HOW TO DISCUSS GENETIC DISEASE WITH YOUR LOVED ONES

RARE TOOLKITS

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Introduction

This toolkit is based on the Global Genes Webinar How to Discuss Genetic Disease with Your Loved Ones that was originally webcast April 1, 2015. A replay can be viewed at http://globalgenes.org/april2015webinar/.

There are currently about 7,000 rare diseases identified worldwide, and approximately 80 percent of these are caused by genetic changes. This toolkit will provide some basics on genetic diseases, how and when patients might want to discuss details of their disease with others, and with whom.

SECTION 1: UNDERSTANDING GENETICS

DNA

Each person has their own genome, a genetic blueprint consisting of deoxyribonucleic acid, or DNA. DNA is a molecule that is shaped like a twisted ladder and is contained in virtually all of the cells of the body. Each person's DNA contains a unique set of instructions that determines the characteristics of an individual.

Chromosomes

Within a person's cells, DNA is coiled up and stored within 23 pairs of chromosomes with one set of 23 coming from the father and the other set of 23 coming from the mother. Within the chromosomes, tiny segments of DNA form genes. Depending on the type of cell, certain genes will be activated to perform specific functions.

Genes

Genes make proteins, which carry out various functions within the body. In the case of a genetic disease, a mutation in the gene may prevent a needed protein from being made or carry out some other interference to the proper functioning within the body. People have two copies of each gene in their body with one derived from their mother and one derived from their father.

One Way to Distinguish Genetic Diseases

One difference in the various genetic diseases is how they are passed on between parent and child. Some genetic diseases require mutations from both parents for them to manifest (autosomal dominant). Other diseases may require that just one parent pass on the mutation in a gene (autosomal recessive). In some cases, someone may carry a genetic disease, but show no signs for having the disease themselves. Still, in other cases, a person with a genetic disease may have a mutation that is not present in either the mother or father (de novo).

Autosomal dominant

If one parent carries a mutation for an autosomal dominant genetic disease, the couple's child has a one in two (50 percent) chance of having that genetic disease.

Autosomal recessive

If both partners carry mutations for an autosomal recessive genetic disease, their child has a one in four (25 percent) chance of having that genetic disease.

