Dystonia Support Group of Greater Washington DC

October 2015

In Association with the Dystonia Medical Research Foundation

Message from Sally Presti
Support Group Leader of the Dystonia Support Group of Greater Washington DC

Dear Friends, I hope you enjoyed the summer months and are doing well. Our next meeting is on November 15, 2015. It promises to be an especially exciting one as we try to provide information that is not only interesting but also useful for coping with all forms of dystonia. Our speaker will be Karin Mente, M.D. a research fellow with the Human Motor Control Section (HMCS} at the National Institute of Neurological Disorders and Strokes of the National Institutes of Health (NINDS/NIH). Dr. Mente works with Dr. Mark Hallett, director of HMDS at NINDS/NIH, and will speak on local and national dystonia research projects and the importance of this research for understanding and developing treatments for dystonia. Our meeting will conclude with our popular medical advisor, Dr. Stephan Grill, M. D. who always speaks on a timely topic followed by an active Q and A discussion.

This should be a very informative and interesting meeting with time before and after for socializing and meeting new friends. Put November 15th on your calendar and we look forward to seeing you there.

Always,
Sally

IN THIS ISSUE...

Knights of Pythias Fund Clinical Trial

The Knights of Pythias, Pythian Sisters of Maryland, have graciously funded a clinical trial for treating cervical dystonia. Dr. Stephen Grill and his team at the Parkinson's and Movement Disorders Center of Maryland will conduct a randomized investigator-blinded trial of specific physical therapy to treat cervical dystonia. The trial will be a cross-over design so that patients will be randomized to active therapy for ½ of the duration of the trial either for the first or second three months of the 6 month study. Patients will continue to receive whatever other treatments they are currently receiving.

Dystonia Support Group of Greater Washington DC Support Group Meeting November 15, 2015

Location: Holy Cross Hospital, 1500 Forest Glen Road, Silver Spring, MD 20910-1484

When: November 15, 2015 Social starts at 12:30PM, Speaker starts at 1:00PM

Speakers: Karin Mente, M.D., Clinical Fellow in the Human Motor Control Section of the National Institute of Health, National Institute of Neurological Disorders and Stroke (NIH/NINDS)
Dr. Mente will discuss the Human Motor Control research studies and research in the dystonia community worldwide.

Stephen Grill, M.D., Our Support Group's Medical Advisor will provide a short talk on very timely and relevant information. Dr. Grill will be available for questions and answers.

If you like, bring a snack to share. Beverages will be provided.

Directions to Holy Cross Hospital 1500 Forest Glen Rd, Silver Spring, MD 20910-1484 301-754-7000

From I-495, take exit 31, Georgia Ave - Wheaton (Rt. 97 North), Turn right onto Forest Glen Rd, Follow 4 blocks (.3 miles) to Holy Cross Hospital on the right, at the corner of Forest Glen and Dameron Drive

Metro Directions to Holy Cross Hospital

Holy Cross Hospital is located five blocks from the Forest Glen (Red Line) Metro station. From the station, cross Georgia Avenue then walk five blocks down Forest Glen Road. Hospital is on the right.

CALENDAR OF EVENTS

WHAT	WHERE	WHEN	SPEAKER/TOPIC
Meetings of the Dystonia Support Group of Greater Washington DC	Holy Cross Hospital 1500 Forest Glen Road Silver Spring, MD 20910-1484	**Tentative** 2016 Schedule March 16, 2016 April 3, 2016 September 18, 2016 November 13, 2016	• To be announced. We need your suggestions on topics. Please call Sally Presti at 301-627-1657 with your suggestions.

BRAIN DONORS ESSENTIAL FOR IMPORTANT RESEARCH: Consider brain donation. For more information or to begin the registration process, visit https://www.dystonia-foundation.org/get-involved/participate-in-research/become-a-brain-donor or contact the DMRF at 800-377-3978.

