Genetics of Dystonia

Individuals diagnosed with dystonia may be concerned that their children are at risk of inheriting the disorder. Being informed about the genetics of dystonia can also be important in the diagnosis and treatment process. There are forms of dystonia that are known to be genetically inherited and forms that may or may not have a genetic component—researchers simply cannot confirm or rule it out at this time. Currently, several dystonia genes with numerous mutations and other abnormalities have been linked to specific forms of dystonia.

A genetic counselor can help individuals and families learn more about the genetics of dystonia and whether genetic testing may be appropriate. Researchers are actively seeking to better understand the genetics of all dystonias and to identify additional gene mutations.

DYSTONIA MEDICAL RESEARCH FOUNDATION

serving all dystonia-affected persons

What Forms of Dystonia are Inherited?

If an individual has a form of dystonia that is known to be genetic then there is a chance that the person may pass the disorder to his/her children. This is especially true if other family members exhibit symptoms or are already diagnosed. The degree of risk varies with the form of dystonia and what is known about inheritance patterns of those specific forms.

Genetic dystonias that are known to run in families include:

- Primary torsion dystonia (which may include childhood and adult onset, generalized and focal symptoms)
- Dopa-responsive dystonias
- Myoclonus dystonia
- Paroxysmal dystonias/dyskinesias
- Rapid-onset dystonia-parkinsonism
- X-linked dystonia-parkinsonism

However, not everyone who inherits a dystonia-causing gene mutation will develop symptoms. This phenomenon is known as *reduced penetrance*.

Also, some people develop dystonia due to a gene mutation without any apparent family history. And to complicate things further, there are families in which many members are diagnosed with dystonia but no specific genetic mutation has yet been identified.

Secondary Dystonias

If an individual's dystonia is secondary to an injury to the brain or nervous system (including exposure to certain medications or stroke), his/her children are in all likelihood not at increased risk of inheriting a known dystonia-causing mutation. However, researchers do not know at this time whether individuals who develop secondary dystonias have a genetic factor that makes them vulnerable to dystonia. It could also be that individuals who do not develop dystonia, despite injuries to the nervous system, have a protective factor that is lacking in those who do develop secondary dystonias. Moreover, dystonia can occur as a symptom of various genetically-caused diseases, in which the inheritance patterns vary.

Dystonia Gene Mutations

Each gene consists of DNA (deoxyribonucleic acid) that contains a code for a specific protein. Proteins participate in virtually every process in the human body. When a gene becomes mutated, this changes the protein associated with that gene and, ultimately, how that protein functions. When a changed protein cannot properly fulfill its function, this may disrupt normal biological processes and lead to a disease or disorder, including dystonias.

Identifying dystonia gene mutations is important for patients because it may clarify complex dystonia diagnosis, point to specific treatments, and give families the information needed to explore, if they choose, measures to reduce the risks of dystonia in future generations.

Dystonia mutations also give researchers an important clue to help unravel the complicated series of biochemical events that causes dystonia symptoms. Every time a new dystonia gene or gene mutation is discovered, it provides a new therapeutic target for the development of new treatments.

Inheritance Patterns

One of the greatest mysteries that dystonia researchers are working to solve is that not everyone who inherits a dystonia gene mutation will develop symptoms.

Most of the dystonias for which gene mutations have been identified are dominantly inherited, meaning that only one parent needs to have the mutation for a child to inherit the disorder. However, most dystonia mutations also exhibit *reduced penetrance*, which means that not every person who inherits the gene will develop symptoms. Research is ongoing to better understand this phenomenon.

Who is a Candidate for Genetic Testing for Dystonia?

Genetic testing is available to determine if an individual has a specific gene mutation associated with certain dystonias. These include:

- Certain early onset dystonias
- Dopa-responsive dystonias
- Myoclonus dystonia
- Paroxysmal dystonias/dyskinesias
- Rapid-onset dystonia-parkinsonism
- X-linked dystonia-parkinsonism

The first step for individuals and families who wish to learn more about genetic testing for dystonia is to consult a genetic counselor who is trained to educate families and prospective parents on the likelihood and risks of inherited diseases.

Genetic testing is only available for specific forms of dystonia for which a gene mutation or other abnormality has been identified. An individual can still have dystonia without testing positive for a specific dystonia mutation. Testing negative for known dystonia mutations does not necessarily negate a clinical diagnosis. As additional dystonia gene mutations are discovered, genetic testing will become informative for more dystonia patients.

A genetic counselor can help individuals and families understand what testing may be appropriate for them. Testing may be suggested for adults and children who exhibit clinical symptoms that resemble the forms of dystonia for which gene tests are available.

Adult biological relatives of individuals who have been identified as having a genetic form of dystonia may also be eligible for testing.

Genetic testing in children who do not exhibit symptoms is generally not recommended, even if a biological relative tests positive for a dystonia mutation. Options exist for individuals with specific genetic forms of dystonia who wish to decrease the likelihood of passing the mutation onto their children. These options include prenatal testing and pre-implantation genetic diagnosis (PGD). PGD uses *in vitro* fertilization and sophisticated gene testing techniques prior to pregnancy to dramatically reduce the chance of a baby inheriting a disease-causing mutation.

How Do I Find a Genetic Counselor?

Individuals may choose to locate a genetic counselor by consulting their movement disorder specialist or health insurance provider. Several professional organizations can also provide contact information for genetic counselors:

GeneTests - National Center for Biotechnology Information
http://www.genetests.org

National Society of Genetic Counselors
http://www.nsgc.org

How Do I Learn More About Dystonia?

Visit the Dystonia Medical Research Foundation (DMRF) website for more information. The DMRF is dedicated to advancing research for more treatments and ultimately a cure, promoting awareness, and supporting the well-being of affected individuals and families.

DYSTONIA MEDICAL RESEARCH FOUNDATION
serving all dystonia-affected persons

One East Wacker Drive, Suite 2810
Chicago, Illinois 60601-1905
Toll free: 800-377-DYST (3978)
Phone: 312-755-0198
Email: dystonia@dystonia-foundation.org
Web: http://www.dystonia-foundation.org

Find the DMRF on Facebook, Twitter, and YouTube.

Many thanks to Laurie Ozelius, PhD for reviewing this publication.