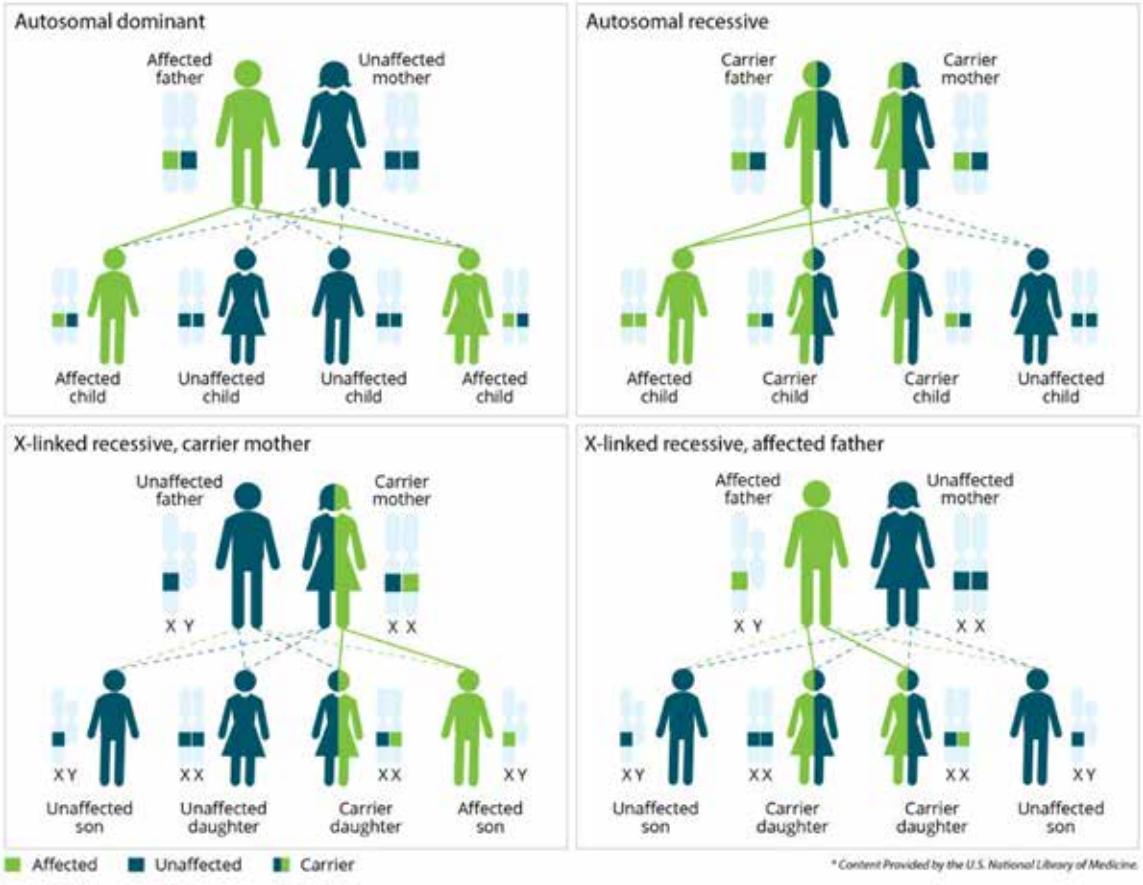
SECTION 1: UNDERSTANDING GENETICS

X-linked recessive

X-linked genetic diseases are passed on by the X chromosome that determines the sex of a person. Males have a Y chromosome from their father and an X chromosome from their mother. Females have an X chromosome from their father and a second X chromosome from their mother. If the female partner is a carrier of an X-linked genetic disease, her male child has a one in two (50 percent) chance of having that genetic disease. Because females have two X chromosomes, whereas males only have one, these diseases tend to show up predominantly in males or are generally more severe in males.

De novo mutations

Some genetic mutations are not passed on from a person's parent, but begin with the individual. These types of genetic mutations are referred to as "de novo."



SECTION 2:
HOW TO DIAGNOSE A GENETIC CONDITION

People will seek genetic testing to get a diagnosis for a possible genetic disease, but while some people want answers, others may find more comfort in denial. For many parents concerned that their child may have a genetic disease, knowing is better than not knowing and finding an explanation for an illness or being able to give a condition a name can provide some comfort.

> "Often, that is a relief, but it's only the beginning of the answer because as we get the answer, we have to go forward," says Michelle Fox, an independent genetic counselor. "What does it mean for the child? What does it mean for the family? What does it mean for reproductive options? There's a lot of information that is just the beginning."

A diagnosis is only a starting point. Genetic counselors can help newly diagnosed patients put a plan in place to tackle the range of challenges that a genetic-based disease brings. This includes connecting with support efforts, finding other patients, considering whether to participate in research, and more.

Michelle notes that genetic counselors don't always deliver bad news and that as treatment options for genetic conditions continue to grow, there are now more reasons than ever to find an underlying diagnosis.

Pre-Natal Testing

Before having children, some people will chose to be tested to identify their risk of having a child with a genetic disease. These tests work by looking at specific genes associated with a variety of genetic diseases to see if people carry any of the genetic mutations associated with a number of diseases. They are a means of identifying the risk of having a child with a genetic disease, but will not be comprehensive. It's still possible that someone with a genetic mutation for a very rare disease will not be detected by a pre-natal test that doesn't specifically test for that disease. This is something that should be discussed with a genetic counselor prior to taking a test.

Diagnostic Testing

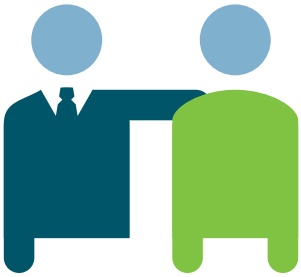
Because rare diseases often begin with symptoms that can be indicative of more common diseases, getting a correct diagnosis can often take years. Eventually, the diagnostic odyssey may lead to genetic testing. Genetic testing can determine changes in chromosomes, genes, or proteins. These tests can confirm, or rule out, suspected genetic conditions.

