CCM

Comprehensive Clinical Management

WORKSHOPS

- ☑ Patient History
- ☑ Clinical Assessment
- ☑ Neurotoxin Injection
- ☑ Follow-up Therapies (PT/OT/SLP)
- ☑ Evaluation of Clinical Outcome

Comprehensive Clinical Management - Focus on Patients With Spasticity

Saturday, May 1, 2021

Meeting Information
&
Key Slides

CCM WORKSHOP

Virtual Workshop Description

The Comprehensive Clinical Management (CCM) workshops provide clinically relevant education that fosters an integrated and comprehensive interdisciplinary approach to achieve the best clinical outcomes for patients with spasticity using a combination of neurotoxin therapy and appropriate follow-up care.

The live virtual CCM workshop will feature didactic presentations with Q & A sessions as well as video grand rounds featuring patients with spasticity, attendee polling, and an interactive expert panel discussion.

Learning Objectives:

- Recognize the importance, benefits, challenges, and practical concerns regarding the interdisciplinary team approach for management of patients with spasticity, in order to develop individualized treatment plans
- Interpret the clinical evidence, guidelines, and recommendations on the use of neurotoxins and adjunctive rehabilitation interventions (PT/OT/SLP), both alone and in combination, in order to establish appropriate treatment strategies for these patients
- Assess neuromuscular pathology and individual patient functional goals, in order to identify appropriate muscles, determine dosing, maximize therapeutic benefit, and minimize complications
- Evaluate methods of guidance and localization (ie, EMG, e-stim, ultrasound), in order to incorporate best practices for proper placement of neurotoxin
- Facilitate interaction and improve communication among members of the interdisciplinary treatment team, in order to encourage appropriate referrals for both neurotoxin injection and adjunctive therapy that may optimize patient outcomes

CCM WORKSHOP

Program Agenda	
11:45 AM - 12:25 PM	Managing Patients with Spasticity: From Evidence to Best Practice *Cindy Ivanhoe, MD*
12:25 PM - 1:10 PM	Guidance, Localization, and Placement of Botulinum Toxin: What Works Best? (Pediatric and Adult Limb Spasticity) *Katharine Alter, MD*
1:10 PM - 1:50 PM	Optimizing Patient Outcomes Post-BoNT Using Rehabilitation Therapy *Laura Wiggs, PT, NCS, CBIS*
1:50 PM - 2:10 PM	The Speech-Language Pathologist's Perspective: A Key Member of the Comprehensive Clinical Management Team *Sofia Tilton, MS, CCC-SLP*
2:10 PM - 2:30 PM	Break / Virtual Lunch
2:30 PM - 4:15 PM	Interactive Video Grand Rounds: Patient Assessments, Neurotoxin Injections, Rehabilitation Therapy and Recommendations for Aftercare The Treatment Team *Cindy Ivanhoe, Katharine Alter, Laura Wiggs, Sofia Tilton and Craig Davis*

CCM WORKSHOP

The Treatment Team

Katharine Alter, MD
Senior Physiatrist
Mount Washington Pediatric Hospital
Baltimore, Maryland

Craig P. Davis, OTR
Hancock Regional Hospital
Hospital & Health Care
Greenfield, Indiana

Cindy Ivanhoe, MD
Clinical Professor
Physical Medicine and Rehabilitation
The University of Texas Health Science Center
Houston, Texas
Director
Spasticity and Associated Syndromes of Movement
TIRR-Memorial Hermann
Houston, Texas

Sofia Tilton, MS, CCC-SLP
Speech-Language Pathologist
Words of Wisdom, PLLC
Houston, Texas

Laura Wiggs, PT, NCS, CBIS
Harris Health Systems
Houston, Texas

CCM WORKSHOP

Accreditation Statement:

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the University of Utah and Scientiae, LLC.

The University of Utah is accredited by the ACCME to provide continuing medical education for physicians.

AMA Credit: The University of Utah School of Medicine designates this other activity: virtual and live for a maximum of *5.25 AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

All attendees are encouraged to use the CME system to claim their attendance. Physicians will be awarded AMA PRA Category 1 Credit(s)™; all other professions will be awarded attendance at a CME event credit that they may use for their re-credentialing purposes. All users will be able to print or save certificates. For questions regarding the CME system, please contact the University of Utah Continuing Medical Education Office. For questions regarding re-credentialing process or requirements, please contact your re-credentialing organization.

AOTA Credit: Scientiae, LLC, is an AOTA Approved Provider of professional development. Course approval ID# 1947. This Distance Learning — Interactive Course is offered at 0.4 CEUs.

Nondiscrimination and Disability Accommodation Statement:
The University of Utah does not exclude, deny benefits to or otherwise discriminate against any person on the basis of race, color, national origin, sex, disability, age, veteran's status, religion, gender identity/expression, genetic information, or sexual orientation in admission to or participation in its programs and activities. Reasonable accommodations will be provided to qualified individuals with disabilities upon request, with reasonable notice. Requests for accommodations or inquiries or complaints about University nondiscrimination and disability/access policies may be directed to the Director, OEO/AA, Title IX/Section 504/ADA Coordinator, 201 S President's Circle, RM 135, Salt Lake City, UT 84112, 801-581-8365 (Voice/TTY), 801-585-5746 (Fax).

