh, PA 15224

Ph: 412.578.5000

www.wpahs.org/wph/services/index.cfm?mode=view&medicalspecialty=501

VIRGINIA RESOURCES

Children with Special Healthcare Needs

Virginia Department of Health
 CSHCN Program
 Office of Family Health Services
 109 Governor Street, 8th Floor
 Richmond VA 23219
 Ph: 804.864.7708
www.vahealth.org/specialchildren

Maternal and Child Health (Title V)

Virginia Department of Health
 Policy and Assessment
 109 Governor Street, 7th Floor
 Richmond, VA 23218
 Janice M. Hicks, PhD
 Ph: 804.864.7662

Newborn Screening Laboratory

Virginia Department of Health
 Division of Child and Adolescent Health
 Pediatric Screening and Genetic Services
 109 Governor Street, 8th Floor
 Richmond, VA 23219
 Ph: 804.864.7712
www.vahealth.org/genetics

Newborn Screening Follow-up

Virginia Department of Health
 Newborn Screening Services
 109 Governor Street, 8th Floor
 Richmond, VA 23219
 Ph: 804.864.7712
www.vahealth.org/genetics

Newborn Hearing Screening

Virginia Department of Health
 Early Hearing, Detection and
 Intervention Program
 109 Governor Street, 8th Floor
 Richmond, VA 23219
 Ph: 804.864.7713
www.vahealth.org/hearing

State Genetic Services Program

Virginia Department of Health
 Pediatric Screening and Genetic Services
 109 Governor Street, 8th Floor
 Richmond, VA 23219
 Ph: 804.864.7712
www.vahealth.org/psgsl/index.htm

Family Voices of Virginia

Ph: 202.494.8383
www.familyvoices.org/states.php?state=VA

March of Dimes: Virginia Chapter

10128-A West Broad Street
 Glen Allen, VA 23060
 Ph: 804.968.4120
www.marchofdimes.com/virginia

VIRGINIA GENETICS PROVIDERS/REFERRALS

Children's Hospital of the King's Daughters

601 Children's Lane
 Norfolk, VA 23507
 Ph: 757.668.9723
www.chkd.org/Services/Genetics

Inova Health System

8301 Arlington Boulevard
 Fairfax, VA 22031
 Ph: 703.776.4001
www.inova.org/inova_fairfax_hospital/index.jsp

University of Virginia Children's Hospital

1215 Lee Street
 Charlottesville, VA 22908
 Ph: 434.924.2665
www.healthsystem.virginia.edu/UVAHealth/peds_genetics

VCU Health System Children's Medical Center

1001 East Marshall Street
 Richmond, VA 23219
 Ph: 804.828.7035
www.vcu.edu/pediatrics/overview/add_div.html#humgen



WEST VIRGINIA RESOURCES**Children with Special Healthcare Needs**

Children with Special Healthcare
Needs Program

350 Capitol Street, Room 427

Charleston, WV 25301

Ph: 304.558.5388

www.wvdhhr.org/cshcn

Maternal and Child Health (Title V)

West Virginia Department of Health and
Human Resources

Office of Maternal, Child, and Family Health

350 Capitol Street, Room 427

Charleston, WV 25301

Ph: 304.558.5388

www.wvdhhr.org/mcfh

Newborn Screening Laboratory

West Virginia Department of Health and
Human Resources

Newborn Metabolic Screening Program

Office of Maternal, Child, and Family Health

350 Capitol Street, Room 427

Charleston, WV 25301

Ph: 304.558.3588

www.wvdhhr.org/labservices/labs/newborn/index.cfm

Newborn Screening Follow-up

West Virginia Department of Health and
Human Resources

Office of Maternal, Child, and Family Health

Newborn Metabolic Screening Program

350 Capitol Street, Room 427

Charleston, WV 25301

Ph: 304.558.5388

www.wvdhhr.org/nbms

Newborn Hearing Screening

West Virginia Department of Health and
Human Resources

Office of Maternal, Child, and Family Health

Right From The Start Project

350 Capitol Street, Room 427

Charleston, WV 25301

Ph: 800.642.8522

www.wvdhhr.org/rfts/newbornhearing.asp

State Genetic Services Program

West Virginia Department of Health and
Human Resources

Office of Maternal, Child, and Family Health

350 Capitol Street, Room 427

Charleston, WV 25301

Ph: 304.558.5388

Family Voices of West Virginia

Ph: 888.835.5669

www.familyvoices.org/states.php?state=WV

March of Dimes: West Virginia Chapter

3508 Staunton Avenue, SE, 2nd Floor

Charleston, WV 25304

Ph: 304.720.2229

www.marchofdimes.com/westvirginia

**West Virginia University School of
Medicine (Teratogen)**

OB/GYN Department

P.O. Box 9186

Robert C. Byrd Health Science Center

Morgantown, WV 26506

Ph: 800.442.6692

**WEST VIRGINIA GENETICS
PROVIDERS/REFERRALS****West Virginia University Children's Hospital**

1 Medical Center Drive

Morgantown, WV 26506

Ph: 304.598.4000

www.wvukids.com/index.html

REGIONAL RESOURCES*Health Resources and Services*

*Administration (HRSA) Regional Genetics
and Newborn Screening Collaboratives*

**Heartland Genetics and Newborn
Screening Collaborative**

University of Oklahoma Health

Sciences Center

940 N.E. 13th Street, CHO Room 2418

Oklahoma City, OK 73104

Ph: 405.271.8685

www.heartlandcollaborative.org

**Mountain States Genetics Regional
Collaborative Center**

8501 North Mopac Expressway, Suite 420
Austin, TX 78759
Ph: 303.978.0125
www.msgrcc.org

The New England Genetics Collaborative

University of New Hampshire
Durham, NH 03824
Ph: 603.862.3454
www.negenetics.org/index.html

**NYMAC: New York – Mid-Atlantic
Consortium for Genetic and Newborn
Screening Services**

New York State Department of Health
Wadsworth Center, Room E-299
Albany, NY 12201
Ph: 518.486.2215
www.wadsworth.org/newborn/nymac

Region 4 Genetics Collaborative

Michigan Public Health Institute
2364 Woodlake Circle, Suite 180
Okemos, MI 48864
Ph: 517.381.8247
www.region4genetics.org

**Southeast Newborn Screening and
Genetics Collaborative**

Emory University
2165 North Decatur Road
Decatur, GA 30033
Ph: 404.778.8551
www.southeastgenetics.org

**Western States Genetic
Services Collaborative**

Hawai'i Department of Health
Genetics Program
741 Sunset Avenue
Honolulu, HI 96816
Ph: 808.733.9063
www.westernstatesgenetics.org/index.htm

NATIONAL RESOURCES

**Advisory Committee on Heritable Disorders
in Newborns and Children**

Health Resources and Services Administration
Genetic Services Branch
Maternal and Child Health Bureau
Parklawn Building
5600 Fishers Lane, Room 18A-19
Rockville, MD 20857
Ph: 301.443.1080

**Early Hearing Detection and Intervention
(EHDI) Program**

Centers for Disease Control and Prevention
National Center on Birth Defects and
Developmental Disabilities
Division of Human Development
and Disability
Early Hearing Detection and
Intervention Program
1600 Clifton Road, Mail-Stop E-88
Atlanta, GA 30333
Ph: 404.498.3032

Family Voices, Inc.

