Botulinum Neurotoxin
Chemodenervation Procedures: Limb Spasticity and Dystonia

Katharine E. Alter MD
Senior Physiatrist
Mount Washington Pediatric Hospital
Baltimore Maryland
Senior Research Clinician, National Institutes of Health
Bethesda MD

Chemodenervation Procedures for Limb Spasticity and Dystonia:
Agenda

• Which conditions?
• Who needs treatment and why?
  • Patient assessment
  • Setting Goals
  • Muscle selection
• Which treatment option?
  • Selecting the optimal procedure
  • Toxin dosing
• Optimizing procedure outcome
  • Guidance/localization
  • Post procedure care
• Putting it all together: Case studies

Spasticity, lumbricals:
MCP joint flexion,
IP joint extension

Focal lower limb dystonia:
True equinus
International Classification of Functioning, Disability, and Health

Health Condition (Muscle Overactivity)

Body function/structure

Activities
Functional Motor Abilities

Participation (Restriction)

Environmental Factors

Personal Factors

http://who.int/classifications/icf/en/

BoNTs

Treatment Goals
BoNT/Chemodenervation for Treatment of Limb Spasticity and Dystonia: Caveats

• Only problematic spasticity or dystonia require treatment
• Problems may include
  • Passive function
    • ADLs, transfers, skin integrity, positioning
  • Active function
    • ADLs, Mobility, other
  • Quality of life
    • Sleep
    • Pain

BoNT/ for Treatment of Limb Spasticity and Dystonia: Caveats

• BoNT: first line treatment for focal, multifocal or segmental dystonia or spasticity
BoNT for Treatment of Limb Spasticity and Dystonia: **Caveats**

- **BoNT for generalized spasticity or dystonia:**
  - A limited number of muscles can be treated at one session
    - Minimum effective dosage/muscle
    - Maximum total dosage/session

- **BoNT may be useful**
  - To treat a focal problem
  - As an adjunct to other treatment
    - Oral medications
    - Other chemodenervation agents
    - Surgery: DBS, ITB, SDR

---

**BoNT/Chemodenervation, Which Conditions?**

*Limb Spasticity* and *Dystonia*
UMNS Related Spasticity: *Motor Disorder Characterized by*

- **Spasticity**
  - Is a motor disorder characterized by
  - **Velocity-dependent** increase in tonic stretch reflexes (muscle tone)
    - Exaggerated tendon jerks
  - Results from hyperexcitability of the stretch reflex
  - **One component of the upper motoneuron syndrome**


UMNS Related Motor Disorders and Function

**Negative**
- Weakness
- Poor selective motor control
- Sensory deficits
- Balance and coordination problems

**Positive**
- Abnormal reflexes
- Hypertonia
  - Spasticity
  - Dystonia
- Involuntary movements

**MSK Consequences:** Contractures, torsion, dislocation

**BoNTs**

**Function**

UMNS
- Stroke
- Acquired Brain Injury
- Cerebral Palsy
- Spinal Cord Injury
- MS
- Others
UMNS Motor Impairments: Who Needs Treatment?

Cerebra Palsy, Diplegia:
Spasticity limiting gait

Cerebral Palsy, Quadriplegia:
Hypotonia/weakness: limiting gait

Classification of Spasticity: Distribution and Severity

- **Generalized/diffuse**, but may
  - Be asymmetric
  - Affect upper or lower limbs differently

- **Regional/multi-limb**
  - E.g., spastic diplegia

- **Multifocal**
  - E.g., several joints affected in the same limb

- **Focal**
  - **Striatal toe**, flexed elbow, adducted thigh
  - **Caveat**: Spasticity may be generalized but cause a focal functional problem amenable to local treatment

- **Severity**:
  - Mild, moderate, severe

Chemodenervation, which Conditions?

**Limb Dystonia**

**Dystonia**

- Motor disorder characterized by postures which may be
  - Sustained or intermittent
  - Often have a twisting characteristic
  - May be tremulous
  - May be fixed or hyperkinetic
Dystonia: May be Associated with

- **Movements/postures can be**
  - Hyperkinetic
  - Fixed
- **Muscle tone:**
  - Normal
  - Hypotonic
  - Hypertonic

Dystonia: May be Associated with

- **Tone:**
  - Normal tone
  - Hypotonia
  - Hypertonia
- **Postures**
  - Hyperkinetic
  - Fixed
- **Mirror dystonia**
- **Overflow movements**
- **Tremor**
Spectrum of Limb Dystonia