Conflict of Interest Statement: As a provider approved by the Accreditation Council for Continuing Medical Education (ACCME), The University of Utah School of Medicine Continuing Medical Education Office (UUCME) meets the ACCME Standards for Integrity and Independence expectations. UUCME requires everyone in control of content, including all speakers and planners, to disclose financial relationships with ACCME-defined ineligible companies in any amount within the past 24 months and any relevant financial relationships must be mitigated prior to the activity start.

Accreditation Statement *(Cont'd)*

Speaker and Planning Committee Disclosure Summary:

The University of Utah School of Medicine Continuing Medical Education Office (UUCME) meets ACCME Standards for Integrity and Independence expectations regarding the identification and mitigation of relevant financial relationships with ACCME-defined ineligible companies. Everyone in control of content, including all speakers and planners, must disclose financial relationships in any amount within the past 24 months and any relevant financial relationships must be mitigated prior to the activity start.

Disclosure: Neither planners, speakers, or anyone in control of content have any relevant financial relationships with an ACCME-defined ineligible company to disclose or mitigate.

American Occupational Therapy Association
Approved Provider
Scientiae, LLC, is an AOTA Approved Provider of professional development. Course approval ID# 1947. This Distance Learning — Interactive Course is offered at 0.4 CEUs.
AOTA does not endorse specific course content, products, or clinical procedures.

This activity is jointly provided by the University of Utah School of Medicine and Scientiae, LLC.

Supported by an independent educational grant from Allergan, an AbbVie company.

Managing Patients With Spasticity: From Evidence to Best Practice

Cindy Ivanhoe, MD
Clinical Professor, Physical Medicine and Rehabilitation
The University of Texas Health Science Center at Houston
Director, Spasticity and Associated Syndromes of Movement
TIRR-Memorial Hermann
Houston, Texas

1

Disclosure

- Cindy Ivanhoe, MD, has no relevant financial relationships with commercial interests
- During the course of this lecture, Dr. Ivanhoe may mention the use of medications for both FDA-approved and non-approved indications

2

Key Concepts

- ***Interdisciplinary team care*** is essential for effective management of complex patients[1]
- ***Evidence-based medicine*** is current best practice[2]
  - The conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients
  - Integration of individual clinical expertise with the best available external clinical evidence from systematic research
- Evaluating evidence for team approach for management of patients with spasticity
  - Use of neurotoxin
  - Use of rehabilitation therapy
  - Use of combination/team approach (neurotoxin + rehabilitation)

1. Royal College of Physicians, *Spasticity in Adults: Management Using Botulinum Toxin. National Guidelines*. London: RCP; 2018. 2. Sackett DL et al. *BMJ*. 1996;312:71-72.

3

Upper Motor Neuron Syndrome

- Abnormal patterns of muscle activity expressed as negative signs (muscle underactivity) and positive signs (muscle overactivity) as in spasticity
- Muscle overactivity in upper motor neuron syndrome (UMNS) is due to
  - Abnormal signal processing in the spinal cord
  - Altered supraspinal inputs and/or dysfunction of segmental spinal modulation
- Pathologic changes in muscles — biomechanical hypertonia
- Possible etiology of lesions: traumatic brain injury (TBI), stroke, spinal cord injury (SCI), multiple sclerosis (MS), cerebral palsy (CP)

Segal M. *Phys Med Rehabil Clin N Am.* 2018;29:427-436.

4

Positive and Negative Features of UMNS

Negative Symptoms	Positive Symptoms
Weakness	Hyperreflexia and reflex irradiation
Loss of dexterity	Clonus
Fatigue	Spasticity
Impaired motor planning	Positive Babinski sign/other primitive reflexes
Disordered motor control	Flexor and extensor spasms
	Positive support reaction
	Co-contraction
	Associated reactions (synkinesis)
	Spastic dystonia

Segal M. *Phys Med Rehabil Clin N Am.* 2018;29:427-436.

5

Spasticity

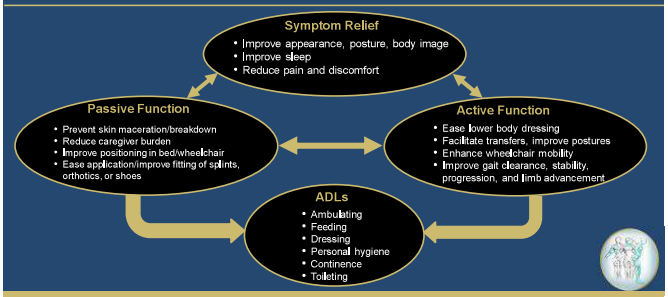
- Common but not inevitable result of UMNS[1]
- "Disordered sensory-motor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles" [2]
- Characterized by muscle overactivity and increased tone and spasms[3]
- May result in muscle and soft tissue contracture if untreated[3]
- Complex problem[3]
  - Can cause profound disability
  - Best treated by interdisciplinary team

1. Kuo C-L, Hu G-C. *Int J Gerontol.* 2018;12:280-284. 2. Pandyan AD, et al. *Disabil Rehabil.* 2005;27(1-2):2-6. 3. Royal College of Physicians, *Spasticity in Adults: Management Using Botulinum Toxin. National Guidelines.* London: RCP; 2018.

