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Appendix Q. National Coalition for Health Professionals Education in Genetics (NCHPEG)—Principles of Genetics for Health Professionals
Appendix R. Centers for Disease Control and Prevention (CDC)—Genomic Competencies for All Public Health Professionals and Clinicians
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**


[www.genhome.nm.gov/handbook/mutationsanddisorders/mutationscausedisease](http://www.genhome.nm.gov/handbook/mutationsanddisorders/mutationscausedisease)
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/famhixfsi.htm](http://www.cdc.gov/genomics/public/famhixfsi.htm)

**Resources**

Centers for Disease Control and Prevention, National Office of Public Health Genomics

[www.cdc.gov/genomics](http://www.cdc.gov/genomics)

Genetic Alliance

[www.geneticalliance.org/familyhealthhistory](http://www.geneticalliance.org/familyhealthhistory)

National Society of Genetic Counselors

[www.nsgc.org/consumer/familytree](http://www.nsgc.org/consumer/familytree)

U.S. Surgeon General’s Family History Initiative

[www.hhs.gov/familyhistory](http://www.hhs.gov/familyhistory)
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: _________________________

<table>
<thead>
<tr>
<th>Health History</th>
<th>Yes</th>
<th>No</th>
<th>Not Sure</th>
<th>Age of Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Blood Pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Cholesterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart Disease or Heart Attack</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Diabetes/Sugar Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Type(s)________________</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alzheimer’s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth Defects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vision Loss/Hearing Loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscarriage/Stillbirth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>How many? __________</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Check one:

- - Smoker  - - Ex-smoker  - - Nonsmoker  - - Not Sure

Other Health Concerns:

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

**HEALTH CONCERNS/RISK FACTORS**

- □ Heart Disease or Heart Attack
- □ Stroke
- □ Diabetes/Sugar Disease
- □ High Blood Pressure
- □ High Cholesterol
- □ Breast Cancer
- □ Ovarian Cancer
- □ Colon Cancer
- □ Endometrial(Uterine) Cancer
- □ Other Cancer: ______________________
- □ Asthma
- □ Vision Loss at a Young Age
- □ Hearing Loss at a Young Age
- □ Genetic Conditions: ______________________
- □ Mental Health: ______________________
- □ Mental Retardation/Developmental Delay
- □ Alzheimer's/Dementia

**PRENATAL CONCERNS**

- □ Birth Defects
- □ Genetic Conditions: ______________________
- □ Miscarriage/Stillbirth

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.)

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Condition</th>
<th>Age of onset</th>
<th>Current age</th>
<th>Age at death, cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brother</td>
<td>High Blood Pressure</td>
<td>35</td>
<td>45</td>
<td>65, Stroke</td>
</tr>
<tr>
<td>Mother</td>
<td>High Blood Pressure</td>
<td>40</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 non-insulin-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

Pedigrees demonstrating clustering of different primary cancers consistent with a family cancer syndrome were high-risk. Pedigrees demonstrating clustering of cardiovascular disease and non-insulin-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/famhist.htm)
4. American Academy of Family Physicians (AAFP) Family History Resources (www.aafp.org)
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.

<table>
<thead>
<tr>
<th>Inheritance Pattern</th>
<th>Characteristics</th>
<th>Disease Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal Dominant</td>
<td>Each affected person usually has an affected parent; occurs in every generation</td>
<td>Huntington’s disease, neurofibromatosis, achondroplasia, familial hypercholesterolemia</td>
</tr>
<tr>
<td>Autosomal Recessive</td>
<td>Both parents of an affected person are carriers; not typically seen in every generation</td>
<td>Tay-Sachs disease, sickle cell anemia, cystic fibrosis, phenylketonuria (PKU)</td>
</tr>
<tr>
<td>X-linked Dominant</td>
<td>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</td>
<td>Hypophatemic rickets (vitamin D-resistant rickets), ornithine transcarbamylase deficiency</td>
</tr>
<tr>
<td>X-linked Recessive</td>
<td>Males are more frequently affected; affected males often present in each generation</td>
<td>Hemophilia A, Duchenne muscular dystrophy</td>
</tr>
<tr>
<td>Mitochondrial</td>
<td>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</td>
<td>Leber’s hereditary optic neuropathy, Kearns-Sayre syndrome</td>
</tr>
</tbody>
</table>

**RESOURCES**

**GeneTests**

www.genetests.org

**Online Mendelian Inheritance in Man (OMIM)**

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.)
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
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.
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
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

www.labcorp.com/genetics/basic_guide/index.html

RESOURCE
GeneTests 
www.genetests.org
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
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](http://www.cdc.gov/ncbddd/bd)

**Medline Plus**

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.
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
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**


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

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_sp.html)

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**
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
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
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*


*Cross Cultural Healthcare Program*

[www.xculture.org](http://www.xculture.org)

*Diversity Rx*

[www.diversityrx.org](http://www.diversityrx.org)

*EthnoMed*

[www.ethnomed.org](http://www.ethnomed.org)

*JAMARDA Resources*

[www.jamardaresources.com](http://www.jamardaresources.com)

*March of Dimes–GENE (Genetics Education Needs Evaluation) Project*

[www.marchofdimes.com/geneproject](http://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](http://www.gucchd.georgetown.edu/nccc/index.html)

*The National Multicultural Institute*

[www.nmci.org](http://www.nmci.org)
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.
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.


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.
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.
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.
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

www.cdc.gov/genomics/training/competencies/comps.htm