Yesterday

- Dystonia was a seriously debilitating condition, affecting thousands of Americans with disabling involuntary muscle contractions that often produce twisting, abnormal postures, or repetitive movements.
- Although some clinicians had speculated that dystonia could be inherited, its potential genetic causes were unknown and the cellular biology underlying the development of the disease was not understood at all.
- Treatment for dystonia was mainly limited to surgeries that destroyed small regions of brain tissue or severed peripheral nerves believed to be responsible for the abnormal movements. The use of oral medications to treat dystonia was just beginning, but none were very effective.

Today

- Today, scientists and clinicians have a much greater understanding of the causes of dystonia and patients have many more treatment options, thanks to advances in dystonia research.
- Researchers have identified more than 15 different genetic mutations that can contribute to dystonia. To expedite genetic studies, the NINDS Human Genetics Repository (http://ccr.coriell.org/sections/collections/NINDS/?Ssid=10) now serves as a resource for the research community to share clinical information and patient samples.
- Among the most important gene findings were the identification of mutations in the gene DYT1 that cause primary torsion dystonia, a whole-body or “generalized” form of the disorder. Genetic testing is now available to people with dystonia and their family members to determine whether they have a DYT1 mutation.
- Investigators are beginning to understand how genetic mutations and environmental influences lead to abnormal changes in the cells of the nervous system that contribute to the disease. Animals models of dystonia – based in some cases on the manipulation of the genes linked to the disorder in humans – are making a substantial contribution to these basic science research efforts.
- Some patients who have a specific form of dystonia may experience considerable relief by taking levodopa, a drug that the body uses to synthesize the nerve chemical dopamine. Drugs that interfere with another neurochemical, acetylcholine (which stimulates muscle movements), may also be effective.
- Deep brain stimulation (DBS) – the electrical stimulation of very small regions of brain tissue by surgically implanted electrodes – is effective for some people with dystonia. DBS has reduced the use of older, usually less effective forms of surgery that created permanent damage to the nervous system.
- Other very effective treatment options are also available for some types of dystonia, including minute injections of botulinum toxin (sold under the trade names of Botox® and Myobloc™) into dystonic muscles. This therapy has revolutionized the treatment of focal dystonias, that is, dystonias that are limited to a single area of the body such as the neck, eyelid, hand, or voicebox (larynx). The toxin works by blocking the release of acetylcholine in the local area of injection, and it can improve symptoms for several months.

Tomorrow

- Better understanding of the molecular and cellular mechanisms of dystonia is revealing targets for development of therapies that stop the development of abnormal movements, rather than interfering with downstream events to simply quell the symptoms.
- Imaging techniques show abnormal activation patterns in motor and sensory brain areas. This is critical to understanding how current therapies interact with the nerve circuits that cause abnormal movements and how to improve the effectiveness of these treatments.
• With improved surgical techniques and a better understanding of the mechanisms of dystonia and of deep brain stimulation (DBS), clinicians and surgeons are developing more personalized DBS therapy for people who have different types of dystonia, through selection of electrode target sites and adjustment of stimulation parameters.

• The NIH-funded Dystonia Coalition ([http://rarediseasesnetwork.epi.usf.edu/dystonia/index.htm](http://rarediseasesnetwork.epi.usf.edu/dystonia/index.htm)) is working to advance the pace of therapy development. The Coalition brings together 40 clinical sites in 9 countries, working with 9 patient advocacy groups, as well as private sector pharmaceutical companies. This extensive cooperation will greatly facilitate research because there are many types of dystonia, often seen by different subspecialists, and each type may be uncommon, making it difficult for any single center to see enough patients to rapidly conduct meaningful clinical studies.

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