6

7

Spasticity Management Goals



Adapted from Moon DK, Johnson AMF. Lower extremity problem-solving: Challenging cases. *Phys Med Rehabil Clin N Am.* 2018; 29: 619-631.

8

Spasticity Management Principles

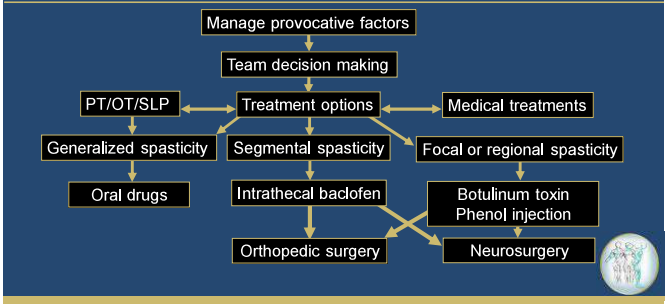
- Observe both active and passive movement and function
- Remove noxious stimuli that exacerbate spasticity
  - Urinary tract infection
  - Constipation
  - Ingrown toenails
  - Pressure ulcers
  - Poorly fitting brace or wheelchair
- Initiate conservative management measures
  - Rehabilitative therapy (PT/OT/SLP)
  - Orthopedic prostheses
  - Positioning

PT=Physical therapy; OT=Occupational therapy; SLP=Speech-language pathology.

Royal College of Physicians, *Spasticity in Adults: Management Using Botulinum Toxin. National Guidelines.* London: RCP; 2018.

9

Management Strategy: Adult Spasticity



Royal College of Physicians, *Spasticity in Adults: Management Using Botulinum Toxin. National Guidelines.* London: RCP; 2018.

10

Oral Drugs Commonly Used to Treat Spasticity

Drug	Mechanism of action	Common side effects include
Baclofen	GABA analog; inhibits muscle stretch reflex	Somnolence, dizziness, weakness, hallucinations with sudden withdrawal
Tizanidine	α-adrenergic receptor agonist	Dry mouth, sedation, dizziness
Clonidine	α-adrenergic receptor agonist	Bradycardia, hypotension, depression
Gabapentin	GABA analog	Somnolence, dizziness, ataxia
Dantrolene	↓Ca^{2+} release from muscle SR	Generalized muscle weakness, hepatotoxicity
Nabiximols	Partial agonist CB1 and CB2 receptors	Psychotropic effects, dizziness, cognitive blunting

GABA, gamma aminobutyric acid; SR, sarcoplasmic reticulum; CB, cannabinoid.

Ambrose AF, et al. Muscle overactivity in the upper motor neuron syndrome. *Phys Med Rehabil Clin N Am.* 2018; 29: 483-500. Kuo C-L, Hu G-C. *Int J Gerontol.* 2018;12:280-284.

11

Injected and Intrathecally-Delivered Drugs Used to Treat Spasticity

Drug	Route	Mechanism of action	Side effects and limitations include
Botulinum Neurotoxins	Injection	Chemodenervation ↓Acetylcholine release at neuromuscular junction	Weakness of adjacent musculature
Phenol	Injection	Chemodenervation Chemical neurolysis; penetrates peripheral nerves and denatures proteins	Vascular damage, dysesthesia, pain
Baclofen	Intrathecal pump	GABA analog; inhibits muscle stretch reflex	Hospital admission required for placement; clinic visits required for refilling; risk of infection

Ambrose AF, et al. Muscle overactivity in the upper motor neuron syndrome. *Phys Med Rehabil Clin N Am.* 2018; 29: 483-500.

12

Chemodenervation for Management of Spasticity

- Insufficient evidence to determine if oral agents improve function[1]
- Intrathecal baclofen (ITB) has shown some benefit in gait velocity[2]
- Chemodenervation has the greatest evidence of functional improvement[3,4]
  - Several evidence-based reviews provide recommendations for use
  - Chemodenervation is key component of combination therapy

1. Lindsay C, et al. *Cochrane Database Syst Rev.* 2016. Issue 10. Art.No.:CD010362. 2. Lee BS, et al. *J Neurosurg.* 2018;129:1056-1062. 3. Simpson DM, et al. *Neurology.* 2016;86(19):1818-1826. 4. Royal College of Physicians, *Spasticity in Adults: Management Using Botulinum Toxin. National Guidelines.* London: RCP; 2018.

13

BoNT for Limb Spasticity: A Meta-Analysis

- 27 RCTs (N=2793)
- Upper limb (UL) spasticity: BoNT-A significantly improved tone, Physician Global Assessment score, and Disability Assessment Scale score
- Lower limb (LL) spasticity: BoNT-A significantly improved Fugl-Meyer score; no significant effects on tone or gait velocity

Sun L-C, et al. *BioMed Res Int.* 2019:8329306.

14

Repeat BoNT-A Effective in UL Spasticity Over 2 Years

- International prospective, observational study of integrated UL spasticity treatment, including repeat BoNT-A, over 2 years (N=953)
- Most patients received rehab therapy — most frequently passive stretch — post-BoNT-A
- Pain, involuntary movement, and active and passive function improved over each treatment cycle by standardized measures
- Higher rates of achievement for passive vs active function goals
- Repeat BoNT-A injections showed sustained benefit over 2 years in UL spasticity

Turner-Stokes L, et al. *Toxicon.* 2021; 190S1:S74.