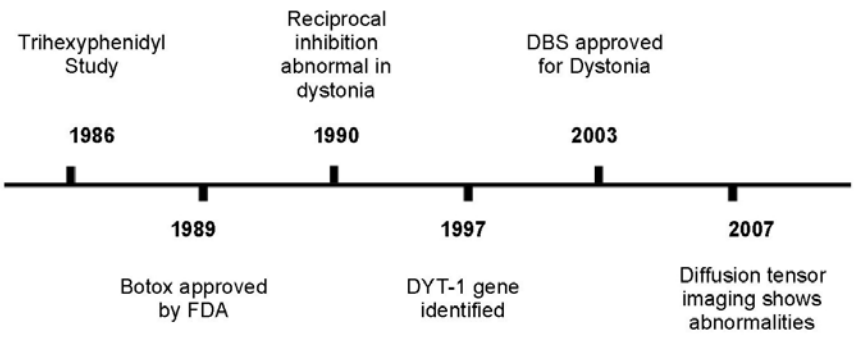
STAY IN TOUCH: Sign up for the DMRF monthly e-newsletter for the latest updates and announcements at https://www.dystonia-foundation.org/get-involved/stay-connected or contact the DMRF at 800-377-3978.

ADVANCES IN DYSTONIA OVER 25 YEARS
Topic Presented by Dr. Stephen Grill at our September 27, 2015 Support Group Meeting

Dr. Stephen Grill began his presentation with an overview of the major milestones in the understanding and treatment of dystonia. They were

1. Progress in identifying effective treatments.
2. New approaches to understanding pathophysiology, which is the disturbance of function that a disease causes in an organ.
3. Understanding of genetics.

Dr. Grill spoke to each of the major dates on the dystonia timeline which are identified in this graph.



Dr. Stephen Grill is a neurologist and director of the Parkinson's and Movement Disorders Center of Maryland. Dr. Grill has been our group's medical advisor for over 25 years. He has attended over 84 of our support group meetings where he provides information on the treatment and research on dystonia.

In 2013 Dr. Grill was awarded the Castle Connolly's Top Washington DC and Baltimore Doctor award as well as the Compassionate Doctor Recognition in 2014.

His office is at 8180 Lark Brown Rd, Suite 101; Elkridge, MD 21075
Phone: (443) 755-0030

1986 Trihexyphenidyl (Artane) Study

The first double-blind placebo-controlled trial of anti-cholinergic medication was conducted in 1986. Anti-cholinergics are a class of drugs that block the action of the neurotransmitter acetylcholine in the brain. The drugs help to block involuntary movements of the muscles. They also balance the production of dopamine and acetylcholine in the body. The patient population where individuals with childhood onset generalized dystonia but without perinatal insults (i.e. patients who suffered strokes while still in the womb). It was a thirty-six week study; cross-over design, meaning everyone was given the "real" drug but researchers and patients did not know when the drug was administered. Trihexyphenidyl (Artane) was increased weekly by 5 mg up to 30 mg/day. 40 patients enrolled; 31 completed study Videotapes were reviewed by a blinded observer using a "global assessment" seven (7) point scale where 4 was no difference, 1 was worst, and 7 was best. 22 (71%) had a clinically significant response. The benefit outweighed side effects such that patient elects to continue medication at conclusion of study. Most common adverse events were blurred vision (19) and dry mouth (10) which were usually transient. Seven patients were forgetful/confused. 21/31 remained on medication after a mean follow up time of 2.4 yrs. (Burke et al, 1986, Neurology).

1989 BOTOX (Botulinum Toxin Type A)

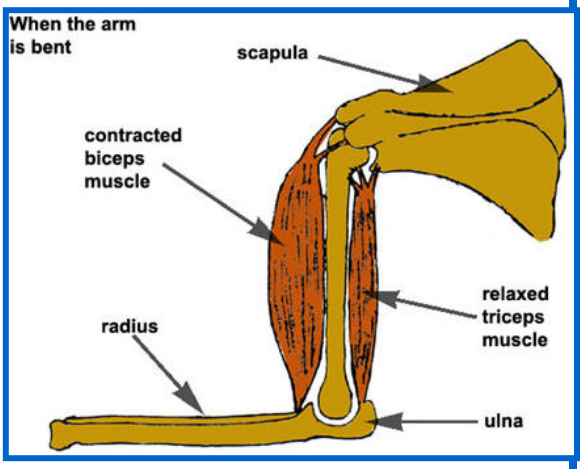
Today BOTOX is approved for multiple indications in 70 countries worldwide Over 900,000 patients have been treated worldwide. More than 11 years of clinical experience worldwide. Endorsed by the American Academy of Neurology (AAN) and the NIH since 1990. During the 1700s and 1800s, scientists identified the cause of botulism. In 1944, E. Schantz, et al began purifying botulinum toxin type A. In 1968, Dr. Allan Scott was the first to use BOTOX to treat eye movement disorders in children. In 1970s and 1980s, BOTOX was used to treat blepharospasm and strabismus. In 1989, it was used to cervical dystonia.

