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Fact Sheet
Genetic Testing

Introduction

In recent years, much energy has been put into genetic research both through the individual efforts of interested scientists and through the collaboration of international teams in the Human Genome Project. Through this work, we have learned a great deal about how genes function and how they can cause certain problems. We now know how to look for mutations (changes in the gene) that can lead to specific disorders. Genetic testing is possible for some conditions because we can recognize the difference between a normal gene and a disease gene.

Genetic testing presents us with both opportunity and concern. There is opportunity for diagnoses and definitive information and, indeed, a hope that cures may ultimately be possible. On the other hand, we have seen that genetic information can have far-reaching effects on individuals being tested and on their families—emotionally, socially, ethically.

What are genes?

Genes are specific pieces of information that tell our bodies how to grow, function, and develop. It is estimated that each person has between 50,000-100,000 genes. These genes, which are contained on our 23 pairs of chromosomes, make up our genetic blueprint. Each gene codes for a particular set of instructions, and a gene's function is determined by its unique *DNA* code. DNA consists of four basic building blocks called bases that are linked in a specific order. When a change occurs in the ordering or number of bases, a gene may not function properly. A gene change which can cause a disease is called a *mutation*.

How can genes influence disease?

Genes come in pairs, with one copy inherited from each parent. A condition is called dominantly inherited when only one copy of a disease gene is needed to lead to symptoms of that disease. One example of dominant inheritance is Huntington's Disease (HD). The HD gene can be passed from one generation to the next and a person who has the HD gene has a 50% chance of passing that gene on to each of his or her children. A person affected by a recessively inherited condition inherits a particular disease gene from each parent. One example is cystic fibrosis in which both parents, by chance, have passed on a CF gene.

Some diseases do not follow simple patterns of inheritance. Many factors influence how a gene works or who will get a disease and when. Mutations in several different genes can lead to the same disease, as we see in some forms of Alzheimer's disease. Genes that increase one's risk of getting a certain disease are called *susceptibility genes.*

What is genetic testing?

Genetic testing involves analyzing a person's DNA. Usually a blood sample is taken, and a molecular genetics lab performs special tests to look for mutations in a gene that lead to disease. Genetic testing is available for only a fraction of the many genetic conditions in existence. There is no test that analyzes a person's DNA and gives him or her a clean bill of health.

Who might want genetic testing?

Genetic testing can be done to confirm or rule out a certain diagnosis. Testing might interest a person who knows or suspects that he/she is at risk for a genetic disease for which treatment options or preventative measures *are* available. Also, couples considering having children may wish to know the risk of passing on an inherited disorder (e.g., Huntington's disease) to offspring.

What testing is available?

Some of the more common genetic diseases for which genetic tests are available include sickle cell disease, myotonic dystrophy, cystic fibrosis, Duchenne's muscular dystrophy, and Fragile X syndrome.

There are also tests available for some inherited adult-onset disorders, including those described below:

- **Alzheimer's Disease**
  Persons with Alzheimer's disease have progressive impairment in multiple cognitive areas. These areas may include memory, language, calculation, orientation, judgment and personality. Genetic research has found connections between a number of genes and Alzheimer's disease in a small percentage of families with Alzheimer's. Three genes on different chromosomes are associated with early onset familial Alzheimer's. A fourth gene, located on chromosome 19, codes for a protein called APOE. APOE4 is now considered a susceptibility gene for AD and increases the risk for developing AD. Not all people who have this gene will get AD and other people may get AD without having the APOE4 gene. There is evidence for additional Alzheimer's disease genes which have not yet been identified.

  At this time, routine predictive testing of Alzheimer's disease genes is not recommended. The APOE4 gene is only a risk factor and it cannot provide definitive information. Since there is no cure for Alzheimer's disease, the benefit of learning about a possible predisposition to the disease is questionable.

- **Amyotrophic Lateral Sclerosis (ALS)**
  ALS, also known as Lou Gehrig's disease, is a neurodegenerative disorder of motor neurons in the cortex, brainstem and spinal cord. It involves muscle weakness, and as the disease progresses, severe impairment of mobility, speech, swallowing, and respiratory function. One's mind is typically unaffected.

  ALS is inherited in aproximately 10% of cases in an autosomal dominant or autosomal recessive manner. Familial ALS (FALS) has been studied closely to determine that in some families, a mutation in a gene called SOD1 (on chromosome 21) is likely the cause. The vast majority of ALS cases are sporadic with no clear cause. The hope now is that the discovery of a gene causing a disease in certain families may give scientists the lead they have been searching for to reach a cure.

- **Ataxia**
  Ataxia means a lack of coordination and can be associated with a degenerative disorder. Testing is currently available for spinocerebellar ataxia (SCA) Types 1, 2 and 3. Type 3 is also known as Machado-Joseph disease. Dementia is not typically seen in SCA Types 1, 2 and 3. They are inherited in an autosomal dominant manner, meaning that either men or women can be affected and that an affected person has a 50% chance of passing the gene on to each of his/her children. The genes for SCA Types 1, 2 and 3, like the HD gene, have repeated sections of DNA that are larger than those in the normally functioning gene.

- **Cerebrovascular Disease (Stroke)**
  Scientists studying cerebrovascular disease have suggested that many risk factors for stroke are under genetic influence, for example, having a family history of stroke may be associated with an increased risk. Greater understanding of these factors may lead to early recognition of and intervention in stroke. Genetic effects are subject to environmental influences (e.g., diet, weight).

- **DRPLA**
  Dentatorubral-pallidoluysian atrophy includes ataxia and dementia. Genetic testing is possible by looking for an expanded repeat in the gene.

