Dystonia

U.S. DEPARTMENT OF HEALTH
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Dystonia

What is dystonia?

Dystonia is a disorder characterized by involuntary muscle contractions that cause slow repetitive movements or abnormal postures. The movements may be painful, and some individuals with dystonia may have a tremor or other neurological symptoms. There are several different forms of dystonia that may affect only one muscle, groups of muscles, or muscles throughout the body. Some forms of dystonia are genetic but the cause for most cases is not known.

What are the symptoms?

Dystonia can affect many different parts of the body and the symptoms are different depending upon the form of dystonia. Symptoms may include:

- a foot cramp or a tendency for one foot to turn or drag—either sporadically or after running or walking some distance
- a worsening in handwriting after writing several lines
- the neck may turn or pull involuntarily, especially when the person is tired or under stress

- both eyes might blink rapidly and uncontrollably; other times, spasms will cause the eyes to close
- tremor
- difficulty speaking

The initial symptoms can be very mild and may be noticeable only after prolonged exertion, stress, or fatigue. Over time, the symptoms may become more noticeable or widespread; sometimes, however, there is little or no progression.

In some cases, dystonia can affect only one specific action, while allowing others to occur unimpeded. For example, a musician may have dystonia when using a hand to play an instrument, but not when using the same hand to type.

Dystonia typically is not associated with pain or problems thinking or understanding, but depression and anxiety may occur.

What do researchers know about dystonia?

Researchers believe that dystonia results from an abnormality in or damage to the basal ganglia or other brain regions that control movement. There may be abnormalities in the brain's ability to process a group of chemicals called neurotransmitters that help cells in the brain communicate with each other. There also may be abnormalities in the way the brain processes information and generates commands to move. In most cases, no abnormalities are visible using magnetic resonance imaging or other diagnostic imaging.

The dystonias can be divided into three groups: idiopathic, genetic, and acquired.

Idiopathic dystonia refers to dystonia that does not have a clear cause. Many instances of dystonia are idiopathic.

There are several **genetic** causes of dystonia. Symptoms may vary widely in type and severity even among members of the same family. In some instances, people who inherit the defective gene may not develop dystonia. Having one mutated gene appears to be sufficient to cause the chemical imbalances that may lead to dystonia, but other genetic or even environmental factors may play a role.

Forms of dystonia for which the genetic cause is known include:

- **DYT1 dystonia** is a rare form of dominantly inherited generalized dystonia that can be caused by a mutation in the *DYT1* gene. It typically begins in childhood, affects the limbs first, and progresses, often causing significant disability. Because the gene's effects are so variable, some people who carry a mutation in the *DYT1* gene may not develop dystonia.
- **Dopa-responsive dystonia** (DRD), also known as *Segawa's disease*, is another form of dystonia that can have a genetic cause. Individuals with DRD typically experience onset during childhood and have progressive difficulty with walking. Symptoms characteristically fluctuate and are worse late in the day and after exercise. Some forms of DRD are due to

mutations in the *DYT5* gene. People with this disorder have dramatic improvements in symptoms after treatment with levodopa, a medication commonly used to treat Parkinson's disease.

Recently, researchers have identified other genetic causes of dystonia, including one resulting from mutations in the *DYT6* gene. Dystonia caused by *DYT6* mutations often presents as cranial dystonia, cervical dystonia, or arm dystonia. Rarely, a leg is affected at the onset.

Many other genes that cause dystonic syndromes have been found, and numerous genetic variants are known. Some other important genetic causes of dystonia include mutations in the following genes: *DYT3*, which causes dystonia associated with parkinsonism; *DYT11*, which causes dystonia associated with myoclonus (brief contractions of muscles); *DYT12*, which causes rapid onset dystonia associated with parkinsonism, and *DYT28*, which is associated with childhood onset dystonia.

Acquired dystonia, also called secondary dystonia, results from environmental or other damage to the brain, or from exposure to certain types of medications. Some causes of acquired dystonia include birth injury (including hypoxia, a lack of oxygen to the brain, and neonatal brain hemorrhage), certain infections, reactions to certain drugs, heavy metal or carbon monoxide poisoning, trauma, or stroke. Acquired dystonia often plateaus and does not spread to other parts of the body.

Dystonia that occurs as a result of medications often ceases if the medications are stopped quickly. Dystonia can be a symptom of other diseases, some of which may be hereditary.

When do symptoms occur?

Dystonia can occur at any age, but genetic and idiopathic dystonia are often divided as either early, or childhood onset, versus adult onset.

- Early onset dystonia often begins with symptoms in the limbs and may progress to involve other regions. Some symptoms tend to occur after periods of exertion and/or fluctuate over the course of the day.
- Adult onset dystonia usually is located in one or adjacent parts of the body, most often involving the neck and/or facial muscles. Acquired dystonia can affect other regions of the body.