15

BoNT-A Treatment Effective in Post Stroke Spasticity When Started up to 3 Years Post Stroke

- Compared therapeutic effects of BoNT-A started <1 year, 1-3 years, and 3 years post stroke
- Treatment success
  - Goal Attainment Scaling (GAS) score: ≥0 per goal
- BoNT-A effective in all groups
  - GAS score ≥0 in 80% of injections, regardless of time started
  - No significant difference in GAS scores among BoNT-A preparations
- BoNT-A very effective in post-stroke spasticity even when started >3 years post stroke

Freitas M, et al. *Toxicon*. 2021; 190S1:S26.

16

BoNT-A Effective for Spasticity Associated With ALS

- Retrospective chart analysis (N=91; 234 injections)
- Examined safety and efficacy of BoNT-A in spasticity in ALS patients
- Eighty-three patients injected in LL; 4 in UL; 4 in both UL and LL
- Fifty-one patients satisfied with treatment; injection repeated
- BoNT treatment was effective in over half of the patients
- Ten reports of adverse events; 2 of rare AE: transient respiratory degradation

ALS=amyotrophic lateral sclerosis.
Deffontaines Rufin S,et al. *Toxicon*. 2021; 190S1:S64.

17

Botulinum Neurotoxin Therapy for Patients With Spasticity

18

Botulinum Neurotoxins: FDA-Approved Spasticity Indications

Serotype A	FDA-Approved for Treatment of
OnabotulinumtoxinA (ona) Botox®	Adult and pediatric UL and LL spasticity[1]
AbobotulinumtoxinA (abo) Dysport®	Adult and pediatric UL and LL spasticity[2]
IncobotulinumtoxinA (inco) Xeomin®	Adult and pediatric UL spasticity (excluding spasticity caused by cerebral palsy)[3]
Serotype B	
RimabotulinumtoxinB (rima) Myobloc®	Not approved for treatment of spasticity[4]

1. Botox® (onabotulinumtoxinA) Prescribing Information. 2. Dysport® (abobotulinumtoxinA) Prescribing Information. 3. Xeomin® (incobotulinumtoxinA) Prescribing Information. 4. Myobloc® (rimabotulinumtoxinB) Prescribing Information.

19

FDA Recommendations for Health Care Professionals Using Botulinum Toxins

- Understand that dosage strength (potency) in "units" is different among the botulinum toxin products and that *clinical dosages expressed in units are not interchangeable from one product to another*
- Educate patients and caregivers about possible effects following administration of botulinum toxins such as
  - Unexpected loss of strength or muscle weakness
  - Trouble swallowing or breathing
  - Double or blurred vision or drooping eyelids
- Understand such effects may present from hours to weeks after injection
- Advise patients to seek medical attention for any of these symptoms

Botox® (onabotulinumtoxinA) Prescribing Information; Dysport® (abobotulinumtoxinA) Prescribing Information; Xeomin® (incobotulinumtoxinA) Prescribing Information; Myobloc® (rimabotulinumtoxinB) Prescribing Information.

20

Important Safety Information (class labeling)

- Spread of toxin effects. The effect of botulinum toxin may affect areas away from the injection site and cause serious symptoms including loss of strength and all-over muscle weakness, double vision, blurred vision and drooping eyelids, hoarseness or change or loss of voice (dysphonia), trouble saying words clearly (dysarthria), loss of bladder control, trouble breathing, trouble swallowing
- Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junctional disorders (eg, myasthenia gravis or Lambert-Eaton syndrome) should be monitored particularly closely when given botulinum toxin
- Patients with neuromuscular disorders may be at increased risk of clinically significant effects including severe dysphagia and respiratory compromise from typical doses of Botox, Dysport, Xeomin, and Myobloc

Botox® (onabotulinumtoxinA) Prescribing Information; Dysport® (abobotulinumtoxinA) Prescribing Information; Xeomin® (incobotulinumtoxinA) Prescribing Information; Myobloc® (rimabotulinumtoxinB) Prescribing Information.

21

Chemodenervation With BoNT for Management of Spasticity

- Clinical effect[1]
  - Apparent in 7-14 days
  - Optimal at 4-6 weeks
  - Lasts approximately 3-4 months
- Weakening of agonist allows rehabilitative strengthening of antagonists to restore balance[2]
- Early BoNT treatment may prevent contractures or delay need for surgery[2]
- Oral medications and/or intrathecal baclofen may be used effectively as part of combination treatment[3]

1. Jacinto J, et al. *Front Neurol.* 2020;11:388. 2. Royal College of Physicians, *Spasticity in Adults: Management Using Botulinum Toxin. National Guidelines.* London: RCP; 2018. 3. Ambrose AF, et al. *Phys Med Rehabil Clin N Am.* 2018; 29: 483-500.