- **Dystonic postures/movements**
  - Typically triggered by movement or attempted movement
  - Even by attempts to relax
- **Impairs motor coordination including**
  - Timing, speed, excursion, directionality, smoothness, effort
- **Presentation** is variable: postures differ between patients
- **May involve any muscle or groups of muscles**
- **Postures/Involvement** in a specific patient are typically repetitive/similar
- **Postures** may have
  - A wide ranging impact on function, quality of life
  - Unpredictable/adverse effect on interventions targeting other impairments

Spectrum of Dystonia: Generalized Dystonia
Spectrum of Dystonia: Adult Focal Limb Dystonia:

• Examples
  • Lower limb runner’s Dystonia with foot inversion
  • Upper limb, focal hand dystonia
    • Writer’s or musician's cramp
    • Others
• May be associated with sensory tricks or geste

Focal Limb Dystonia:

• Task Specificity
  • **Upper limb**: typically remains task specific
  • **Lower limb**: Task specific at onset but may generalize
• Task specificity should be assessed in all patients with focal dystonia
  • Upper limb: writing, typing, playing musical instrument
  • Lower limb: walking, running, marching, backwards walking
Which Patient’s Need Treatment?
Patient assessment identifies if Spasticity or Dystonia Requires Treatment

Patient Evaluation and Treatment Planning

• Treatment is only required for problematic spasticity and dystonia, assessed by

• History:
  • Onset, progression, diurnal variation, factors that provoke or improve MoA
  • Comorbidities

• Impairment Assessment
  • Neurological exam
    • Tone, reflexes, motor control weakness
    • Involuntary movements/postures
    • Severity/scope of the problem
  • Musculoskeletal exam
    • Contractures or ROM limitations?

• Functional Assessment

CP, diplegia, Spasticity

Dystonia, Involuntary Movements/Overflow with talking
Impairment Assessment: Spasticity Scales: Modified Ashworth Scale (MAS)

**Modified Ashworth Scale (MAS)**

<table>
<thead>
<tr>
<th>MAS</th>
<th>mMAS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>No increase in muscle tone</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>Slight increase in muscle tone, manifested by a catch and release</td>
</tr>
<tr>
<td>1+</td>
<td>2</td>
<td>Slight increase in muscle tone, manifested by a catch, followed by minimal resistance</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>More marked increase in muscle tone, but affected part (s) can easily be moved</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>Considerable increase in muscle tone, passive movement difficult</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>Affected part (s) rapid in flexion or extension</td>
</tr>
</tbody>
</table>

**Does the MAS assess spasticity as defined by Lance?**

- **Performed at one speed**
  - Speed of the limb falling with gravity (1 second)
- **Not performed at a rapid speed**
- **Resistance is influenced by**
  - Any increased tone: spasticity, rigidity, hypertonic dystonia with co-contraction
  - Non-contractile elements of muscle
- **Therefore the MAS is more a measure of stiffness or resistance to ROM than spasticity**
Impairment Assessment, Beyond the MAS: Tardieu or Modified Tardieu Scale (MTS)

• **Advantage 1**
  - Assesses muscle tone at 2 speeds
    - Slowly (V1 or R2)
    - As fast as possible (V2 or R1)
      - Measures velocity dependent tone

• **Measure**
  - **Slow speed/V1 or R2:**
    - Assesses the extent of PROM
  - **Fast speed/V2 or R1:**
    - Assesses velocity dependent muscle tone

MTS: Knee extensors & flexors

Spasticity Scales: Tardieu Scale

• **Advantage 2**
  - Quantitative, not ordinal measure of spasticity
    - A “Spasticity or catch angle” is calculated
      - $R_2(V1) - R_1(V2) = \text{Spasticity angle}$
    - **Large angle or difference** = greater contribution of dynamic spasticity
    - **Small angle or difference** = limited ROM more than dynamic tone issue
      - Indicates some level of contracture

Gracies JM et al Arch Phys Med Rehabil 2010

Spasticity Angle $= V_1 \text{ or } R_2 (150^\circ) - V_2 \text{ or } R_1 (40^\circ) = 110^\circ$
Hypertonia Assessment Tool

• Discriminative Scale
  • Spasticity
  • Dystonia
  • Rigidity

• Evaluates
  • Velocity dependent increased tone
  • Abnormal postures, co-contraction
  • Biphasic tone

Marsico P, J Child Neurol 2017, Mink JA et al Dev Med Child Neurol. 2010
Hypertonia Assessment Tool

• Discriminative Scale
  • Spasticity
  • Dystonia
  • Rigidity

• Evaluates
  • Velocity dependent increased tone
  • Abnormal postures, co-contraction
    • Tactile stimulation
    • Movement of distant body part
  • Biphasic increased tone

