



Genetic Testing

*A Growing Approach to
Disease Diagnosis and Treatment*

By Amy Scanlin, MS

The growing interest in genetic testing has spurred the field of genetic counseling, leading to better health outcomes and treatment options.

WITH MORE THAN 1,800 genetic tests available through research centers and direct-to-consumer kits, and more than 10 million genetic variants, the interest in genetic testing is rapidly gaining momentum, with some estimates showing a market growth of as much as 25 percent annually. Alongside this rise comes increased access to information about health status and susceptibility to health concerns, diseases and potential expectations for projected life span. “The field of genetics has grown tremendously,” explains James P. Evans, MD, PhD, Bryson Distinguished Professor of Genetics and Medicine at the University of North Carolina, Chapel Hill. While the possibilities for this information seem endless, it is important to gain a better understanding of what genetic testing is, what can be gained from it and how results can best be interpreted.

What Is Genetic Testing and How Is It Used?

Genetic tests identify changes in chromosomes, genes or proteins that may be able to confirm or rule out a genetic condition or help determine a person’s chance of developing or passing on a genetic disorder. For instance, scientists can look at a single gene’s short DNA strands to identify mutations that can lead to a genetic disorder. They can look at whole chromosomes or long lengths of DNA to see if there are large genetic changes such as an extra copy of a chromosome that can cause a genetic condition. Or, they may consider biochemical genetic tests to study the activity level or number of proteins since abnormalities can indicate changes to DNA that result in a genetic disorder.

In a clinical setting, genetic testing is generally a simple blood draw that allows for a better quality DNA sample. In some cases, only one gene is looked at such as with the rare condition of fragile X syndrome. In others, multiple genes are tested at once such as with suspected autoimmune disease in which a mutation or error in any number of genes collectively can increase a person’s risk. In some cases, doctors know which gene they are specifically testing for, but in others, they aren’t sure. Complex diseases such as those with known strong genetic and environment components make testing and forming conclusions more difficult. Multiple sclerosis (MS), for example, is known to be caused by both genetic and environmental factors. “The field of genetics doesn’t really understand what to test for with MS,” explains Erynn Gordon with the National Society of Genetic Counselors. “Research tells us there is clearly a genetic component, but we don’t yet know the gene to test for.” In these cases, testing multiple genes at one time can provide a cost-effective look at a number of genetic causes.

Genes are DNA inherited from parents that can tell one version

of a person’s risk for disease, its potential severity and other factors. Typical reasons for genetic testing referrals differ between adults and children. For instance, in adults, the most common testing referral occurs because of an unusual cancer diagnosis such as young age or other suspicious factors. In children, a birth defect is the most common reason. Patients with suspected or familial immune disorders are frequently referred for genetic testing to assist with diagnosis and clinical prognosis and to narrow successful pharmacogenetic treatment options. “While most diseases aren’t genetic in nature,” explains Dr. Evans, “our development is driven by our genes.”

Understanding a person’s genetic makeup can help guide patients and physicians in making healthcare choices. It can guide families in deciding about future pregnancies by identifying genes that can be passed on to children, and it can better inform expectant and new parents about any conditions their newborn may be susceptible to both in utero and after birth. Obstetrics is an area in which genetic testing is common because it is a noninvasive prenatal look via amniotic fluid or placenta tissue samples. Once a child is born, a heel stick screening can identify any abnormalities that warrant further exploration.