22

Individualized Spasticity Treatment With BoNT

- Treatment should be tailored to individual patients' symptoms, clinical need, and desired outcomes[1,2]
- Treatment considerations[1]
  - Target muscles
  - BoNT dose (per session/muscle/injection site)
  - Number and location of target sites
  - Interval between treatments
- Symptom re-emergence between BoNT-A injections common[3,4]
- Patient/practitioner surveys support tailored treatment and flexibility in dosing and dosing intervals[5]

1. Wissel J. *Toxicon.* 2018; 147:100-106. 2. Francisco GE. *J Rehabil Med.* 2021;53:jrm00134. 3. Esquenazi A, et al. *Toxicon.* 2021; 190S1: S23. 4. Esquenazi A, et al. *Toxicon.* 2021; 190S1: S23-S24. 5. Bensmail D, et al. *J Med Econ.* 2014;17(9): 618-625.

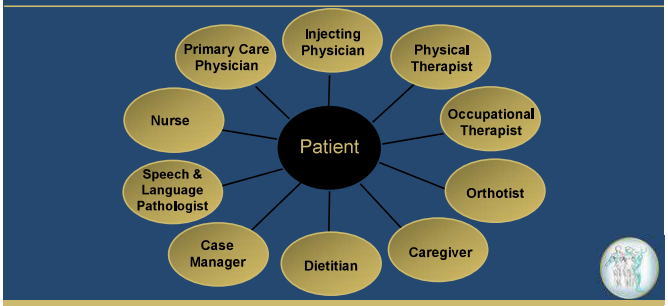
23

Summary

- Spasticity is a consequence of many neurologic disorders
- Spasticity is one component of the UMNS
- Impact varies from subtle to severe
- Clinical management is complex
  - Best handled by interdisciplinary team incorporating medical and rehabilitative approaches
  - Individualized, patient-centered treatment important
  - Neurorehabilitation involving combination treatment often produces best patient outcomes

24

Multidisciplinary Team Approach



25

Guidance, Localization, and Placement of Botulinum Toxin: What Works Best? Pediatric and Adult Limb Spasticity

Katharine E. Alter, MD
Senior Physiatrist
Mount Washington Pediatric Hospital
Baltimore, Maryland

1

Disclosures

I have the following potential conflicts of interest to report:

- Receipt of honoraria or consultant's fees: Paradigm Medical Communications, Catalyst Medical Consulting
- Royalties: Demos Medical Publishing

2

Optimizing Treatment Outcomes — Which of These Comes First?

- Determining Who Needs Treatment?
- Selecting a Localization Technique?

3

Optimizing BoNT Treatment Outcomes: Prerequisites for Successful Treatment

- Patient Selection, Pre-Procedure Planning

4

Optimizing Outcomes From BoNT Injections for Limb Spasticity

Caveats

- Failure to respond to BoNT
  - Is ***very unlikely*** to be due to neutralizing antibodies/resistance
  - Is ***more likely*** to be due to one of the following:
    - Patient selection
    - Treatment goals
    - Clinical pattern recognition/muscle selection
    - Dosage
    - ***Targeting/localization errors***
    - Lack of follow-up treatment

5

BoNT for MOA, To Treat or Not to Treat, That is the Question

Determined by…

- Does the patient have problematic spasticity?
- Are there identifiable treatment goals?
  - Quality of life: sleep, pain relief
  - Passive function: Care/hygiene/positioning
  - Active function: ADLs, mobility, others
- Access to care/follow-up
  - PT/OT/splinting/bracing
  - Transportation
  - Compliance/commitment to post intervention care

MOA=Muscle overactivity

6

Optimizing Outcomes From BoNT Injections

Caveats

Outcomes are more likely to be successful when clinicians recognize/identify

- Clinical pattern
  1. Elbow flexed and pronated
  2. Elbow flexed and supinated
- Muscles contributing to the clinical pattern
  1. Brachialis
  2. Biceps
- If the problem is caused by
  - Agonist muscle overactivity/out-of-phase recruitment
    - Example: Dynamic foot equinus
  - Antagonist muscle weakness/impaired control or timing
    - Equinus from foot drop/weak dorsiflexion

7

Optimizing Outcomes From BoNT Injections

Caveats

Outcomes are more likely to be successful when clinicians recognize/identify

- All muscles contributing to a patient's problem, including
  - Prime movers
    - Example: Foot inversion/ankle equinus
      - Tibialis posterior (Tib. post)
      - Tibialis anterior
  - Secondary contributors
    - Example: Foot inversion/ankle equinus
      - Flexor digitorum longus (FDL)
      - Flexor hallucis longus (FHL)

8

Guidance and Localization for Limb Spasticity BoNT Procedures: What Works Best?

- Optimizing BoNT Treatment Outcomes

9

Localization and Guidance for Limb Spasticity:
Manual Techniques (Palpation, PROM, Reference Guides)

- Rely on clinician's knowledge of
  - Surface and cross-sectional anatomy
  - Functional anatomy
  - Inspection
  - Palpation
  - Passive range of motion/active range of motion
- No equipment needed
  - Other than reference guides

10

Muscle Localization Techniques for Limb Spasticity:
Electrophysiological Techniques (EMG, E-Stim)

- Electromyography (EMG)
  - Relies on observation of muscle activity: visual/auditory
- Electrical stimulation (E-stim)
  - Relies on observation of muscle twitch or movement
- Equipment is accessible and relatively inexpensive
- Most clinicians have some experience with these techniques
  - *At least for diagnostic procedures*




11

Muscle Localization Techniques for Limb Spasticity:
Imaging-Based Guidance Techniques

- Of the available imaging-based guidance techniques
  - Ultrasound (US)
  - Fluoroscopy
  - CT
  - MRI
- US is the most commonly utilized
  - Accessible/portable
  - Low cost
  - No ionizing radiation
- B-mode imaging for
  - Continuous tracking of the needle to the target and injectate location
- Color Doppler to visualize vascular structures

12

Localization and Guidance for Limb Spasticity:
What Works Best?