Spasticity and Dystonia: Caveats

• Spasticity:
  • It is appreciated or “felt” by the examiner on
    • During physical exam

• Dystonia
  • Is most often appreciated or “seen”
    • When a patient initiates movement
    • Attempts to move
    • Or attempts to relax
    • Or when performing non-movement tasks like talking
Beyond Impairment: Assessing Function

- **Assessment of function/movement should detail**
  - Pattern, scope, severity
  - At rest/with activities
  - Impact on function

- **How?**
  - Observation
  - Observation + video
  - Motion analysis

- **Assess various conditions or tasks**
  - Upper limb: Reaching, grasping, playing instrument etc.
  - Lower limb: Walking, running, backwards walking, marching
  - Provoking/non-provoking tasks

- **Assessment provides information about:**
  - Muscle involvement
    - Informing treatment planning/goals
  - Response to treatment
  - Change in pattern over time

When do we Treat?

Is Spasticity or Dystonia Causing Problems?
What are the treatment goals?
BoNT for MOA, To Treat or Not to Treat, That is the Question .......... Determined by

• Identifiable Treatment Goals
  • Quality of life: sleep, pain relief
  • Passive function
  • Active function

• Access to care/follow up
  • Compliance
  • Commitment to post intervention care

Setting Goals for BoNT Treatment for Spasticity or Dystonia

• Goals must be patient focused
  • Clearly communicated to the patient
  • Consider Goal Attainment Scaling (GAS)

• Goals may include
  • Improved active function
  • Improved passive function
  • Comfort: less pain, better sleep, splint tolerance
  • Reduced disfigurement
  • Reduced burden of care

Setting Treatment Goals

• Goals should be **SMART**
  • **Specific:**
    • Ex: decreased fist to improve skin hygiene, pain
  • **Measurable:**
    • Ex: measurable improvement in ROM, skin breakdowns
  • **Achievable/Attainable:**
    • Patient has access to therapy etc.
  • **Relevant/realistic**
    • For the patient/family/situation
  • **Timely:**
    • Can be achieved within the proposed time frame

What?
Are the treatment options?
## Chemodenervation Options

<table>
<thead>
<tr>
<th></th>
<th>Local Anesthetics*</th>
<th>Phenol and Alcohol</th>
<th>Botulinum Toxins Type A &amp; B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism of Action</strong></td>
<td>Blocks sodium channels/action potential</td>
<td>Protein denaturation/axonal necrosis</td>
<td>Presynaptic inhibition of acetylcholine release</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>1-4 hours</td>
<td>20 days-7-18 months</td>
<td>3-7 months</td>
</tr>
<tr>
<td><strong>Side Effects</strong></td>
<td>Injection site pain, Temporary weakness, paralysis, sensory loss</td>
<td>Pain, skin necrosis, paresthesias</td>
<td>Injection site pain, weakness, atrophy</td>
</tr>
<tr>
<td><strong>When?</strong></td>
<td>Temporary Block</td>
<td>Long term effect</td>
<td>Long term effect</td>
</tr>
</tbody>
</table>

* Lidoicaine, Bupivacaine, Etidocaine

---

### Combining Chemodenervation Agents: BoNT + Neurolytics, Why?

- BoNT and neurolytics each have dose limitations
- Combining BoNT and neurolytics allows greater number of muscles to be treated
- **Approach**
  - BoNT for smaller distal muscles; smaller dose or when less “permanent effect” is desired
  - Phenol/ETOH for large proximal muscles innervated by easy-to-access motor nerves and motor points

---

**References**
Limb Spasticity and Dystonia: BoNT Dose Calculation Basics

- Dose information is available from
  - Manufacturers
  - Published studies, injection guides
- Rather than using a fixed dose per muscle
- Consider dose calculation in 3 dimensions based on
  - Muscle size
  - Severity of the problem
  - Functional goal

Optimizing Treatment

Improving the accuracy of muscle targeting
Should You Rely Only on Anatomic/Manual Guidance for Chemodenervation Procedures?

• **Knowledge of surface/functional anatomy is essential**
  - Recognizing muscle contributions to abnormal movements/postures
  - Prerequisite for
    - Any invasive procedure including BoNT/phenol/nerve blocks etc.
    - Any use of supplemental guidance

• **Limitations to relying solely on anatomic guidance**
  - Knowledge of anatomy
  - Reference guides not specific for chemodenervation
    - Cannot position the patient as described in atlas
    - Patient cooperation, involuntary movements
    - Anatomic rearrangements/contracture
  - Cannot assess depth of target or muscle thickness

Chemodenervation Procedures: Why Use a Supplemental Localization or Guidance Technique?