- **Huntington's Disease (HD)**
  Huntington's disease is the most common inher-

ited neurological disease. It is characterized by progressive deterioration. Motor effects progress to uncontrollable movements (chorea) and deterioration of handwriting, speech and swallowing. Cognitive symptoms can include memory loss and progress to dementia. Emotional problems may include personality change and depression.

A person with symptoms of Huntington's disease may have a genetic test to confirm that he/she has HD. People at risk for HD (meaning that one of their parents has HD) may consider presymptomatic testing to learn if they carry the HD gene and therefore will ultimately develop HD symptoms.

After many years of intense research, the HD gene was identified in 1993. It was discovered that a three base pair section of the DNA of the HD gene is repeated many times in individuals who have HD. The normal functional gene does not have this enlargement. Current testing analyzes the HD gene to look for the presence or absence of this enlargement (or expanded repeat). At this time, the function of the HD gene and how it causes HD is not known.

- **Multiple Sclerosis (MS)**
  Multiple sclerosis is a disease that randomly attacks the central nervous system. Familial occurrence (not necessarily genetic) in MS is documented, but uncommon. It is thought that the major causes for MS will prove to be immunological and possibly infectious, but certain genes may be required for susceptibility.

Implications of Testing

Benefits

Although there are no cures for these adult-onset disorders, genetic testing for actual gene mutations can provide an accurate diagnosis or rule out a specific condition. Having a clear diagnosis can allow a person and his/her family to anticipate disease progression and make informed decisions about the future. In some cases, treatment options may be available to slow the progression of symptoms.

Persons at risk (e.g., a person with a parent with Huntington's disease) might feel uncertain about their own future and that of their children. A negative test (indicating that a person does not have the gene) can give a tremendous sense of relief. A positive test result can relieve uncertainty and let the person plan for
the future.

Limitations

There are not tests available for every adult-onset disorder. One important limitation for gene testing is that diagnostic information often is not matched by effective treatment strategies or therapies.

Risks

Since most genetic tests involve only a blood sample, there is no significant physical risk. Any potential risks have more to do with the way the results of the test might change a person's life.

There can be a major psychological impact on people considering and undergoing genetic testing. The knowledge that one does or does not carry a disease gene can provoke many emotions. Many people with a family history of certain diseases have already seen relatives become affected by the disorder. The news that they have the disease gene can lead to depression or anger. These emotions can impact the person and reverberate throughout the family. A person who finds he/she does not carry a disease gene may feel guilty.

There is also concern about confidentiality. People have expressed concern that testing information could someday be used against them.

Genetic discrimination

As knowledge about the genetic basis of common disorders grows, so does the potential for discrimination in obtaining health or life insurance. People also have concerns about discrimination in employment.

At the state and federal levels, legislation is being pursued to help ensure that genetic information is not used against people. The Americans with Disabilities Act (ADA) provides employment anti-discrimination protection for people with disabilities and neurological disorders. In addition, as an example of state law, the State of California prohibits insurers, to varying degrees, from requiring or requesting genetic tests or their results, from denying

coverage on the basis of genetic tests, and from using tests to determine rates and benefits. California law has provisions to protect the privacy of genetic information. However, in this time of flux and changing health care systems, it is not clear to what extent consumers are protected. People considering genetic testing need to consider potential risks for discrimination.

Whom to contact

Your primary care physician may be able to make a referral to a specialist such as a neurologist and genetic counselor as appropriate. The National Society of Genetic Counselors may also be a helpful source of referrals. A trained professional can help evaluate family history, document diagnosis and discuss whether testing options are available. In addition, in California there is a Genetically Handicapped Persons Program (see *Resources* section of this fact sheet).

How can genetic counseling help?

Genetic counselors are specially trained health professionals who help families learn about and cope with genetic conditions. If a person is considering testing, a genetic counselor would discuss risks, benefits, and limitations and provide balanced information for the individual to make an informed decision about whether to proceed with testing. There are many issues to consider including psychological impact, family issues, and privacy. Genetic counseling can be helpful in addressing these issues. Genetic counselors support families and individuals in making decisions about genetic testing and in adjusting to test results.

How do people decide about genetic testing?

The decision about whether to have testing is a very personal one. It should also be voluntary; people should have the test only if they want the information and should not be pressured into testing by relatives or health care providers.

Because the issues are so complex and the consequences so profound, the decision to have a genetic test deserves careful preparation and thought.

As a final note, it is also important to understand that the available information is changing rapidly as genetic research continues. It is likely that more information and genetic tests will be available in the future. Please use the Resource listings below to help stay informed and up to date.

Resources

Huntington's Disease Society of America
140 West 22nd St., 6th Flr.
New York, NY 10011-2420
(212) 242-1968
(800) 345-HDSA

HDSA maintains a list of genetic testing centers across the U.S.

Genetically Handicapped Persons Program
State of California Department of Health Services
714 P St., Rm. 300
Sacramento, CA 95814
(916) 654-0503
(800) 639-0957

Alliance of Genetic Support Groups
35 Wisconsin Circle, Suite 440
Chevy Chase, MD 20815
(800) 336-4363
(301) 652-5553

National Alliance for Rare Disorders
P.O. Box 8923
New Fairfield, CT 06812
(800) 999-6673
(203) 746-6518

National Society of Genetic Counselors
233 Canterbury Dr.
Wallingford, PA 19086-6617
(610) 872-7608

Human Genome Management Information System
Oak Ridge National Lab
1060 Commerce Park MS 6480
Oak Ridge, TN 37830
(423) 576-6669
Publishes a *Primer on Molecular Genetics.*

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families and caregivers of brain-impaired adults. Funded by the Californ
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