2340 Alamo SE, Suite 102
Albuquerque, NM 87106
Ph: 888.835.5669
www.familyvoices.org

Genetic Alliance

4301 Connecticut Avenue, NW, Suite 404
Washington, DC 20008
Ph: 202.966.5557
www.geneticalliance.org

**National Coordinating Center
for the Genetics and Newborn
Screening Collaboratives**

American College of Medical Genetics
9650 Rockville Pike
Bethesda, MD 20814
Ph: 301-634-7127
www.nccrcg.org



**National Newborn Screening and Genetics
Resource Center**

1912 West Anderson Lane, Suite 210
Austin, TX 78757
Ph: 512.454.6419
genes-r-us.uthscsa.edu/index.htm

Prenatal/Pregnancy Resources

March of Dimes

1275 Mamaroneck Avenue
White Plains, NY 10605
Ph: 914.997.4488
www.marchofdimes.com

**National Healthy Mothers, Healthy
Babies Coalition**

2000 North Beauregard Street, 6th Floor
Alexandria, VA 22311
Ph: 703.837.4792
www.hmhb.org

**National Newborn Screening and Genetics
Resource Center**

1912 West Anderson Lane, Suite 210
Austin, TX 78757
Ph: 512.454.6419
genes-r-us.uthscsa.edu

**National Sudden Infant Death
Resource Center**

Georgetown University
P.O. Box 571272
Washington, DC 20057
Ph: 866.866.7437
www.sidscenter.org

Resolve: The National Infertility Association

1760 Old Meadow Road, Suite 500
McLean, VA 22102
Ph: 888.623.0744
www.resolve.org

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

St. Joseph Health Center
300 First Capitol Drive
St. Charles, MO 63301
Ph: 800.821.6819
www.nationalshareoffice.com

Resources for Specific Genetic Conditions

GeneTests

9725 Third Avenue NE, Suite 602
Seattle, WA 98115
Ph: 206.616.4033
www.genetests.org

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

P.O. Box 8126
Gaithersburg, MD 20898
Ph: 888.205.2311
TTY: 888.205.3223
Fax: 240.632.9164
Email: GARDinfo@nih.gov
www.genome.gov/10000409

Genetics Home Reference

Reference and Web Services
National Library of Medicine
8600 Rockville Pike
Bethesda, MD 20894
Ph: 888.346.3656
Fax: 301.496.2809
Email: custserv@nlm.nih.gov
www.ghr.nlm.nih.gov

**National Organization for Rare
Disorders (NORD)**

55 Kenosia Avenue, P.O. Box 1968
Danbury, CT 06813
Ph: 800.999.6673
Ph: 203.744.0100
Fax: 203.798.2291
www.rarediseases.org

Genetics Professional Organizations

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

9650 Rockville Pike
Bethesda, MD 20814
Ph: 301.634.7127
Fax: 301.634.7275
www.acmg.net

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

9650 Rockville Pike
Bethesda, MD 20814
Ph: 800.HUM.GENE
Ph: 301.634.7300
www.ashg.org

**International Society of Nurses in Genetics,
Inc. (ISONG)**

461 Cochran Road, P.O. Box 246
Pittsburgh, PA 15228
Ph: 412.344.1414
Fax: 412.344.1599
Email: isongHQ@msn.com
www.isong.org

National Coalition for Health Professional

Education in Genetics (NCHPEG)
2360 West Joppa Road, Suite 320
Lutherville, MD 21093
Ph: 410.583.0600
Fax: 410.583.0520
www.nchpeg.org

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

401 North Michigan Avenue
Chicago, IL 60611
Ph: 312.321.6834
Fax: 312.673.6972
www.nsgc.org





APPENDICES

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|---|--|
| Appendix A. Basic Genetics Information | Appendix M. Pharmacogenomics and Pharmacogenetics |
| Appendix B. Family History is Important for Your Health | Appendix N. Integrated Health Data System |
| Appendix C. Family Health History Questionnaire | Appendix O. Making Sense of Your Genes: A Guide to Genetic Counseling |
| Appendix D. Healthcare Provider Card | Appendix P. Cultural Competency in Genetics |
| Appendix E. Inheritance Patterns | Appendix Q. National Coalition for Health Professionals Education in Genetics (NCHPEG)—Principles of Genetics for Health Professionals |
| Appendix F. Chromosomal Abnormalities | Appendix R. Centers for Disease Control and Prevention (CDC)—Genomic Competencies for All Public Health Professionals and Clinicians |
| Appendix G. Genetic Testing | |
| Appendix H. Prenatal Screening and Testing | |
| Appendix I. Genetic Testing Methodologies | |
| Appendix J. Newborn Screening | |
| Appendix K. Birth Defects | |
| Appendix L. Genetics and the Environment | |

APPENDIX A. BASIC GENETICS INFORMATION

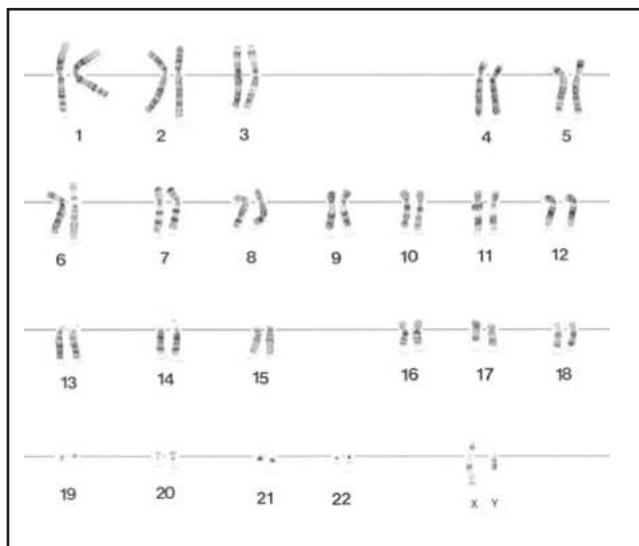
Cells are the body's building blocks. Many different types of cells have different functions. They make up all of your body's organs and tissues. Nearly every cell in a person's body has the same deoxyribonucleic acid, or DNA. DNA is the hereditary material in humans and almost all other organisms. Most DNA is located in the cell nucleus (where it is called nuclear DNA), but a small amount of DNA can also be found in the mitochondria (where it is called mitochondrial DNA).

DNA contains the code for building and maintaining an organism. The code is spelled out in the order, or sequence, of four chemical bases—adenine (A), cytosine (C), guanine (G), and thymine (T)—in the same way that letters of the alphabet come together to form words, sentences, and paragraphs. Human DNA consists of about three billion bases, and more than 99 percent of those bases are the same in all people.

DNA bases pair with each other—A with T, C with G—to form units called base pairs. Each base is attached to a sugar molecule and a phosphate molecule. Together, base, sugar, and phosphate are called a nucleotide. Nucleotides are arranged in two long strands that form a spiral called a double helix. The structure of the double helix is like a ladder, with base pairs running through the middle like rungs and sugar and phosphate molecules along the outside.

Genes are small sections of the long chain of DNA. They are the basic physical and functional units of heredity. In humans, genes vary in size from a few hundred DNA bases to more than two million bases. The Human Genome Project has estimated that humans have between 20,000 and 25,000 genes. Every person has two copies of each gene, one inherited from each parent. Most genes are the same in all people, but a small number of genes (less than one percent of the total) are slightly different between people. Alleles are forms of the same gene with small differences in their sequence of DNA bases. These small differences contribute to each person's unique features.

Genes act as instructions to make molecules called proteins. To function correctly, each cell depends on thousands of proteins to do their jobs in the right places at the right times. Sometimes changes in a gene, called mutations, prevent one or more of these proteins from working properly. This may cause cells or organs to change or lose their function, which can lead to a disease. Mutations, rather than genes themselves, cause disease. For example, when people say that someone has “the cystic fibrosis gene,” they are usually referring to a mutated version of the CFTR gene, which causes the disease. All people, including those without cystic fibrosis, have a version of the CFTR gene.