Genetic testing can provide vast amounts of information to patients, as well as patients’ first-, second- and, in some cases, third-degree relatives who may also choose to undergo genetic

Direct-to-Consumer Genetic Testing

With the thousands, and by some reports tens of thousands, of genetic tests available, curiosity about direct-to-consumer (DTC) genetic testing is increasing. While the lure of quick and easy answers draw consumers, the U.S. Food and Drug Administration, Centers for Disease Control and Prevention, Federal Trade Commission and some healthcare associations such as the American College of Medical Genetics and the American Society of Human Genetics urge consumers to use caution and remember there are many complex layers of information surrounding both the decision to undergo a genetic test and how to interpret the results. Without the context of a medical evaluation, a full interpretation of the results and what to do next, DTC test results may be meaningless to the consumer. And, while many DTC test kits suggest contacting a professional to discuss results, the onus is on the patient to do so.

testing based on results. For example, while there may be a familial pattern of autoimmunity, autoimmune diseases seen in each family member may be different. The ability to genotype family members for their own genetic information and identify appropriate donors can be critical to patients' health and healthcare. This information may inspire patients to make different decisions, which can be overwhelming because it can completely change the trajectory of their lives.

The good news is geneticists (doctors who specialize in genetics), genetic counselors (certified healthcare workers who counsel patients on genetic testing plans and results), nurses, social workers and other specialists trained in genetics can help patients evaluate the decisions surrounding testing and how to interpret the results. Patients can then be armed with the best available information and how to use it.

HELP FROM GENETICISTS AND GENETIC COUNSELORS CAN DETERMINE CLINICAL UTILITY, OR WHETHER THE INFORMATION CAN LEND INSIGHT INTO A DIAGNOSIS, MANAGEMENT OR TREATMENT.

What Genetic Test Results Mean

The term "genetic mutation" sounds scary. However, most disease-causing genetic mutations are rare. Mutations, or alterations, also apply to things as simple as eye color and blood type.

If a test comes back "positive," it means the genetic alteration tested for was detected. If it comes back "negative," it means it was not detected or it is inconclusive, which means either not enough information was gleaned or further testing may be warranted.

The terms "positive," "negative" and "inconclusive" may also suggest a "bad result," "good result" or "question mark." For instance, testing positive for a gene mutation doesn't mean the disease is inevitable (just as not everyone who carries the BRCA1 or BRCA2 genes develop breast or ovarian cancer). Also, the course or severity of a disease can't be predicted. And, just because a test doesn't reveal a gene mutation, it's still possible the disease will develop (like those who develop breast cancer even though they don't carry BRCA1 or BRCA2 genes).

Confusing results is just one reason it is so important for individuals making the decision to undergo genetic testing to do so under the guidance of healthcare professionals who can discuss family history, available tests and the analytical (accuracy) and clinical (whether they actually provide the information sought) validity of the tests. Taken together, help from geneticists and genetic counselors can determine clinical utility, or whether the information can lend insight into a diagnosis, management or treatment.

What to Expect from Genetic Testing and Genetic Counseling

Why is genetic testing important? Why not just diagnose the disease and treat it if possible? According to Gordon from the National Society of Genetic Counselors, there are many important reasons: "In some cases, the phenotype, what the patient is experiencing, can have multiple different causes as in the case of peripheral neuropathy. Sometimes it is caused by diabetes, and sometimes there are hereditary causes. Another example is Charcot-Marie-Tooth disease, which can have different versions and be inherited in different ways."

Another reason is the symptom being tested for may be one of many, and an evaluation can help determine what other organ systems may be involved and whether an evaluation of family members may lead to a bigger picture of the disease. "Some diseases are more clearly genetic than others," Gordon explains. "In many cases, the disorders of interest will be more diverse, and a test may rule in or rule out hereditary forms."

Gordon says that, oftentimes, people are not referred to geneticists when they should be: "There is a tendency, rightfully so, for specialists to focus on their area of expertise, but that may mean multisystem disorders are missed. If you are a patient and have multiple systems involved in your disease, ask your doctor if something could be tying them all together. There are probably more genetic disorders than we realize because we tend to focus on the primary system rather than the bigger picture."

Genetic counselors are facilitators and educators for both patients and primary care physicians. They primarily deal with face-to-face patient interaction to help address concerns and to ease patients into the process. It starts with a discussion of family history to better understand who else might be affected and whether other considerations need to be addressed. They then discuss the type of tests to be performed, any risks, how long the results will take and what types of information the tests will provide.