Dystonia often progresses through various stages. Initially, dystonic movements may be intermittent and appear only during voluntary movements or stress. Later, individuals may show dystonic postures and movements while walking and ultimately even while they are relaxed. Dystonia can be associated with fixed postures and shortening of tendons.

How is dystonia classified?

Dystonia is classified along two distinct axes.

- Axis I is based on clinical features which include age at onset, body region affected, specific features, and whether there are associated clinical problems.
- Axis II is based on etiology or cause. This classification includes dystonia caused by genetics or abnormalities in the brain, and idiopathic dystonia, for which the cause is unknown.

What are the different forms of dystonia?

There are many different forms of dystonia. Within Axis I, some are grouped by the regions of the body which they affect:

- **Generalized dystonia** affects most or all of the body.
- **Focal dystonia** is localized to a specific part of the body.
- **Multifocal dystonia** involves two or more unrelated body parts.
- **Segmental dystonia** affects two or more adjacent parts of the body.
- **Hemidystonia** involves the arm and leg on the same side of the body.

Some of the more common focal forms are:

Cervical dystonia, also called *spasmodic torticollis* or *torticollis*, is the most common of the focal dystonias. The muscles in the

neck that control the position of the head are affected, causing the head to turn to one side or to be pulled forward or backward. Sometimes the shoulder is pulled up. Cervical dystonia can occur at any age, although most individuals first experience symptoms in midlife. It often begins slowly and usually reaches a plateau over a few months or years. About 10 percent of those with torticollis may experience a spontaneous remission, but unfortunately the remission may not be lasting.

Blepharospasm, the second most common focal dystonia, is the involuntary, forcible contraction of the muscles controlling eye blinks. The first symptoms may be increased blinking, and usually both eyes are affected. Spasms may cause the eyelids to close completely, causing "functional blindness" even though the eyes are healthy and vision is normal.

Cranial dystonia affects the muscles of the head, face, and neck (such as blepharospasm). The term *Meige syndrome* is sometimes applied to cranial dystonia accompanied by blepharospasm. **Oromandibular dystonia** affects the muscles of the jaw, lips, and tongue. It may cause difficulties with opening and closing the jaw, and speech and swallowing can be affected. **Spasmodic dysphonia**, also called *laryngeal dystonia*, involves the muscles that control the vocal cords, resulting in strained or breathy speech.

Task-specific dystonias tend to occur only when undertaking a particular repetitive activity. Examples include *writer's cramp* that affects the muscles of the hand and sometimes the forearm, and only occurs during handwriting. Similar focal dystonias have also been called typist's cramp, pianist's cramp, and musician's cramp. **Musician's dystonia** is a term used to classify focal dystonias affecting musicians, specifically their ability to play an instrument or to perform. It can involve the hand in keyboard or string players, the mouth and lips in wind players, or the voice in singers.

What treatments are available?

Currently, there are no medications to prevent dystonia or slow its progression. There are, however, several treatment options that can ease some of the symptoms of dystonia, so physicians can select a therapeutic approach based on each individual's symptoms.

- **Botulinum toxin**. Botulinum injections often are the most effective treatment for the focal dystonias. Injections of small amounts of this chemical into affected muscles prevent muscle contractions and can provide temporary improvement in the abnormal postures and movements that characterize dystonia. First used to treat blepharospasm, such injections are now widely used for treating other focal dystonias. The

toxin decreases muscle spasms by blocking release of the neurotransmitter acetylcholine, which normally causes muscles to contract. The effect typically is seen a few days after the injections and can last for several months before the injections must be repeated. The details of the treatment will vary among individuals.

- **Medications**. Several classes of drugs that affect different neurotransmitters may be effective for various forms of dystonia. These medications are used "off-label," meaning they are approved by the U.S. Food and Drug Administration (FDA) to treat different disorders or conditions but have not been specifically approved to treat dystonia. The response to drugs varies among individuals and even in the same person over time. These drugs include:
  - *Anticholinergic agents* block the effects of the neurotransmitter acetylcholine. Drugs in this group include trihexyphenidyl and benztropine. Sometimes these medications can be sedating or cause difficulties with memory, especially at higher dosages and in older individuals. These side effects can limit their usefulness. Other side effects such as dry mouth and constipation can usually be managed with dietary changes or other medications.

- *GABAergic agents* are drugs that regulate the neurotransmitter GABA. These medications include the benzodiazepines such as diazepam, lorazepam, clonazepam, and baclofen. Drowsiness is their common side effect.