Sections of DNA form genes, and many genes together form chromosomes. People inherit two sets of chromosomes (one from each parent), which is why every person has two copies of each gene. Humans have 23 pairs of chromosomes.

REFERENCE

National Library of Medicine. *Genetics Home Reference*. **How can gene mutations affect health and development?**

www.ncbi.nlm.nih.gov/handbook/mutationsanddisorders/mutationscausedisease

APPENDIX B. FAMILY HISTORY IS IMPORTANT FOR YOUR HEALTH



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 such as curly hair, dimples, leanness, or athletic ability that run in their families. 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 cannot 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 cancer 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 a disease.

LEARNING ABOUT YOUR FAMILY HISTORY

To learn about your family history:

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



Collect information about your grandparents, parents, aunts, uncles, nieces, 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
- 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
- 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 if 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 DON'T UNCOVER A FAMILY HISTORY OF DISEASE?

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

REFERENCE

Centers for Disease Control and Prevention. **Family history is important for health.**
www.cdc.gov/genomics/public/fambix/fs.htm

RESOURCES

Centers for Disease Control and Prevention, National Office of Public Health Genomics
www.cdc.gov/genomics

Genetic Alliance
www.geneticalliance.org/familyhealthhistory

National Society of Genetic Counselors
www.nsgc.org/consumer/familytree

U.S. Surgeon General's Family History Initiative
www.hhs.gov/familyhistory

APPENDIX C. FAMILY HEALTH HISTORY QUESTIONNAIRE

These cards are designed to help you organize your family health history information to bring to your healthcare provider. They also serve as resources for your provider. These and other family health history materials can be found at www.geneticalliance.org/ccfhh.

FAMILY HEALTH HISTORY QUESTIONNAIRE

Instructions: Fill out the questionnaire on the right for yourself and make copies for others to fill out. You can also fill out a questionnaire for people who are deceased or cannot do it themselves. Not all health conditions are listed. Many other conditions, including many mental health conditions and single gene disorders, also run in families.

REFERENCE

Genetic Alliance

www.geneticalliance.org/ccfhh



Instructions: Fill out one of these questionnaires for yourself and make copies for others to fill out. You can also fill out one for people who are deceased or cannot do it themselves.

Name: _____ Today's Date: _____

Place of Birth: _____ Date of Birth: _____

If Deceased,
Cause of Death: _____ Date of Death: _____

Ethnicity: _____

<u>Health History</u>	<u>Yes</u>	<u>No</u>	<u>Not Sure</u>	<u>Age of Onset</u>
High Blood Pressure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
High Cholesterol	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
Heart Disease or Heart Attack	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
Stroke	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
Diabetes/Sugar Disease	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
Cancer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
Type(s) _____				
Asthma	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
Alzheimer's	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
Birth Defects	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
Vision Loss/Hearing Loss	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
Miscarriage/Stillbirth	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____
How many? _____				

Check one:

_____ Smoker _____ Ex-smoker _____ Nonsmoker _____ Not Sure

Other Health Concerns:

APPENDIX D: HEALTHCARE PROVIDER CARD

I am concerned about my family history of: *(Please check all that apply.)*

HEALTH CONCERNS/RISK FACTORS

- | | |
|--|---|
| <input type="checkbox"/> Heart Disease or Heart Attack | <input type="checkbox"/> Breast Cancer |
| <input type="checkbox"/> Stroke | <input type="checkbox"/> Ovarian Cancer |
| <input type="checkbox"/> Diabetes/Sugar Disease | <input type="checkbox"/> Colon Cancer |
| <input type="checkbox"/> High Blood Pressure | <input type="checkbox"/> Endometrial(Uterine) Cancer |
| <input type="checkbox"/> High Cholesterol | <input type="checkbox"/> Other Cancer: _____ |
| <input type="checkbox"/> Asthma | <input type="checkbox"/> Mental Health: _____ |
| <input type="checkbox"/> Vision Loss at a Young Age | <input type="checkbox"/> Mental Retardation/Developmental Delay |
| <input type="checkbox"/> Hearing Loss at a Young Age | <input type="checkbox"/> Alzheimer's/Dementia |
| <input type="checkbox"/> Genetic Conditions: _____ | |

PRENATAL CONCERNS

- | | |
|--|---|
| <input type="checkbox"/> Birth Defects | <input type="checkbox"/> Miscarriage/Stillbirth |
| <input type="checkbox"/> Genetic Conditions: _____ | |

Identify family members with each condition circled, including age of diagnosis, current age or age at death and cause of death. (Use extra sheets if needed.)

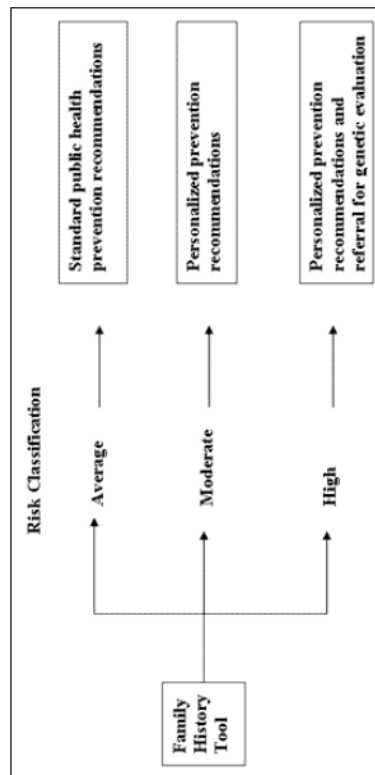
Relationship	Condition	Age of onset	Current age	Age at death, cause
<i>Example:</i>				
<i>Brother</i>	<i>High Blood Pressure</i>	<i>35</i>	<i>45</i>	
<i>Mother</i>	<i>High Blood Pressure</i>	<i>40</i>		<i>65, Stroke</i>

Please include information about your children, brothers and sisters, mother, (mother's side: aunts, uncles, grandparents), father, (father's side: aunts, uncles, grandparents).



Recognizing Family Risk (Genetic Red Flags)

- Family history of known genetic disorder
- Multiple affected family members with same or related disorders
- Earlier age than expected at onset of disease
 - Breast, ovarian, and endometrial cancer < 50 yrs (pre-menopausal)
 - Colon and prostate cancer < 50 yrs
 - Stroke and noninsulin-dependent diabetes < 50 yrs
 - Dementia < 60 yrs
 - Coronary artery disease < 55 yrs for males and < 65 yrs for females
- Sudden cardiac death in a person who seemed healthy
- Multifocal or bilateral occurrence in paired organs
- Ethnic predisposition to certain genetic disorders



General Guidelines for Risk Stratification

High Risk

1. Premature disease in a first-degree relative (sibling, parent or child)
2. Premature disease in a second-degree relative (CAD only)
3. Two affected first-degree relatives
4. One first-degree relative with late or unknown disease onset and an affected second-degree relative from the same lineage with premature disease
5. Two second-degree maternal or paternal relatives with at least one having premature onset of disease
6. Three or more affected maternal or paternal relatives
7. Presence of a “moderate risk” family history on both sides of the pedigree

Moderate Risk

1. One first-degree relative with late or unknown onset of disease
2. Two second-degree relatives from the same lineage with late or unknown disease onset

Average Risk

1. No affected relatives
2. Only one affected second-degree relative from one or both sides of the pedigree
3. No known family history
4. Adopted person with unknown family history

Scheetner et al., Am J Med Genet 1997; 71:315-324

Pedigrees demonstrating clustering of different primary cancers consistent with a family cancer syndrome were high-risk. Pedigrees demonstrating clustering of cardiovascular disease and noninsulin-dependent diabetes consistent with [metabolic syndrome] were considered high-risk.