ADVANCES IN DYSTONIA OVER 25 YEARS (Continued)

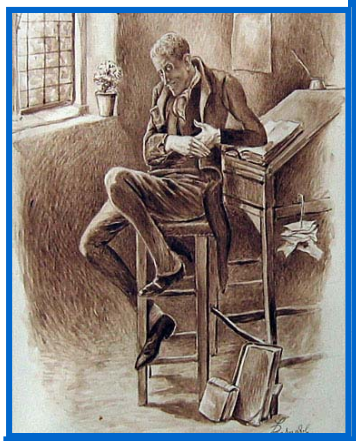
Botulinum toxin targets motor nerve terminals. It weakens the connection between the nerve and the muscle. BOTOX works in the muscle but does not address the disorder inside the brain that causes the brain to send the errant signals. The administering doctor may use an Electromyography, (EMG) to identify the "correct" muscle in which to inject the BOTOX. It may take days after the injection before the patients feels the effect of the BOTOX which will "wear off" within several months.

1990 Reciprocal Inhibition Was Noted to be Abnormal in Dystonia

Dr. Marcela Panizza, Dr. Stefania Lelli, Dr. Mark Hallett and Jan Nilsson BSEE, studied H-reflex and reciprocal inhibition in upper limbs. They studied patients with Cervical dystonia (10), Generalized (5), blepharospasm (5), writer's cramp (14). During normal movement, muscles are activated to move a limb and the muscles opposing the movement are inhibited. This is called Reciprocal Inhibition. In dystonia, there is "overflow" so that inappropriate muscles are activated. Normally, when you bend your arm, your biceps muscle is contracted and your triceps muscles relax. With dystonia, the triceps muscles contract as well as the biceps contract causing abnormal movements or postures. Even before this abnormal posturing was medically studied, it is possible to find precise descriptions of dystonia in art and literature. It is thought that Charles Dickens depicted several of his characters in Dave Copperfield as having dystonia. Dickens character, Uriah Heep, may have had generalized dystonia. Dickens described Uriah Heep's movements as jerking and writhing. Dickens described his other character, Mr. Sharp, as a man whose head was too heavy for him to hold straight which could have been describing cervical dystonia. Mr. Creakle could have had spasmodic dysphonia.



Ancient Representation of Meige's Syndrome in Moche Culture (pre-Columbian Peru)



Drawing of Uriah Heep by Fred Barnard

1990 DYT-1 Gene Identified

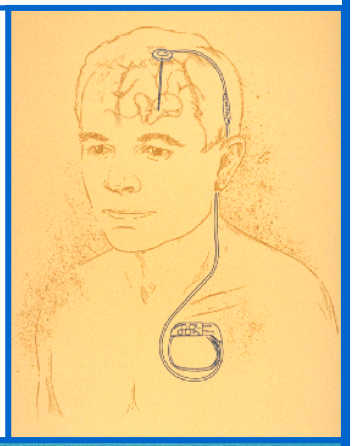
DYT-1 gene defect found on chomosome 9q34 to be responsible for disease. It codes for TorsinA protein.

- Deletion of a single 3 base-pair
- Accounts for 80% of early-onset primary dystonia.

Frequent in Ashkenazi Jews

- Inherited as autosomal dominant trait with reduced penetrance
- Deletion results in loss of one of a pair of glutamic-acid residues
- Other deletions in the vicinity may produce dystonia
- TorsinA is associated with a variety of cellular activities. Restricted to neurons
- Normally associated with endoplasmic reticulum. Defective protein associated with nuclear envelope Defect results in loss of function (Nature Genetics 1997)

ADVANCES IN DYSTONIA OVER 25 YEARS (Continued)



2003 Deep Brain Stimulation (DBS) approved for Dystonia

- Surgeons noticed that low-frequency stimulation of the pallidum caused abnormal movements but high frequencies may suppress them.
- Mundinger 1977: targeted the thalamus and subthalamic nucleus; appeared favorable
- Andy 1983: Reported favorable results in 2 patients with torticollis
- Use of pallidotomy in PD demonstrated improvement in dyskinesias and dystonias in 1990's
- This was proposed as a treatment in young persons with dystonia. An 8 year old girl with severe dystonia returned to independence.
- Lesion or lead is placed within posterior (sensorimotor region)