Anatomic/Manual Guidance

Advantages: *Are there any advantages?*
Limitations: Accuracy limited by a variety of factors

- Clinician
  - Anatomical knowledge
  - Challenges in estimating
    - Muscle depth or position
    - Path to the target
- Anatomic
  - Variations, rearrangements
- Patient
  - Positioning
  - Estimating muscle depth/size
  - Presence of contractures
- Caveats: Only a few superficial muscles can be accurately targeted relying solely on anatomic guidance
  - This strategy is no longer recommended by most expert clinicians

13

Localization and Guidance for Limb Spasticity:
What Works Best?

Anatomy and localization/guidance

- Caveat
  - Extensive knowledge of regional and functional anatomy is required when performing BoNT procedure
- Without this knowledge
  - No supplemental localization technique will increase the accuracy of BoNT Injections

14

Localization and Guidance for Limb Spasticity:
What Works Best?

EMG

Advantages

- Provides information about level of muscle activity
- Caveat
  - Is the observed muscle activity coming from the target muscle?

Disadvantages

- Anatomic factors
  - Cannot estimate muscle depth, safe path to target, anatomic rearrangements or variations
- Patient-related factors
  - Positioning
  - Muscle synergies/co-contraction
- Clinician-related factors
  - Misinterpretation of EMG activity
- Equipment-related factors
  - Cost of insulated needles
  - Insulated needles more painful to insert

15

Localization and Guidance for Limb Spasticity: What Works Best?

E-Stim

Advantages: Available evidence suggests that E-Stim

- Provides more accurate information about needle location than EMG (or anatomic guidance) when treating patients with spasticity/involuntary movements/co-contraction*
- Facilitates precise isolation of individual muscle fascicles

Disadvantages

- Anatomical factors
  - Cannot estimate muscle depth/location, safe path to target
- Patient-related factors
  - Positioning: Cannot position patient as recommended
  - Pain from stimulation may require sedation
    - Always required for children
- Clinician-related factors
  - Over stimulation and resulting volume conduction may cause targeting errors
    - Needle may be outside of the target muscle
    - Needle may be in an untargeted muscle

16

Localization and Guidance for Limb Spasticity: What Works Best?

Ultrasound

Disadvantages

- Anatomical factors: None
- Patient-related
  - Positioning may remain challenging
- Equipment-related: cost
- Clinician-related
  - Steep learning curve to become proficient in US

Advantages

- Anatomical
  - Identifies complex/overlapping anatomy
  - Provides direct assessment of target
    - Depth
    - Location
    - Safe path to target/structures to be avoided
- Procedure-related safety:
  - Needle is observed continuously on its path to the target
  - Enables precise targeting/avoidance of neurovascular and other structures

17

Localization and Guidance for Limb Spasticity: What Works Best?

Caveats

Which technique works best?

Dependent in part on

- Clinician training
- Access to equipment

Evidence suggests that any supplemental guidance (EMG, E-stim, US) is superior to anatomical guidance alone*

What works best for me?

- US guidance for all limb, cervical, and oromandibular targets
- US + EMG for
  - All cervical muscles
  - Some deep limb muscle injections
- US + E-stim for
  - All nerve or motor point blocks (not BoNT)
- If US is not available?
  - E-stim for limb spasticity injections
  - EMG for cervical and focal limb dystonia

* Chan and Finlayson 2017; Grigoriu 2015; Walker 2015; Lim 2011.

18

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 should be applied?**
  - 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

19

BoNT for Limb Spasticity and Dystonia: Summary (Cont'd)

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 and EMG
  - Reduces dysphagia
  - Increases procedural safety
  - Helps determine muscle contribution to an abnormal posture

20

Optimizing Patient Outcomes Post-BoNT Using Rehabilitation Therapy

Laura Wiggs, PT, NCS, CBIS
Harris Health Systems
Houston, Texas

1

Disclosure

- Laura Wiggs has no relevant financial relationships with commercial interests
- She has disclosed that she may reference the use of medications for both FDA-approved and non-approved indications during the course of this presentation

2

State of the Evidence for Combined Team Approach

- Evidence supports comprehensive multidisciplinary approach to spasticity management
- Studies vary widely on methodology, populations, interventions, outcomes
- Heterogeneity poses challenge to integrating complex rehab interventions
  - Studies mainly address chronic stroke
  - Fewer studies on lower limb (LL) vs upper limb (UL) spasticity
  - Etiology, onset, and degree of spasticity vary
  - Variety of outpatient rehab programs employed
- Further research needed to elucidate optimal rehab protocols

3

Potential Benefits of Comprehensive Approach

- Decreased pain
- Improved mobility
- Improved ability to perform activities of daily living (ADLs)
- Reduced risk of secondary complications
- Improved fit of orthosis
- Decreased caregiver burden
- Improved tolerance for more aggressive therapy