Family History Website Resources

1. CDC's Office of Genomics and Disease Prevention – Using Family History to Promote Health (www.cdc.gov/genomics/famhistory/famhst.htm)
2. AMA Pocket-sized Pedigree Information (www.ama-assn.org/ama/pub/category/14399.html)
3. U.S. Surgeon General's Family History Initiative (www.hhs.gov/familyhistory/)
4. American Academy of Family Physicians (AAFP) Family History Resources (www.aafp.org)

APPENDIX E. INHERITANCE PATTERNS

It is important to understand the basic laws of inheritance to appreciate how conditions are passed on in a family. An accurate family health history is a valuable tool to illustrate how conditions are passed down through generations.

A person has two copies of almost every gene, one copy from mom and one copy from dad. Scientists have studied human genes to learn how they normally work and how changes in genes can change how they work. Some changes are very minor and do not affect the way a gene works. These changes are often called single nucleotide polymorphisms (SNPs, pronounced “snips”) or gene variants. Other changes, called mutations, affect how a gene works and can lead to disease.

For some conditions, family members with the same mutation may not have the same symptoms. For other conditions, individuals with different mutations can have similar characteristics. This is because gene expression is influenced by genes, as well as by the environment.

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. This is often referred to as Mendelian inheritance because Gregor Mendel first observed these patterns in garden pea plants. Most single gene disorders are rare; but, in total, they affect millions of people in the United States.

Several basic modes of inheritance exist for single-gene disorders: autosomal dominant, autosomal recessive, X-linked dominant, and X-linked recessive. However, not all genetic conditions will follow these patterns, and other rare forms of inheritance such as mitochondrial inheritance exist. (See table at the end of this section.)

Dominant mutations are expressed when only one copy of that mutation is present. Therefore, anyone who inherits one dominant disease mutation such as the mutation for Huntington’s disease will have that disease. Dominantly inherited genetic diseases tend to occur in every generation of a family. Each affected person usually has one affected parent. However, dominant mutations can also happen in an individual for the first time, with no family history of the condition (spontaneous mutation).

Recessive mutations require two mutated copies for disease to develop. Recessive genetic diseases are typically not seen in every generation of an affected family. The parents of an affected person are generally carriers: unaffected people who have a copy of a mutated gene. If both parents are carriers of the same mutated gene and both pass it to the child, the child will be affected.

Inheritance patterns differ for genes on sex chromosomes (chromosomes X and Y) compared to genes located on autosomes, non-sex chromosomes (chromosomes numbers 1-22). This is due to the fact that, in general, females carry two X chromosomes (XX), while males carry one X and one Y chromosome (XY). Therefore, females carry two copies of each X-linked gene, but males carry only one copy each of X-linked and Y-linked genes. Females carry no copies of Y-linked genes.



Diseases caused by mutated genes located on the X chromosome can be inherited in either a dominant or recessive manner. Since males only have one X chromosome, any mutated gene on the X chromosome, dominant or recessive, will result in disease. Because females have two copies of X-linked genes, they will not be affected by inheriting of a single recessive mutation on an X-linked gene. For X-linked recessive diseases to occur in females, both copies of the gene must be mutated. Families with an X-linked recessive disorder often have affected males, but rarely affected females, in each generation.

For X-linked dominant diseases, however, a mutation in one copy of an X-linked gene will result in disease for both males and females. Families with an X-linked dominant disorder often have both affected males and affected females in each generation.

A striking characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons; fathers only pass X chromosomes to their daughters and Y chromosomes to their sons. In contrast, mothers pass X-linked genes to both sons and daughters.

Inheritance Pattern	Characteristics	Disease Examples
Autosomal Dominant	Each affected person usually has an affected parent; occurs in every generation	Huntington's disease, neurofibromatosis, achondroplasia, familial hypercholesterolemia
Autosomal Recessive	Both parents of an affected person are carriers; not typically seen in every generation	Tay-Sachs disease, sickle cell anemia, cystic fibrosis, phenylketonuria (PKU)
X-linked Dominant	Females are more frequently affected because all daughters and no sons of an affected man will be affected; can have affected males and females in same generation if the mother is affected	Hypophatemic rickets (vitamin D-resistant rickets), ornithine transcarbamylase deficiency
X-linked Recessive	Males are more frequently affected; affected males often present in each generation	Hemophilia A, Duchenne muscular dystrophy
Mitochondrial	Can affect both males and females, but only passed on by females because all mitochondria of all children come from the mother; can appear in every generation	Leber's hereditary optic neuropathy, Kearns-Sayre syndrome

RESOURCES

GeneTests

www.genetests.org

Online Mendelian Inheritance in Man (OMIM)

www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM

APPENDIX F. CHROMOSOMAL ABNORMALITIES

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 are called autosomes. The 23rd pair consists of the sex chromosomes, X and Y. Females usually have two X chromosomes, and males usually have one X and one Y chromosome in each cell. All of the information that the body needs to grow and develop comes from the chromosomes. Each chromosome contains thousands of genes, which make proteins that direct the body's development, growth, and chemical reactions.

Many types of chromosomal abnormalities exist, but they can be categorized as either numerical or structural. Numerical abnormalities are whole chromosomes either missing from or extra to the normal pair. Structural abnormalities are when part of an individual chromosome is missing, extra, switched to another chromosome, or turned upside down.

Chromosomal abnormalities can occur as an accident when the egg or the sperm is formed or during the early developmental stages of the fetus. The age of the mother and certain environmental factors may play a role in the occurrence of genetic errors. Prenatal screening and testing can be performed to examine the chromosomes of the fetus and detect some, but not all, types of chromosomal abnormalities.

Chromosomal abnormalities can have many different effects, depending on the specific abnormality. For example, an extra copy of chromosome 21 causes Down syndrome (trisomy 21). Chromosomal abnormalities can also cause miscarriage, disease, or problems in growth or development.

The most common type of chromosomal abnormality is known as aneuploidy, an abnormal chromosome number due to an extra or missing chromosome. Most people with aneuploidy 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. Besides trisomy 21, the major chromosomal aneuploidies seen in live-born 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 chromosomal segments. A range of structural chromosomal abnormalities result in disease. Structural rearrangements are defined as balanced if the complete chromosomal set is still present, though rearranged, and unbalanced if information is additional or missing. Unbalanced rearrangements include deletions, duplications, or insertions of a chromosomal 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 duplicates.

Balanced rearrangements include inverted or translocated chromosomal regions. Since the full complement of DNA material is still present, balanced chromosomal rearrangements may go undetected because 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 nonfunctional 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.



APPENDIX G. GENETIC TESTING

Genetic testing involves examining a person's blood or other tissues to determine whether he or she has a change in his or her genetic material. Genetic testing may be useful in determining whether an individual has a genetic condition or may develop one in the future. The information gained from genetic testing may be helpful in a number of ways such as diagnosing a genetic disease, starting treatment, or initiating prevention strategies, as well as making life decisions such as career choice and family planning. Several types of genetic testing are available, and this appendix provides an overview of the genetic testing available, as well as who may be offered such testing.

WHY GENETIC TESTING?

Genetic testing may be offered for a number of different reasons including:

- To confirm or rule out a diagnosis in an individual with symptoms of a genetic condition
- For individuals with a family history of or a previous child with a genetic condition
- To locate possible genetic conditions in newborn babies so treatment may be started immediately

HOW IS GENETIC TESTING PERFORMED?

Genetic testing involves analyzing an individual's blood, skin, hair, or other body tissue to look at his or her DNA, chromosomes, or proteins for a change, or mutation, that is associated with a genetic condition. When a mutation occurs, it may affect all or part of a gene and can result in an abnormal function leading to disease. Three major types of genetic testing are available in laboratories: cytogenetic (to examine whole chromosomes), biochemical (to measure protein produced by genes), and molecular (to look for small DNA mutations). (See *Chapter 2* and *Appendix I* for more information.)