How the results are interpreted and what type of follow-up is required depends on each situation. For example, in pediatrics, genetic counselors provide “anticipatory guidance” to educate families and their doctors and ensure they are connected with all available resources. “In a pediatric setting, we help the family figure out if there is a genetic condition for what we are seeing,” explains Robin Grubs, assistant professor of human genetics and director of the genetic counseling program at the University of Pittsburgh. “We discuss all the possibilities with the patients and their families, [including discussing] possible outcomes and what a positive or negative result may mean, as well as treatment possibilities. We help patients understand the possible outcomes so they won’t be blindsided by the results. We must ensure they understand that this could be really serious.”

In adults, cancer is the most common type of referral to a genetic counselor, and the relationship between the counselor and patient is generally shorter term because the counselor becomes part of the precision medicine process of disease management. In those for whom increased surveillance is warranted, adapted screening recommendations and testing can help to keep on top of risks.

For prenatal patients, it is hoped the relationship is even shorter, says Janice G. Edwards, MS, CGC, clinical professor and director of the genetic counseling program at the University of South Carolina School of Medicine: “We never see them again if they are healthy.” But, when needed, genetic counselors follow the patient and help the parents get through the crisis.

Genetic Testing Costs

Genetic testing can run anywhere from a few dollars (in the case of some prenatal screenings) to a few thousand dollars. Many insurance companies cover genetic testing, at least in part, so it is important to verify which tests are covered and the co-pay amount.

Many genetic tests today are moving toward what is known as panel testing, or testing multiple genes at once. “Going back to the peripheral neuropathy example,” explains Gordon, “we might look at all the genes that could be associated, rather than guessing which gene could be the underlying cause.” According to Gordon, the field of genetics is moving so fast that costs of testing have dropped significantly: “If multiple genes can have a similar presentation, it makes sense to cast a wider net.”

No matter the results, the Genetic Information Nondiscrimination Act prevents both health insurers and employers (provided the employer has more than 15 employees) from discrimination based on test results. Even with this pro-

tection, however, some elect to undergo genetic testing without going through their insurer because it could affect the cost of insurance. Also, some types of coverage do not fall under this protective umbrella such as long-term care, disability and life insurance.

Genetics of the Future

Genetic disorders were once so rare, most pharmaceutical companies declined to invest in them. But now, pharmacogenetics is a promising field and is beginning to change the way medicine is prescribed, with a focus on tailored treatments. “Now, we are understanding the molecular mechanisms, what is broken and how that affects proteins,” says Gordon. “We can focus in, as is the case with cystic fibrosis and Duchenne muscular dystrophy, and we’ll see this increasing over time.”

“We are trying to better understand precision medicine,” says Grubs. “Our goal is to understand the factors that contribute to disease.” In the meantime, patients can play a role in their health, including the possibility of whether health-harming genes are triggered by environmental factors. For example, some drugs are associated with the development of immune disorders, and some suspect that certain viruses are associated as well. Even iodine has been attributed to the onset of thyroid disease. “We want to give patients a sense of agency in what they can do for their health,” adds Grubs.

In some genetic conditions, dietary changes or enzyme replacement therapy can help. Resources such as the American Cancer Society’s cancer prevention guidelines offer recommendations that should be adopted by most everyone. Eliminating tobacco, maintaining a healthy weight, performing physical activity and eating a healthy diet are important proactive steps people can take. “Everyone can reduce their cancer risk,” says Grubs, “even if they have a hereditary form of cancer.”

“One day, we’ll have lots of changes we can make, but we aren’t there yet,” explains Edwards. “Today, if patients know they have a genetic change that makes them more at risk, as in the case of increased risk for breast cancer, they can have a prophylactic surgery to reduce the risk.” And, in the future, we may have other means and protocols. ■

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Resources

1. National Society for Genetic Counselors Patient Resource: aboutgeneticcounselors.com
2. American Cancer Society Cancer Prevention Guidelines: www.cancer.org/healthy/eat-healthy-get-active/acs-guidelines-nutrition-physical-activity-cancer-prevention.html