4

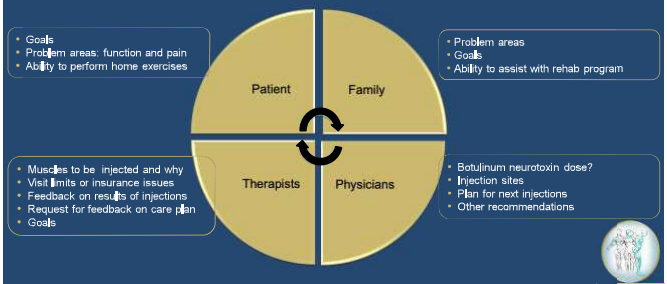
Proper Goal Setting Vital to Success

- Patient and family involvement central to care
- Interventions should align with patient/family priorities
- Consider patient/family's capacity for self-rehabilitation
- Consider neuropsychological, cognitive, and behavioral deficits

Turner-Stokes L, Ashford S, Esquenazi A. *Eur J Phys Rehabil Med.* 2018;54(4):605-617.

5

Communication of Goals Key to Achieving Best Outcomes



6

Focus of Rehabilitation Interventions After Neurotoxin Injections

- Elongation of target tissues
  - Stretching – muscle, joint, nerve
  - Casting/splinting
- Motor control
- Muscle strengthening
  - Power production and endurance
- Home rehabilitation programs

7

Rehabilitation Therapy Interventions

8

Stretching and Spasticity

- Variety of approaches and outcomes makes stretching complicated[1]
- Incomplete understanding of responses to stretch[1]
- Effect of passive stretch on contractures unclear[2]
- Stretch for <7 months ineffective for joint mobility in contracture cases[3]
- Prolonged stretching effective for spasticity affecting the ankle joint[4]

1. Bovend'Eerdt TJ, et al. *Arch Phys Med Rehabil*. 2008;89:1395-1406. 2. **Prabhu RKR, Swaminathan N, Harvey LA. *Cochrane Database Syst Rev*. 2013; 12. doi: 10.1002/14651858.CD009331.pub2.** 3. Harvey LA, Katalinic OM, Herbert RD, et al. *Cochrane Database Syst Rev*. 2017. doi.org/10.1002/14651858.CD007455.pub3. 4. Bani-Ahmed A *Top Stroke Rehabil*. **2019; 26 (2): 153-161.**

9

Daily Stretching Is a Lifestyle Change

- Stretching modulates stretch reflex, decreasing spasticity
- Stretching increases range of motion (ROM)
- Determine intensity and duration for each patient (pt) in order to maintain function

Gracies JM. *Phys Med Rehabil Clin N Am*. 2001;12(4):747-768.

10

BoNT Injection With Casting

- BoNT-A + PT + casting significantly improved passive ROM and gait in children with CP[1]
- BoNT-A + casting + orthoses produced significant improvement in R1 angles of gastrocnemius and hamstrings in non-ambulatory children with CP[2]
- BoNT-A + casting increased passive ROM, decreased MAS scores, and improved gait in pts with UL spasticity[3]

PT=Physical therapy; CP=Cerebral palsy; MAS=Modified Ashworth Scale

1. Dursun N, Gokbel T, Akarsu M, Dursun E. *Am J Phys Med Rehabil*. 2017;96:221-225. 2. Aydil S, Akpinar FM, Akpinar E, Beng K, Yagmurlu MF. *Med Princ Pract*. 2019;28:309-314. 3. Ganzert C, Reebye R, Winston P. *Toxicon*. 2018; 156:S38-S39.

11

BoNT and Strengthening

12

Role of Strengthening

Strengthening Does Not Increase Spasticity

- Strength training improved UL strength and function in stroke pts; no increase in tone or pain[1]
- Resistance training improved strength, gait speed, function, and quality of life (QoL) without exacerbating spasticity[2]
- Resistance therapy strengthened musculature and significantly improved motor function in children with CP[3]

Considerations for Strengthening

- Significant weakness underlies spasticity
- Lack of eccentric control due to spasticity causes concentric firing of muscles

1. Harris JE, Eng JJ. *Stroke*. 2010;41:136-140. 2. Pak S, Patten C. *Top Stroke Rehabil*. 2008;15(3):177-199. 3. Collado-Garrido L, et al. *Int J Environ Res Public Health*. 2019; 16: 4513.

13

BoNT and Strengthening: Lower Limb

- Single-blind, pilot RCT (N=25 chronic CVA pts)
- Control group (N=13): BoNT-A only
- Experimental group (N=12): BoNT-A + ankle strengthening x 4 weeks
- Assessments at baseline, 5, and 8 weeks post-injection
- Experimental group had
  - significantly greater increase in dorsiflexor strength
  - increased gait speed
  - decreased spasticity

RCT=Randomized, controlled trial; CVA=Cerebrovascular accident

Cinone N, Letizia S, Santoro L, et al. *Toxins*. 2019;11: 210. doi:10.3390/toxins11040210

14

BoNT Therapy of Upper Limb: Effect on Gait

- **Successful BoNT-A management of UL spasticity improves gait velocity[1]**
- **BoNT-A treatment of UL spasticity improves step length symmetry[2]**
- **Decrease in stiff knee gait pattern after BoNT-A treatment[3]**

1. Esquenazi A, Mayer N, Garreta R. *Am J Phys Med Rehabil*. 2008;87(4):305-310. 2. Ganzert C, Reebye R, Winston P. *Toxicon*. 2018; 156:S38-S39. 3. Tok F, Balaban B, Yazar E, Alaca R, Tan AK. *Am J Phys Med Rehabil*. 2012; 91:321-326.