WHAT TYPES OF GENETIC TESTING ARE THERE?

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 chance of having a child with a genetic condition.

Prenatal diagnostic testing is used to detect changes in a fetus' genes or chromosomes. This type of testing is offered to couples with an increased chance 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.)

APPENDIX G. GENETIC TESTING (CONTINUED)

Genetic tests may be used to confirm a diagnosis in a symptomatic individual or 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.

Forensic testing is used for identification, not to identify individuals at risk for a genetic disease. Forensic testing is performed for legal purposes such as criminal investigations, questions of paternity, and identification after catastrophic events such as Hurricane Katrina.

WHO SHOULD CONSIDER GENETIC TESTING?

When deciding whether or not to get a genetic test for yourself or a family member, several issues need to be considered, both from a medical and an emotional standpoint. Genetic testing may provide a diagnosis and help provide information for symptom management, treatment, or lifestyle changes. However, genetic testing has limitations. When a genetic test detects a mutation, the test cannot always determine when or what symptoms of the condition may show, which symptoms will occur first, how severe the condition will be, or how the condition will progress over time. Even if a test is negative, an individual may still be at risk for a condition.

Due to the complexity of the medical and emotional issues involved in genetic testing, 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. For information on genetic counseling, preparation for a genetic counseling visit, and sample questions to ask healthcare providers, see *Appendix O*.

REFERENCES

American College of Medical Genetics

www.acmg.net

GeneTests

www.genetests.org

National Society of Genetic Counselors

www.nsgc.org

U.S. National Library of Medicine: Genetics Home Testing

www.ghr.nlm.nih.gov



APPENDIX H: PRENATAL SCREENING AND TESTING

Prenatal testing may be offered to women during pregnancy to determine if the fetus has a possibility to be born with a genetic condition or birth defect. Performing prenatal testing may be useful in determining different options for the pregnancy or special management of the pregnancy and delivery to improve the outlook for the baby. Several types of prenatal testing are available, depending on which trimester of pregnancy the mother is in and the type of condition in question. This appendix provides an overview of different prenatal tests that may be offered to pregnant women.

WHO IS OFFERED TESTING?

All pregnant women, regardless of age, have the option to undergo prenatal testing. However, as women age, the chance of having a baby with a chromosomal abnormality increases. So the age of the mother is the most common reason for prenatal testing.

Other reasons that a woman may be offered prenatal testing include:

- Family history or a previous child with a genetic condition
- Parents who are known carriers of a specific genetic condition
- Abnormal ultrasound findings
- Screening test results

Any woman who desires more information about the developing fetus can consider prenatal testing. The decision is an individual choice. A woman should discuss the various options outlined above with her obstetrician or a genetic counselor to determine which are right for her.



HOW ARE TESTS PERFORMED?

Two main types of prenatal testing are performed during pregnancy. The first type of testing is known as screening. Screening tests are used to identify women with an increased chance to have a baby with certain chromosomal abnormalities. Screening tests do not identify birth defects such as genetic diseases. Results that reveal a chance over a certain cutoff level are called “positive results,” and these women are

offered further testing. Screening tests are not diagnostic. And while the majority of fetuses with a chromosomal condition are identified through screening, some affected fetuses with a chromosomal condition receive a normal or “negative” screening result.

The second type of prenatal testing is known as diagnostic testing because these tests can determine definitively if the developing fetus has a certain genetic condition or birth defect.

APPENDIX H: PRENATAL SCREENING AND TESTING (CONTINUED)

Screening and diagnostic tests may be performed in either the first or second trimester of pregnancy as follows.

SCREENING TESTS

Screening tests can be performed in both the first and second trimesters of pregnancy. First trimester screening involves an ultrasound examination and a sample of the mother's blood, while second trimester screening involves just the blood sample. Some women may also be offered a combination of first and second trimester screening, known as either "integrated" or "combined" screening. The blood results and ultrasound results are then combined with maternal factors such as age and weight to calculate the chance for certain chromosomal conditions in the current pregnancy.

Screening results are usually available within a week, and those who receive a positive result are offered diagnostic testing. The detection rate for screening tests varies by the type of test performed. The only way to know for certain whether or not a developing baby has a chromosomal condition is by performing a diagnostic test.

DIAGNOSTIC TESTS

Certain diagnostic tests are procedures that can determine with greater than 99.9 percent accuracy whether or not a developing baby has a chromosomal difference. The two types of diagnostic tests are chorionic villus sampling (CVS) and amniocentesis. Diagnostic tests for specific genetic diseases must be specially requested. These tests have different accuracy rates, depending on which test is ordered.

CVS is performed between 10.5 to 13.5 weeks of pregnancy. During the procedure, a doctor obtains a small tissue sample from the placenta by either inserting a thin needle through the woman's abdomen or by using a small catheter inserted through the cervix. The method used depends on the location of the baby and the placenta.

Amniocentesis is performed from 15 weeks of pregnancy onward. During amniocentesis, a thin needle is inserted through the woman's abdomen into the amniotic sac to withdraw a small sample of fluid from around the developing baby.

The cells collected from either procedure can be used for chromosomal analysis or other genetic tests, as ordered. The results from the chromosomal analysis usually take two weeks; while the results from other genetic tests may take longer, depending on what test has been ordered.

Diagnostic test procedures are associated with a chance for miscarriage, which is estimated to be up to 1 percent for CVS, and less than 1 percent for amniocentesis.



REFERENCES

American College of Medical Genetics

www.acmg.net

American College of Obstetrics and Gynecology

www.acog.org

March of Dimes Foundation

www.marchofdimes.com

National Society of Genetic Counselors

www.nsgc.org

APPENDIX I. GENETIC TESTING METHODOLOGIES

As the number of genetic tests has expanded rapidly over the last decade, so have the different types of genetic testing methodologies used. The type of test employed depends on the type of abnormality being measured. In general, three categories of genetic testing—cytogenetic, biochemical, and molecular—are available to detect abnormalities in chromosome structure, protein function, and DNA sequence, respectively.

Cytogenetic Testing. Cytogenetics involves the examination of chromosomes to identify structural abnormalities. Chromosomes of a dividing human cell can be analyzed clearly in white blood cells, specifically T lymphocytes, which are easily collected from blood. Cells from other tissues such as bone marrow, amniotic fluid, and other tissues can also be cultured for cytogenetic analysis. Following several days of cell culture, chromosomes are fixed, spread on microscope slides, and 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 the chromosomal structure.

Fluorescent in situ hybridization (FISH) is a process that vividly paints chromosomes or portions of chromosomes with fluorescent molecules to identify chromosomal abnormalities (e.g., insertions, deletions, translocations, and amplifications). FISH is commonly used to identify specific chromosomal deletions associated with pediatric syndromes such as DiGeorge syndrome (a deletion of part of chromosome 22, also called del22) and cancers such as chronic myelogenous leukemia (a translocation involving chromosomes 9 and 22).

Biochemical Testing. Clinical testing for a biochemical disease utilizes techniques that examine the protein instead of the gene. Many biochemical genetic diseases are known as “inborn errors of metabolism” because they are present at birth and disrupt a key metabolic pathway. Depending on the disease, tests can be developed to directly measure protein activity (direct measurement of enzyme activity), level of metabolites (indirect measurement of enzyme activity), and the size or quantity of protein (protein structure). These tests require a tissue sample in which the protein is present, typically blood, urine, amniotic fluid, or cerebrospinal fluid. Because gene products may be more unstable than DNA or RNA and can degrade quickly, the sample must be collected, stored properly, and shipped promptly according to the laboratory’s specifications.