SECTION 2: HOW TO DIAGNOSE A GENETIC CONDITION

> "It was emotional, but also, it was very good for me. Some patients, when they get a serious diagnosis, that's when they feel upset and possibly suicidal," says Janet Mills, Trustee and Patient Advocate, cureCADASIL Association. When she finally had a diagnosis after more than 20 years of living with the symptoms of her disease, she felt relief. "There really is something wrong," she says. "I'm not a hypochondriac. I know what's wrong and I can deal with it better."

The cost of genetic testing is falling rapidly, but whole genome sequencing is used today, usually when other tests fail to provide needed answers. Instead, doctors likely will use more narrow types of genetic tests if a genetic disease is suspected. A fuller discussion of genetic concepts and genetic testing is available in the **Genetic Testing: Is This My Path to a Diagnosis?** toolkit http://globalgenes.org/toolkits/genetic-testing-is-this-my-path-to-a-diagnosis-3/introduction/

Some people may be hesitant to get testing because of concerns about the potential for discrimination. There are specific protections against discrimination on the basis of genetics. In 2008, President George W. Bush signed the Genetic Information Nondiscrimination Act into law. Hailed as the "first civil rights bill of the new century," the law prohibits employers or insurance companies from discriminating against people on the basis of their genetic information. It prohibits insurance companies from using genetic information to make eligibility, coverage, underwriting, or premium-setting decisions. Employers are prohibited from using genetic information to make decisions about hiring, promotion, and certain other terms of employment. To learn more, go to http://ghr.nlm.nih.gov/spotlight=thegeneticinformationnondiscriminationactgina.



SECTION 3: THE ROLE OF GENETIC COUNSELORS

Genetic counselors are specially trained professionals who can provide information, explain tests and results, and deliver ongoing support and guidance to patients. As part of their education, genetic counselors undergo special training on communication, as well as psycho-social issues. When working with patients, they will often begin by gauging a patient's level of understanding, but focus on keeping information simple and straightforward. Rather than weighing deep in concepts of molecular biology, genetic counselors will focus on what's important to their patients, such as understanding a disease's manifestation, what it means for them of their family, and how it might affect reproductive options.

> "In general," says Jenna Miller, a genetic counselor with the clinical genomic testing company Recombine, "I would say keeping it simple is good for everyone."

People have different appetites for information and getting news of a rare disease diagnosis can be overwhelming to absorb along with other information that may be provided. Often doctors may take a very clinical approach and may tend to use scientific terms and focus on delivering the diagnosis. Genetic counselors can translate complex information that a doctor may not have taken the time to explain and can also help patients decide with whom they might want to discuss their condition and how to best do that.

Doctors will treat the physical aspect of the disease, but genetic counselors can provide a more holistic approach to helping patients with the emotional aspect of the disease, cope with the challenges of the disease, and provide resources to help manage their disease over time.

> "It goes way beyond diagnosing. It goes to learning how to manage and care for a dis-ease," says Cynthia Frank, director of patient advocacy and meetings for the National Gaucher Foundation. "Although my doctor really does help me with the treatment and what physical aspects I can expect from the disease, it's genetic counselors, and I call them 'my angels,' who really helped me over the years to cope with my disease and give me the emotional support and the resources to really manage my disease over the long term."

The National Society of Genetic Counselors provides an online directory to help patients find genetic types of specialty, or zip code. It can be accessed at http://nsgc.org/p/cm/ld/fid=164

SECTION 4: WHO TO TELL?

In making a decision about with whom patients might choose to discuss their genetic-based rare disease, one factor to consider is whether the genetic mutation driving the disease is from both parents, one parent, can be carried by siblings, or represents a new mutation.

Though many people may value their privacy and consider their rare disease nobody's business but their own, there are many reasons why patients or parents of children with a rare disease might choose to share that information with others.

Doctors

Any medical professional that provides care should be informed of a patient's rare disease even if the doctor is not treating the patient for that condition. The condition can carry risks for certain procedures or medications and may also explain symptoms that patients think are unrelated to the disease.