- *Dopaminergic agents* act on the dopamine system and the neurotransmitter dopamine, which helps control muscle movement. Some individuals may benefit from drugs that block the effects of dopamine, such as tetrabenazine. Side effects (such as weight gain, depression, and involuntary and repetitive muscle movements) can restrict the use of these medications. Dopa-responsive dystonia (DRD) is a specific form of dystonia that most commonly affects children, and often can be well managed with levodopa.

- **Deep brain stimulation** (DBS) may be recommended for some individuals with dystonia, especially when medications do not sufficiently ease symptoms or the side effects are too severe. DBS involves surgically implanting small electrodes that are connected to a pulse generator into specific brain regions that control movement. Controlled amounts of electricity are sent into the exact region of the brain that generates the dystonic symptoms and interfere with and block the electrical signals that cause the symptoms. DBS also involves follow up and adjustments to optimize an individual's DBS settings.

- **Other surgeries** aim to interrupt the pathways responsible for the abnormal movements at various levels of the nervous system. Some operations purposely damage small regions of the thalamus (thalamotomy), globus pallidus (pallidotomy), or other deep centers in the brain. Other surgeries include cutting nerves leading to the nerve roots deep in the neck close to the spinal cord (anterior cervical rhizotomy) or removing the nerves at the point they enter the contracting muscles (selective peripheral denervation). Some individuals report significant symptom reduction after surgery.
- **Physical and other therapies** may be an adjunct to other therapeutic approaches. Speech therapy and/or voice therapy can be helpful for some affected by spasmodic dysphonia. Physical therapy, the use of splints, stress management, and biofeedback also may help individuals with certain forms of dystonia.

What research is being done?

The ultimate goals of research are to find the cause(s) of the dystonias so that they can be prevented, and to find ways to cure or more effectively treat people who are affected. The National Institute of Neurological Disorders and Stroke (NINDS), a part of the National Institutes of Health (NIH), is the Federal agency with primary responsibility for brain and neuromuscular

research. NINDS sponsors research on dystonia both in its facilities at the NIH and through grants to medical centers and institutions throughout the country. Scientists at other NIH institutes also conduct research that may benefit individuals with dystonia. Scientists at the National Institute on Deafness and Other Communication Disorders (NIDCD) are studying improved treatments for speech and voice disorders associated with dystonia. The National Eye Institute (NEI) supports work on the study of blepharospasm and related problems, and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) supports work on dystonia, including rehabilitation for the disorder.

Scientists at NINDS laboratories and clinics have conducted detailed investigations of the patterns of muscle activity, imaging studies of brain activity, and physiological studies of the brain in persons with dystonia.

Treatment studies, using surgery or medication, are being conducted in many centers, including the NIH. To learn more about clinical studies on dystonia, visit https://www.clinicaltrials.gov/.

The Dystonia Coalition is a clinical research network for dystonia created with support from NINDS and the NIH Office of Rare Disease Research as part of the Rare Disease

Clinical Research Network. For more information on the clinical studies and patient registry established by the Coalition, see https://www.rarediseasesnetwork.org/cms/dystonia.

The search for genes responsible for some forms of dystonia continues. In 1989 a team of researchers mapped the first gene for early-onset torsion dystonia to chromosome 9; the gene was subsequently named *DYT1.* In 1997 the team sequenced the *DYT1* gene and found that it codes for a previously unknown protein now called "torsin A." The discovery of the *DYT1* gene and the torsin A protein provides the opportunity for prenatal testing, and allows doctors to make a specific diagnosis in some cases of dystonia. It also facilitates s the investigation of molecular and cellular mechanisms that lead to disease.

The discovery of the mutation in "torsin A" has enabled scientists to study animal models into which the mutated gene has been introduced. Many more genes have been found and are being studied. Through research with people informed by the latest discoveries from genetics and basic neuroscience, scientists and doctors hope to better understand dystonia and find more effective treatments.

Where can I get more information?

For more information on neurological disorders or research programs funded by NINDS, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
800-352-9424
http://www.ninds.nih.gov

Information also is available from the following organizations:

Dystonia Medical Research Foundation
One East Wacker Drive, Suite 1730
Chicago, IL 60601-1980
312-755-0198
http://www.dystonia-foundation.org

National Spasmodic Dysphonia Association
300 Park Boulevard, Suite 175
Itasca, IL 60143
800-795-6732
www.dysphonia.org

National Spasmodic Torticollis Association
9920 Talbert Avenue
Fountain Valley, CA 92708
714-378-9837; 800-487-8385
http://www.torticollis.org

American Speech-Language-Hearing Association (ASHA)
2200 Research Boulevard
Rockville, MD 20850
800-638-8255
http://www.asha.org

Benign Essential Blepharospasm Research Foundation
P.O. Box 12468
Beaumont, TX 77726-2468
409-832-0788
http://www.blepharospasm.org

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