A variety of technologies such as high performance liquid chromatography (HPLC), gas chromatography/mass spectrometry (GC/MS), and tandem mass spectrometry (MS/MS) enable both qualitative detection and quantitative determination of metabolites. In addition, bioassays may employ fluorometric, radioisotopic, or thin-layer chromatography methods.

Molecular Testing. Direct DNA analysis is applicable when the gene sequence of interest is known. For small DNA mutations, direct DNA testing is typically the most effective method, particularly if the function of the protein is unknown and a biochemical test cannot be developed. A DNA test can be performed on any tissue sample and requires very small amounts



of sample. Several different molecular technologies, including direct sequencing, polymerase chain reaction-based assays (PCR), and hybridization, can be used to perform testing. PCR is a common procedure used to amplify targeted segments of DNA through repeated cycles of denaturation (heat-induced separation of double-stranded DNA), annealing (binding of specific primers of the target segment to parent DNA strand), and elongation (extension of the primer sequences to form a new copy of the target sequence). The amplified product can then be further tested. For some genetic diseases, many different mutations can occur in the same gene and result in the disease, making molecular testing challenging. However, if the majority of cases of a particular genetic disease are caused by a few mutations, this group of mutations is first tested before more comprehensive testing such as sequencing is performed.

Comparative genomic hybridization (CGH) or chromosomal microarray analysis (CMA) is a molecular cytogenetic method for analyzing gains or losses in DNA that are not detectable with routine chromosome analysis. The method is based on the proportion of fluorescently-labeled patient DNA to normal-reference DNA. CGH can detect small deletions and duplications, but not structural chromosomal changes such as balanced reciprocal translocations or inversions or changes in chromosomal copy number.

DNA microarray analysis, also referred to as gene, genome, or DNA chip analysis, is a tool for determining gene expression. Molecules of mRNA bind, or hybridize, specifically to a DNA template, typically a gene or portion of a gene, from which it originated. When an array contains many DNA templates, the expression level of hundreds to thousands of genes from an individual patient sample can be measured using a computer to detect the amount of mRNA bound to each site on the array.

Protein microarray analysis is used to quantify the amount of protein present in biological samples. Similar to chromosome and DNA microarray analysis, the hybridization of labeled target proteins in a patient sample is measured against a reference sample. Also referred to as a biomarker, the presence, absence, increase, or decrease of a particular protein can be an indicator of disease in a person. For example, analysis of the cerebrospinal fluid of a patient for amyloid beta or tau proteins may be used to diagnose Alzheimer's disease.

REFERENCES

Greenwood Genetic Center. *Cytogenetics: Chromosome Analysis.*
www.ggc.org/diagnostics/cytogenetics/cytogenetics.htm

Laboratory Corporation of America. *A Basic Guide to Genetic Testing.*
www.labcorp.com/genetics/basic_guide/index.html

RESOURCE

GeneTests
www.genetests.org

APPENDIX J. NEWBORN SCREENING

Each year, all children born in the United States are screened for a panel of diseases, which differ from state to state. Early detection and treatment of these diseases can lead to significant reduction in disease severity and possibly even disease prevention. Over 100,000 newborns screen positive for a disorder each year.

Newborn screening programs began in the U.S. in the 1960s with the work of Dr. Robert Guthrie, who developed a screening test for phenylketonuria (PKU). PKU is an inherited metabolic disease that is caused by a mutation of the gene for 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 would otherwise lead to brain damage and mental retardation. When Dr. Guthrie introduced a system for collection and transportation of blood samples on filter paper, cost-effective, wide-scale genetic screening became possible.

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 PKU, sickle cell disease, and hypothyroidism. The sample, called a "blood spot," is tested at a state public health laboratory or other participating lab. Each state has its own newborn screening panel that tests for different conditions. Decisions for adding



or deleting tests involve many complex social, ethical, and political issues. Usually, newborn screening disorders are selected based on disease prevalence, detectability, treatment availability, outcome, and overall cost-effectiveness. The American College of Medical Genetics and the March of Dimes recommend that all babies be screened for a core panel of 29 disorders and a hearing screening. Slightly less than half of all states offer screening for this panel of 29 disorders.

REFERENCES

Advisory Committee on Heritable Disorders in Newborns and Children

www.hrsa.gov/heritabledisorderscommittee

Centers for Disease Control and Prevention

www.cdc.gov/nceh/dls/newborn.htm

March of Dimes

www.marchofdimes.com

National Newborn Screening and Genetics Resource Center

genes-r-us.uthscsa.edu



APPENDIX K. BIRTH DEFECTS

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

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. These children can lead healthy lives. But some birth defects are very severe and can even cause death. Some birth defects such as a clubfoot or cleft lip are relatively noticeable, but others such as heart defects may require imaging tests like an ultrasound. Not all birth defects can be detected prenatally (before birth).

Some of the most common birth defects affect the heart. About one in every 200 to 300 babies is born with a heart defect. Depending on the type and severity of the heart defect, it may be corrected by surgery. Another common group of birth defects is called “neural tube” defects. These are due to abnormal development of the baby’s spine or brain and affect about one in 1,000 babies. These defects are sometimes very severe, causing early death or severe paralysis. 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 one in 700 to 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 supplements (4 mg per day) during early pregnancy. Uncontrolled medical conditions of the mother—for example, diabetes or PKU—can lead to birth defects. Some medicines such as Accutane are known to cause birth defects.

To learn more about your risk of having a baby with a birth defect, 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, get help managing their medical conditions, decide which medications are safe to take, and avoid exposure to alcohol, drugs, and tobacco.

RESOURCES

Centers for Disease Control and Prevention

www.cdc.gov/ncbddd/bd

Medline Plus

www.nlm.nih.gov/medlineplus/birthdefects.html

APPENDIX L. GENETICS AND THE ENVIRONMENT

A teratogen is any agent that causes an abnormality following fetal exposure to harmful substances during pregnancy. Teratogens are usually discovered after an increased prevalence of a particular birth defect. For example, in the early 1960s, a drug known as thalidomide was used to treat morning sickness. Exposure of the fetus during the early stages of development results 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 time when fetuses are most vulnerable to teratogen exposures.

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 are also dependent on the genetic susceptibilities of 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, developmental disabilities, and adverse pregnancy outcomes are alcohol and smoking. Alcohol use during pregnancy has significant effects on the fetus. 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 three to eight 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 consumed alcohol during pregnancy. It is the most common known nongenetic (not inherited) cause of mental retardation in the U.S.



It is the most common known nongenetic (not inherited) cause of mental retardation in the U.S.



Smoking cigarettes during pregnancy nearly doubles a woman's risk of having a low birth-weight baby, preterm delivery, or a combination of both. Babies born prematurely and with low birth-weight 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 three 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.

Uncontrolled diabetes during pregnancy poses a risk of birth defects because glucose can act as a teratogen during pregnancy. Women should see their doctors before becoming pregnant to discuss diagnosing and managing medical conditions such as diabetes and to eliminate other teratogens and risk factors if possible.

RESOURCES

Centers for Disease Control and Prevention

www.cdc.gov/ncbddd/fas/faspub.htm

March of Dimes

www.marchofdimes.com

Organization of Teratogen Information Services

otispregnancy.org/otis_about_us.asp

Reprotox

www.reprotox.org

Teratogen Information System

depts.washington.edu/~terisweb/teris

APPENDIX M. PHARMACOGENOMICS AND PHARMACOGENETICS



The impact of genetic makeup on drug response and outcome has been known since the 1950s. Interest reignited with the sequencing of the human genome, leading to the field now commonly known as pharmacogenomics. Genetic variation in drug targets or genes involved in drug disposition are known to result in different drug responses and outcomes for a given group of patients treated with the same

drug. Many genes are likely to influence a single drug response (pharmacogenetics) and obtaining the big picture of the impact of gene variation on drug efficacy and safety has become a cornerstone of drug development.