Family Members

Family members, particularly those who may share the same genes, should be told if they may be carrying a mutation that can cause a rare disease, if they are at risk for having that disease, or at risk for passing it on to a child. They might want to seek genetic testing to determine if they too have the mutation. In discussing a genetic-based rare disease with family members, it is helpful to tell them about a specific test they may want to have performed, provide them with a copy of their test results, and refer them to their genetic counselor. Though the risks are highest for first degree relatives (parents, siblings, children), other relatives may also share an aberrant gene. Family dynamics vary and for some people these are difficult conversations to have. As much as someone with a rare disease may want someone in their family to be tested, they will not be able to force them to do so. For a variety of reasons, some people will not want to know if they carry a genetic condition.

Explaining a Disease to a Child

Genetic counselors will develop a plan with the parents before an actual diagnosis to determine whether they want the child in the room at the time of the diagnosis or if they want to explain it to them. Genetic counselors can help gauge the child's level of understanding and what they need to know. They can also help a parent explain to a child why they are getting a certain test and what the results mean. Children who have a disease will need to know how to live with it and while parents may want to shield their children from unhappy news, they may find their children are more resilient and capable of understanding their condition than they thought. A genetic counselor can help parents work through how to talk to them and what it means to them.

> "Parents think that children don't know things, but they do," says the genetic counselor Michelle Fox. "For instance, if they are coming to the doctor repeatedly, they do know something is wrong with them."

Teachers and Others

There are reasons why patients and their parents may choose to share information with teachers and others about their rare disease. This is not just because of safety issues, but to help them understand certain conditions that have outward manifestations that cause others to have concern either about the individual or their own risks of catching something they don't understand.

SECTION 5: PATIENT STORIES

Everyone's circumstances are different, but below are a few examples of personal experiences with rare diseases and how circumstances led individuals to make others aware of their particular rare condition.

Concerned about Safety

Janet Mills had symptoms of her disease as a teenager, but she wasn't actually diagnosed with CADASIL, until she was 49. CADASIL is a rare genetic disease that causes a progressive degenerative of blood vessels and can cause strokes. Because CADASIL causes a weakening of the blood vessels, medications used to normally treat stroke patients can cause fatal cerebral hemorrhage. Janet not only wears a medical alert bracelet, but she also discusses her condition with her friends because if she blacks out, suffers a migraine, or has a stroke, they need to know where she keeps her medical information and what they can do to help.

A Child's Perspective

At 13, Cyndi Frank was diagnosed with Gaucher's disease, a lysosomal storage disorder. Though enzyme replacement therapy is available today, at the time of her diagnosis, such treatments were about 20 years away from market. She remembers her parents talking over her head with her doctor. She says she had been through more than 100 blood tests and finally confronted her parents and told them she wanted to know what was going on. She told them she was old enough to know what she had and her parents agreed. She says the person with the disease is the one who needs to learn how to live with it.

Ivy's Cards

Jenna Miller, a genetic counselor, tells the story of her niece Ivy, a little girl who has a rare disease called epidermalytic hyperkeratosis or EHK, a genetic disease that can cause very red skin and severe blisters. The skin grows fast and can look yellow, thick, or scaly. Because the manifestations of the disease are very apparent, they can cause people to have unwarranted concerns. Ivy's parents printed up cards that explain Ivy's condition and provide assurance that Ivy is not hurt, neglected, or contagious.

For More Information:

- Check with your genetic counselor or physician for appropriate resources;
- Seek out specialists;
- If you have a diagnosis, find a group focused on that condition; and
- Ask questions about your family history.

SUGGESTED RESOURCES

- To learn more about genetics, try the website **Genes in Life** (http://genesinlife.org/).
- The **Genetics Home Reference Guide** is a helpful resource for understanding issues surrounding genetics (http://ghr.nlm.nih.gov/).
- For help in finding a genetic counselor, try the **National Association of Genetic Counselors** (http://nsgc.org/p/cm/ld/fid=164).
- Download the **RARE Toolkit, Genetic Testing: Is This My Path to a Diagnosis?** here (https://globalgenes.org/wp-content/uploads/2014/05/GG_toolkit_seven_web.pdf).
- View the **Global Genes Webinar How to Discuss Genetic Disease with Your Loved Ones** that was originally webcast April 1, 2015. A replay can be found at (http://globalgenes.org/april2015webinar/).

Global Genes Would Like to Thank All of This Toolkit's Contributors

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