

Background

CERVICAL DYSTONIA

What is cervical dystonia?

Cervical dystonia, also called spasmodic torticollis, is the third most common movement disorder, after Parkinson's disease and tremor,¹ affecting approximately 125,000 people in the United States.² The disorder is characterized by involuntary contractions of the neck muscles that cause twisting, repetitive movements, or abnormal postures of the head. These muscle contractions hinder normal movement and can cause severe, chronic neck pain.

Most often cervical dystonia develops between the ages of 30 and 50, and women are twice as likely to be affected as men.³ Cervical dystonia belongs to a group of movement disorders, collectively known as "focal dystonias," that affect more than 300,000 people in North America,⁴ yet awareness of this condition is extremely limited.

The symptoms of cervical dystonia usually develop gradually over a period of time, with the severity of symptoms leveling off after five years. These symptoms can include painful contractions of the neck muscles that force the head to move forward (anterocollis), backward (retrocollis), sideways (laterocollis), or to twist to the left or right (torticollis). The neck spasms experienced by patients with this disorder may be constant or intermittent. This excessive muscle activity is often painful. In one study of 170 patients, more than 90 percent of cervical dystonia patients experienced chronic pain.⁵

What causes cervical dystonia?

Until recently, cervical dystonia was often misunderstood and misdiagnosed as stress, scoliosis, arthritis, or a variety of other conditions. Although the exact cause of the disorder is unknown, cervical dystonia has been observed to develop in conjunction with an injury to the brain or neck muscles (e.g., whiplash), or after prolonged exposure to certain neuroleptic or antipsychotic drugs. Some forms of dystonia may also be genetic, as mutations in the *DYT-1* gene have been linked to an early-onset form of the disorder.⁶ It is thought that each of these factors may somehow affect the basal ganglia of the brain, which is involved in the control and coordination of muscle activity, and cause the release of excessive and erratic signals to the neck muscles.⁷

Physicians use a variety of tools including function and movement scales, global assessment scales, and pain scales to assess the degree of disease progression and determine which treatment will provide the most benefit to the patient.

How is cervical dystonia treated?

Cervical dystonia is treated by various medical experts, including neurologists and movement disorder specialists, otolaryngologists (ear, nose and throat specialists), and physiatrists (doctors specializing in physical rehabilitation). While there is no cure for cervical dystonia, there are treatment options that can help relieve the excessive muscle spasms of the neck and shoulder muscles and the associated neck pain.

Injection of therapeutic doses of BOTOX[®] (Botulinum Toxin Type A) into the neck and shoulder muscles is the most commonly used treatment for cervical dystonia in adults to decrease the severity of abnormal head position and the associated neck pain. Derived from the bacterium *Clostridium botulinum*, BOTOX[®] therapy inhibits the release of a neurotransmitter, acetylcholine, from nerve cells, blocking the signals that promote involuntary muscle contraction. The effect is temporary and the treatment needs to be readministered approximately every three months depending on the individual patient.

Other current therapies used for cervical dystonia include benzodiazepines, baclofen (an anti-spasmodic agent), anti-cholinergic agents and surgical denervation. While the benzodiazepines interfere with chemical activities between nerve cells in the brain, reducing muscle contractions, baclofen acts primarily on the spinal cord to reduce the amount of contractions. The anticholinergic agents block the release of acetylcholine from nerve cells and are usually administered orally to patients with early-onset cervical dystonia. In severe cases, surgeries in which either the nerve cell is removed from the contracting muscle or a section of the muscle itself is removed are recommended in patients who do not respond to less invasive therapy.

Finally, physical therapy is recommended in all patients with dystonia. Stretching exercises and neck braces have been shown to ease the severity of contractions and are recommended in addition to medication and/or other therapies.

Important Safety Information on BOTOX[®]

BOTOX[®] and BOTOX[®] Cosmetic treatments are contraindicated in the presence of infection at the proposed injection site(s) and in individuals with known hypersensitivity to any ingredient in the formulation. Serious and/or immediate hypersensitivity reactions have been rarely reported. These

reactions include anaphylaxis, urticaria, soft tissue edema, and dyspnea. If such a reaction occurs further injection of BOTOX[®] or BOTOX[®] Cosmetic should be discontinued and appropriate medical therapy immediately instituted. BOTOX[®] and BOTOX[®] Cosmetic should only be diluted with 0.9 percent non-preserved sodium chloride. Individuals with peripheral motor neuropathic diseases (e.g., amyotrophic lateral sclerosis, or motor neuropathy) or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should only receive BOTOX[®] or BOTOX[®] Cosmetic with caution. Patients with neuromuscular disorders may be at increased risk of clinically significant systemic effects including severe dysphagia and respiratory compromise from typical doses of BOTOX[®] or BOTOX[®] Cosmetic. There have been rare reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including cardiovascular disease. The exact relationship of these events to the botulinum toxin injection has not been established.

BOTOX[®] for Cervical Dystonia in Adults: The most frequently reported adverse reactions in patients with cervical dystonia are dysphagia (19%), upper respiratory infection (12%), neck pain (11%), and headache (11%). There have been rare cases of dysphagia severe enough to warrant the insertion of a gastric feeding tube.

Please see enclosed full prescribing information for BOTOX[®] and BOTOX[®] Cosmetic.

BOTOX[®] therapy should only be administered by a trained and qualified physician. Further product and prescribing information is available by visiting www.Botox.com; or by visiting www.BotoxGlobalNews.com, selecting the country of interest and clicking on “Country Resources/Prescribing Information.”

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¹ Dystonia Medical Research Foundation. *Dystonia Defined*. Available at: <http://www.dystonia-foundation.org/defined>. Accessed: December 10, 2003.

² Spasmodic Torticollis/Dystonia. Available at: http://www.spasmodictorticollis.org/newsroom_QASheet.cfm. Accessed: 1/25/07.

³ We Move. Epidemiology of Cervical Dystonia..Available at: http://www.wemove.org/dys/cdys_epi.html. Accessed: March 16, 2004.

⁴ Dystonia Medical Research Foundation. *Dystonia Defined*. Available at: <http://www.dystonia-foundation.org/defined>. Accessed: December 10, 2003.

⁵ Hauser RA, Comella C, et al. A randomized, multicenter, double-blind, placebo-controlled trial of original BOTOX[®] (Botulinum Toxin Type A) purified neurotoxin complex for the treatment of cervical dystonia. Presented at the International Conference 1999: Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Orlando Florida, 1999.

⁶ Ozelius LJ, Hewett JW, et al. The early-onset torsion dystonia gene (DYT1) encodes an ATP binding protein. *Nature Genetics*. 1997.

⁷ Dystonia Medical Research Foundation. *Q&A about dystonia*. April 2000.