The findings from genetic studies facilitate drug discovery and allow drug makers to produce treatments better targeted to the cause of specific conditions. This accuracy not only maximizes therapeutic effects but also decreases damage to nearby healthy cells. Pharmacogenetics aims to improve the likelihood of positive outcomes and reduce the risk of serious adverse responses. Pharmacogenetics has the potential to dramatically reduce healthcare costs associated with the more than 2 million hospitalizations and outpatient visits due to adverse drug responses and multiple drug prescriptions each year in the U.S.

Such knowledge allows physicians to tailor drug treatment to an individual's genetic makeup, sometimes referred to as "personalized medicine." Although environment, diet, age, lifestyle, and health status can all influence a person's response to medicines, understanding an individual's genetic makeup can be the key to prescribing 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.

A number of research and clinical trials are performed for genes involved in drug dosage and response. The most well-known example of a pharmacogenetic intervention involves cytochrome p450 (CYP 450). The CYP 450 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. Currently, panels offering testing for several of the "P450s" are available to patients to determine how effectively they metabolize specific drugs. Those identified as "poor metabolizers" may experience side effects, overdose at a standard dosage, or not receive any relief of symptoms. Such information is valuable in choosing drugs to treat very serious conditions from bleeding disorders (Warfarin) to breast cancer (Tamoxifen).



Despite the successes of pharmacogenetic testing for CYP 450 and identifying the correct drugs for some cases of cancer and HIV, this new field has highlighted the complexity of the interactions between drugs and biochemicals in the body. Understanding the role of genetics in common, chronic conditions remains hopeful; but with many new medical advances, it will take time for pharmacogenomics to enter the mainstream as a standard clinical tool.

RESOURCES

Licinio J & Wong M (eds). *Pharmacogenomics: The Search for Individualized Therapies*, Weinheim (Germany): Wiley-VCH; 2002.

National Center for Biotechnology Information. *One size does not fit all: the promise of pharmacogenomics.*

www.ncbi.nlm.nih.gov/About/primer/pharm.html

National Institute of General Medical Sciences, National Institutes of Health.

Medicines for you.

publications.nigms.nih.gov/medsforyou

(Spanish language: publications.nigms.nih.gov/medsforyou/index_esp.html)

Rothstein M (ed). *Pharmacogenomics: Social, Ethical, and Clinical Dimensions*. Hoboken (New Jersey): John Wiley & Sons. 2003.

APPENDIX N. INTEGRATED HEALTH DATA SYSTEMS

The American Health Information Community (AHIC) is a federal advisory body chartered in 2005 to make recommendations to the Secretary of the U.S. Department of Health and Human Services on how to accelerate the development and adoption of health information technology. AHIC was formed by the Secretary to help advance efforts to achieve President Bush's goal that most Americans have access to secure electronic health records by 2014.

On January 22, 2008, Secretary Michael Leavitt announced the successor of AHIC. LMI and Brookings Institute will collaborate in the creation of AHIC 2.0. Together, their work will further the goals and recommendations put forth by the AHIC:

Full and Secure Information

- Protect health information through different practices
- Create a national internet-based tool that provides information and secure networks

Convenience and Lower Costs

- Establish and manage national and industry-wide health IT standards
- Focus on policy and technical barriers to advance ideas

Reduce Medical Errors and Improve Quality of Care

- Accelerate the creation of interoperable electronic health records (EHRs) across all healthcare providers
- Create compliance certificates and inspection processes for EHRs

Provide Better Information for Patients and Physicians

- Identify breakthrough ideas where health IT is most important and possible

REFERENCE

U.S. Department of Health and Human Services. Health Information Technology.
www.hhs.gov/healthit



APPENDIX O. MAKING SENSE OF YOUR GENES: A GUIDE TO GENETIC COUNSELING

This is an excerpt from *Making Sense of Your Genes: A Guide to Genetic Counseling*. The full guide can be found at www.geneticalliance.org/publications.

WHAT IS GENETIC COUNSELING?

The goal of genetic counseling is to help you learn more about the causes of genetic conditions and how they affect you.

Genetic counselors can:

- Review your family and medical histories
- Explain how genetic conditions are passed down through families
- Figure out whether you or your family members are at risk for disease
- Find and give you information about genetic conditions
- Offer guidance to help you make informed choices or life plans
- Provide information about testing options and help you decide what is best for you and your family
- Help you find referrals to medical specialists, advocacy and support networks, and other resources

WHY MIGHT I SEE A GENETIC COUNSELOR?

You might see a genetic counselor in many situations, such as:

- You are pregnant or considering becoming pregnant and are concerned about the health of your baby
- Your baby had an abnormal result from newborn screening
- You, your child, or a family member has been diagnosed with a genetic condition
- You are concerned that you, your child, or a family member has a genetic or inherited condition and you would like more information
- Your family has a history of developmental disability, birth defects, and/or mental retardation
- Your family has a history of mental illness
- Your family has a history of cancer

APPENDIX O. MAKING SENSE OF YOUR GENES: A GUIDE TO GENETIC COUNSELING (CONTINUED)

HOW CAN I PREPARE FOR A GENETIC COUNSELING VISIT?

Although steps to prepare for specific types of visits are provided later in this booklet, here are a few common areas to think about before your visit. Come to the visit with a list of questions you would like to ask. This will help the counselor focus on your concerns. Genetic counseling visits usually involve collecting family history information. It can be useful to ask your relatives about what types of medical conditions occur in your family before your visit. If you have medical records relating to your concerns, you may want to bring them or ask your doctor to send them to the genetic counselor before your visit.

WHAT CAN YOU EXPECT FROM YOUR VISIT?

At the beginning of the session, you and the genetic counselor should outline what to talk about in the session. Common topics include:

- Talking about your family health history and ethnic heritage
- Helping you understand the causes of genetic conditions
- Helping you understand testing options, diagnosis, or, in some cases, the reason why no diagnosis has been made
- Guiding you through decision-making about genetic testing, family planning, or medical planning
- Helping you deal with emotions associated with having or not having a known genetic condition, having a relative with a genetic condition, or being at risk for a genetic condition
- Finding supportive resources to help you manage a genetic condition
- Understanding the chance of passing a genetic condition on to your children

Your input is very important to the genetic counseling session; the details you provide will allow the genetic counselor to understand your health concerns fully.



QUESTIONS YOU MIGHT ASK YOUR GENETIC COUNSELOR

- Does the disease in question run in families?
- If my family member has a disease, might I get it?
- If I have a disease, are my family members at risk of getting it?
- Is any kind of genetic testing available? If so, what are the benefits and limitations of the testing? How will I pay for it?
- What kind of information can genetic testing give me?
- What does the genetic testing process involve?
- Will the results be given to me over the phone or in person?
- How can knowing more about a genetic risk help me?
- Could I be exposing my family or myself to discrimination based on genetic information?

REFERENCE

Genetic Alliance, *Making Sense of Your Genes: A Guide to Genetic Counseling*
www.geneticalliance.org/publications

RESOURCES

Genetic Alliance
www.geneticalliance.org/familyhealthhistory

National Society of Genetic Counselors
www.nsgc.org

U.S. Surgeon General's Family History Initiative
www.hhs.gov/familyhistory

APPENDIX P. CULTURAL COMPETENCY IN GENETICS

Cultural competency involves attitudes, policies, and structures that enable health professionals to work effectively with people of different cultures. The term “cultural competence” represents a process of working toward a greater understanding of 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. Staff of health organizations and services should acquire and institute cultural knowledge across all aspects of policymaking, administration, practice, and service delivery. They should systematically involve consumers, key stakeholders, and communities.