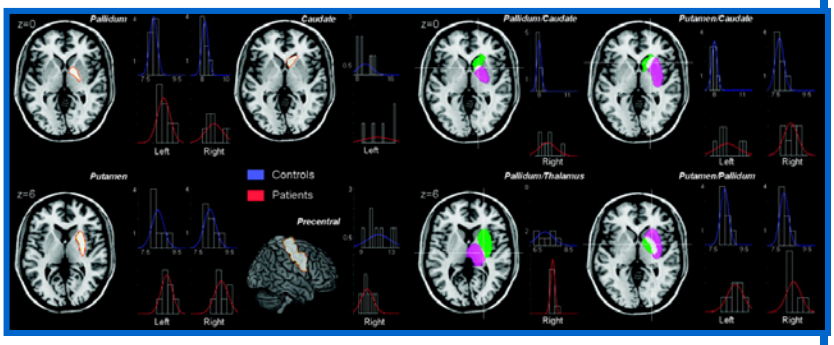
Deep Brain Stimulation Results in Generalized Dystonia

- Coubes 2000: 15 patients showed mean improvement in dystonia scales of 81%; somewhat better in DYT-1 patients
- Kumar 1999; Tronnier 2000; Vercuel 2001 showed similar results
- Fogel 2000: 10 patients treated but one showed no improvement; other patients have also not improved

DBS Results in Cervical Dystonia (Parkin 2001)

- 3 Patients with severe CD unresponsive to medical therapy or botulinum toxin
- Improvement in neck ache, voluntary neck movements and natural head position.
- Effects were immediate in terms of pain. Voluntary movement and natural head position improved slowly over 3 months.
- Perhaps related to geste antagoniste (sensory trick)

2007 Diffusion Tensor Imaging (DTI) Shows Abnormalities



- DTI is a specialized method of using MRI to investigate axonal integrity. It investigate the integrity of an extension of a nerve cell, which is similar in shape to a thread, that transmits impulses outward from the cell body. It looks at the magnitude and directionality of molecular displacement.
- Rather than looking at an individual person's MRI, averages across controls and people with dystonia are done.
- Thus, there are significant differences in the brains of people with dystonia and controls.
- Dystonia is not just a functional disorder but also had structural brain changes.

THE FUTURE

There will be continued study of etiology (the origin) of dystonia. We hope there will be advances in oral medicines and compounds that enhance normal TorsinA activity.

NEWS YOU CAN USE

NORD's Disease Specific Assistance Programs are designed to help patients with out-of-pocket costs associated with their insurance plans such as monthly premiums, deductibles, co-payments, and co-insurance. In addition, some programs may provide financial assistance with other expenses related to a patient's diagnosis such as travel to diagnostic centers/clinics, diagnostic testing, initial consultation with healthcare professionals, and infusion costs for uninsured or underinsured patients.

Are you eligible? Eligibility criteria can vary by program but most of NORD's patient assistance programs require the following:

1. Does the patient have an applicable diagnosis or physician referral?
2. Is the patient a legal US resident?
3. Does the patient meet NORD's financial need criteria?

NORD has a program for eligible patients with Cervical Dystonia (spasmodic torticollis)
To see if you are eligible call 1-855-864-4024 or Email: CervicalDystonia@rarediseases.org
Fax:1-203-349-3003
Website:
http://rarediseases.org/for-patients-and-families/help-access-medications/patient-assistance-programs/

GOODRX.COM

Drug prices vary wildly between pharmacies. GoodRx finds the lowest prices and discounts. They collect and compare prices for every FDA-approved prescription drug at more than 70,000 US pharmacies. GoodRx shows the lowest price at each pharmacy near you. At GOODRX.com you will find free coupons to use at the pharmacy. The website is http://www.goodrx.com/

Programs Provide Brand Name Medications at No or Low Cost to Eligible Patients

The NeedyMeds website provides a list of Patient Assistance Programs that provide brand name medications at no or low cost to eligible patients. These program are provided by various pharmaceutical companies and each program has different eligibility requirements. For further information, visit the NeedyMeds website is at http://www.needymeds.org/pap or call the telephone numbers provided for each program.

Klonopin (Clonazepam) RX Outreach Program provides this medication at low cost.
PO Box 66536
St Louis, MO 63166-6536
TEL: 888-796-1234
FAX: 800-875-6591

Baclofen Tablets Xubex Program provides medication at low cost.
PO Box 1244
Winter Park, Fl 32790-1244
TEL: 866-699-8239 ALT PHONE: 407-478-2663
FAX: 407-671-7960