• **Comparative studies indicate that**
  - **Instrumented guidance is superior to anatomic guidance alone**
    - US and or EMG are superior guiding injections for cervical dystonia
    - US or ESTIM guidance is more accurate than EMG for spasticity indications
    - US is the most anatomically accurate method of guidance

• **Injections in the region of the innervation zone/endplate are more effective than injections outside these regions**


Guidance for BoNT Injections: EMG, E-Stim

**Advantages**
- Clinician familiarity
- EMG: provides info on muscle activity
- ESTIM: muscle twitch or joint movement may confirm needle location

**Disadvantages/Limitations**
- EMG ESTIM cannot
  - Estimate target depth, anatomic variation or rearrangement, safe path to target
  - Position patients per print reference guides
  - Be used for non-muscle targets
- EMG: Co-contraction limits accuracy
- E-STIM: Volume conduction targeting errors, pain may require sedation

US for BoNT Injections: **Advantages**

- US provides information on muscle
  - Depth
  - Location
  - Thickness
- Anatomic variations, rearrangements
- Safe path to target

US/EMG localization of Longus Colli and Capitis Muscles for Cervical Dystonia

Farrell M, Alter KE et al Toxins 2020

Added Benefits of US Guidance for BoNT Injections

- Multiple approaches to a target muscle, example
  - Tibialis Posterior
    - Antero-medial
    - Anterior
    - Posterior
  - Choice of approaches when
    - Multiple muscles are injected
    - Patient positioning is problematic

Problematic MOA ✓
Identifiable Goals ✓
Muscle Pattern Identified ✓
Target Muscle Identified ✓
BoNT dose calculated ✓
Now what?

Optimizing muscle targeting
Putting it all Together

Case Studies

Case 1: Common Gait Patterns, Stiff Knee

- Task Specific Runner’s dystonia
  - Stiff Knee
    - Limited knee flexion in walking/running
    - Task specific
    - EMG: Rectus firing out of phase
    - Task specific
BoNT Treatment of Common Gait Patterns: Stiff Knee

- Recommendation?
  - BoNT-A injections into rectus femoris

Case 2: 14 Year Old Generalized Dystonia: Focal Problem? Equinus Gait
Treatment Plan?

Severe L ankle equinus

Target muscles: Plantar Flexors and Invertors

Injection, medial gastrocnemius
Target muscles: Plantar Flexors and Invertors

Tibialis Posterior, posterior medial approach, “Bathtub View”

Tibialis Posterior, posterior lateral approach, “Chair View”

Target muscles: Plantar Flexors and Invertors

Flexor Digitorum Longus, Tibialis Posterior, Anteromedial Approach

Tibialis Anterior, Tibialis Posterior, Anterior Approach
77 y.o. with Post Stroke Spasticity (PSS) and Pain

• CVA 7 years prior to referral
• Referred by OT for spasticity treatment
• Problems?
  • Severe pain R arm/hand limiting ADLs, sleep, hygiene
  • Maceration, skin breakdown in palm
  • ROM restrictions limiting dressing and positioning
  • Unable to tolerate splints or stretching

Video: Initial Assessment

Case: 77 y.o Referred for Assessment of Post Stroke Spasticity (PSS), Left Upper Limb

• EMG guided BoNT injections into:
  • Wrist flexors: FCR, FCU
  • Finger flexors: FDS, FDP, Lumbricals
• Serial casting/splinting
  • 10 days following BoNT injections x 3 weeks with weekly cast changes

Video: Post Treatment Assessment
BoNT for Limb Spasticity and Dystonia: Summary

- **A detailed History, Physical and Functional Evaluation will determine**
  - Should the patient receive BoNTs?
  - Which muscles require treatment
  - What is the appropriate dosage/volume?
  - What concomitant therapies?
    - BoNT is not administered in insolation

- **BoNT Dosage**
  - Use the lowest effective total dose
    - For large muscles or with spasticity consider increasing volume of dilution/ to enhance spread

- **Instrumented guidance**
  - Improves toxin efficacy
  - Reduces BoNT side effects, procedural risks/complications
  - For Spasticity in Limb muscles: E-Stim and or US may
    - Improve outcomes
    - Identify specific muscles/muscle fascicles
  - For Dystonia US or EMG or combined US EMG
    - Reduce dysphagia
    - Increases procedural safety
    - Helps determine muscle contribution to an abnormal posture