Cross-cultural genetic services focus on the health beliefs and cultural customs of the patient and family. Culturally and linguistically appropriate healthcare 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 healthcare delivery. In particular, reproductive issues and pediatric care may raise culturally-unique issues that require culturally-sensitive discussions about treatment and care.

RESOURCES

Assuring Cultural Competence in Healthcare: Recommendations for National Standards and an Outcomes-Focused Research Agenda

www.pcusa.org/nationalhealth/advocacy/standard-hc.pdf

Cross Cultural Healthcare Program

www.xculture.org

Diversity Rx

www.diversityrx.org

EthnoMed

www.ethnomed.org

JAMARDA Resources

www.jamardaresources.com

March of Dimes—GENE (Genetics Education Needs Evaluation) Project

www.marchofdimes.com/geneproject

National Center for Cultural Competencies at Georgetown University Center for Child and Human Development

www.gucchd.georgetown.edu/nccc/index.html

The National Multicultural Institute

www.nmci.org



APPENDIX Q. 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* (Third Edition, September 2007), provides basic guidance to a broad range of individuals and groups as they plan educational initiatives in genetics and genetically-based healthcare. Their June 2004 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 healthcare. The principles focus on basic biology related to genetics. A subsequent set of principles will address concepts related to patient care and public health more directly.

We are hopeful that these principles will help determine the content for lectures, workshops, seminars, and complete courses. We leave it to individual professionals, who know their audiences and the context of the instruction in genetics, to select the applicable principles, determine the examples selected to illustrate those principles, and define the level of detail appropriate for the audience in question.

We welcome your feedback about the utility of this document. Please send your comments to info@nchpeg.org.

A. PRINCIPLES RELATED TO BIOLOGICAL VARIATION

1. Genetics is the study of heritable biological variation.
2. Genetics in the healthcare 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 structure 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. No differential selection, and therefore no evolution, would occur without mutation and variation. This principle helps 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.

APPENDIX Q. NATIONAL COALITION FOR HEALTH PROFESSIONAL EDUCATION IN GENETICS (NCHPEG) – PRINCIPLES OF GENETICS FOR HEALTH PROFESSIONALS (CONTINUED)

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 healthcare and the 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. No sharp genetic boundaries exist between populations of human beings around the globe, and more genetic variation occurs 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/are 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 healthcare, 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 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 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 other animals, fungi, and plants, cells contain a nucleus that includes 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.

APPENDIX Q. NATIONAL COALITION FOR HEALTH PROFESSIONAL EDUCATION IN GENETICS (NCHPEG) – PRINCIPLES OF GENETICS FOR HEALTH PROFESSIONALS (CONTINUED)

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 deaths 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 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 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 predicted 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. 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 control processes such as prenatal development and ongoing cellular functions.
9. 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.
10. Because proteins direct the operations of cells, statements like “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, 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, individual differences occur in the rate of progression.

APPENDIX Q. NATIONAL COALITION FOR HEALTH PROFESSIONAL EDUCATION IN GENETICS (NCHPEG) – PRINCIPLES OF GENETICS FOR HEALTH PROFESSIONALS (CONTINUED)

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 nongenetic 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. 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 the juvenile period is long. This requires prolonged parental investment and 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 healthcare and basic research, but it also raises concerns about the use of genetic information.

REFERENCE

National Coalition for Health Professional Education in Genetics' (NCHPEG) publication *Core Competencies in Genetics Essential for All Health*, Joseph D. McInerney, MA, MS, Executive Director, NCHPEG and Barton Childs, MD, Professor Emeritus of Pediatrics and Biology, The Johns Hopkins School of Medicine. Reviewed by NCHPEG's working group on content and instruction.

APPENDIX R. CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)—GENOMIC COMPETENCIES FOR ALL PUBLIC HEALTH PROFESSIONALS AND CLINICIANS

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, and 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

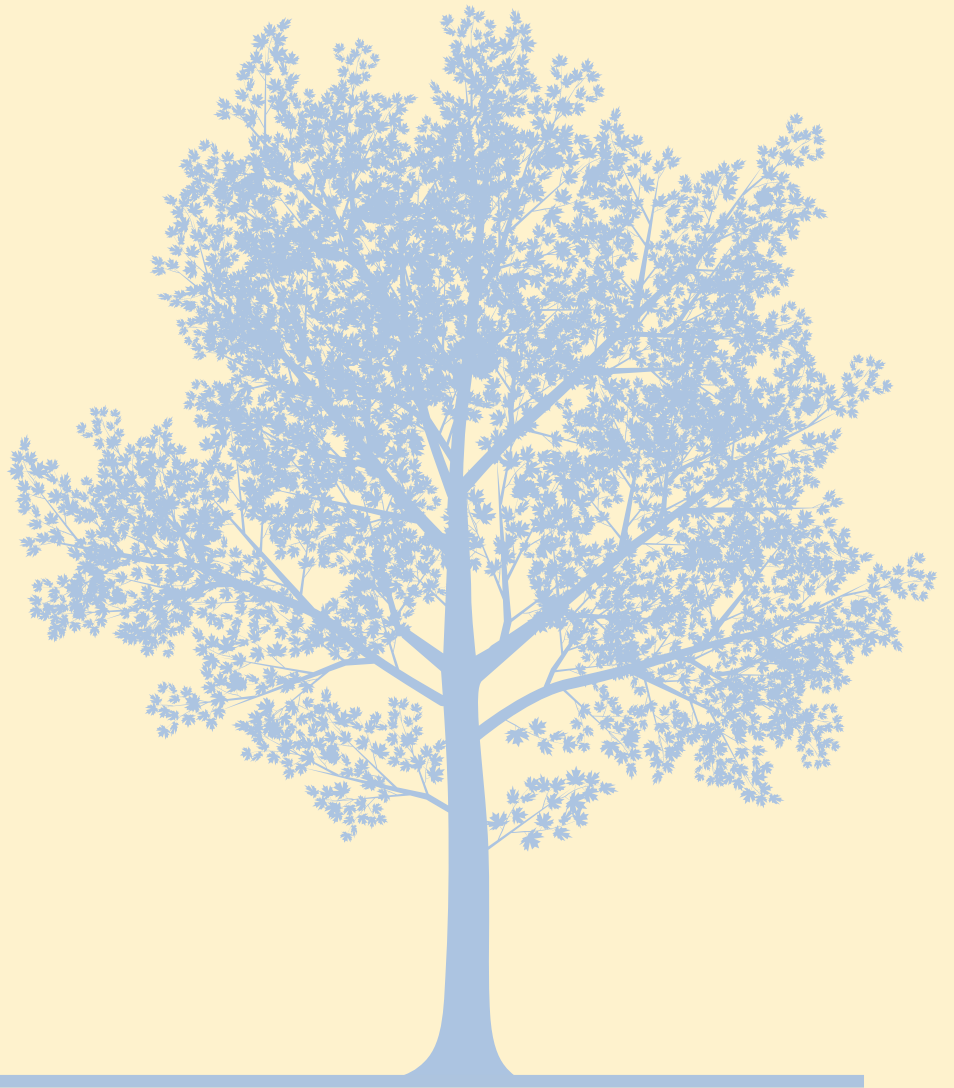
The public health clinician, as appropriate to discipline, agency, or program, is able to:

- 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

REFERENCE

Centers for Disease Control and Prevention. National Office of Public Health Genomics. Genomics Competencies for the Public Health Workforce.
www.cdc.gov/genomics/training/competencies/comps.htm





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