15

Effect of PT Post–BoNT-A on Gait in Hemiparetic Patients

- Single-center, nonrandomized, controlled trial
- Group I (N=18): toxin only — to plantarflexors
- Group II (N=17): toxin + PT, 1 hour twice daily x 2 weeks
- Group II: Significant improvement in gait and walking speed
- Group I: No gait improvement; decreased walking speed in 40% of subjects

Fujita K, Miaki H, Hori H, et al. *Eur J Phys Rehabil Med.* 2019;55(1):8-18.

16

Effect of Combined Therapy on Upper Limb Function

17

Effect of Additional Rehabilitation Post–BoNT-A on Upper Limb Activity in Chronic Stroke

- Multicenter RCT (N= 140)
- Group I: BoNT-A to wrist muscles and HEP
- Group II: BoNT-A and serial casts x 2 weeks + movement therapy x 10 weeks
- Primary outcomes: GAS, Box and Block Test
- Secondary outcomes: spasticity, ROM, strength, pain, burden of care, QoL
- No significant differences between groups
- Additional intensive UL therapy post–BoNT-A is not effective

HEP=Home exercise program; GAS=Goal Attainment Scaling

Lannin NA, Ada L, Coralie English C, et al; InTENSE Trial Group. *Stroke.* 2020;51:556-562.

18

Rehabilitation Plus BoNT-A Improves Motor Function Vs BoNT-A Alone in Post-Stroke Upper Limb Spasticity

- Multicenter, single-blind RCT (N=31)
- All received BoNT-A ± rehab
- Rehab group (N=15): 24 weeks tailored rehab, 1.5 hours/week + 1 hour HEP/day
- Significant improvement in rehab group on Fugl-Meyer UL score
- No improvement in control group
- Spasticity decreased in both groups
- BoNT + rehab improved UL motor function (≥ 7 months) vs BoNT alone

Devier D , Harnar J, Leandro Lopez L, et al. *Toxin*. 2017; 9: 216. http://dx.doi.org/10.3390/toxins9070216.

19

BoNT-A With Therapy for Upper Limb Yields Best Results

- Meta-analysis of nonsurgical UL therapies in children with unilateral CP[1]:
  - Moderate-to-strong effect of BoNT-A + occupational therapy (OT) in improving UL and individualized outcomes vs OT alone
  - Strong evidence goal-directed OT HEP effective
- Better UL outcome with BoNT-A + PT + orthoses vs no BoNT-A in a double-blind RCT in children with unilateral CP[2]

1. Sakzewski L, Ziviani J, Boyd RN. *Pediatrics*. 2014;133:e175-e204.
2. Ferrari A, Maoret AR, Muzzini S, et al. *Res Dev Disabil*. 2014; 35: 2505-2513.

20

BoNT Combined With E-Stim

21

Effect of BoNT-A With E-Stim on Active Hand Function in Chronic Stroke Patients

- Open-label pilot study (N=15)
- BoNT-A injected into finger and/or wrist flexors
- E-stim + wrist brace for 30 minutes, 5 times/week x 4 weeks
- Outcomes assessed at baseline, 2, and 6 weeks post-injection
- BoNT-A + E-stim of finger extensors improved active hand function and UL impairment

Lee J-M, Gracies J-M , Si-Bog Park S-B, et al. *Toxins*. 2018;10:426. http://dx.doi.org/10.3390/toxins10110426.

22

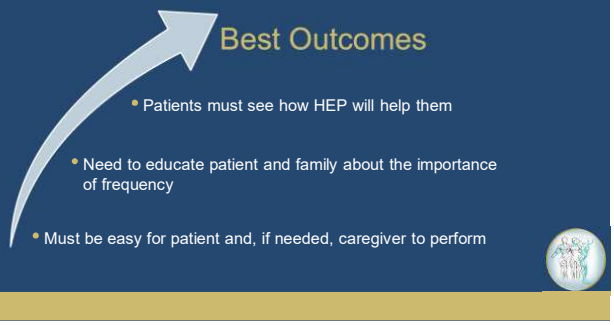
BoNT and E-Stim in Children With Spastic Diplegic CP

- Prospective, randomized study (N=38)
- Group 1: BoNT-A + E-stim , 20 minutes/day x 10 days
- Group 2: BoNT-A alone
- HEP recommended to both groups
- Both treatments reduced spasticity in children with SDCP
- No additional benefit from E-stim to gastrocnemius muscle post-BoNT

Yiğitoğlu P, Erkan Kozanoğlu E. *Turk J Phys Med Rehab* 2019;65(1):16-23.

23

Home Program or Self-Habilitation Yields Best Outcomes



24

The Speech-Language Pathologist's Perspective: A Key Member of the Comprehensive Clinical Management Team

Sofia Tilton, MS, CCC-SLP
Speech-Language Pathologist
Words of Wisdom, PLLC
Houston, Texas

1

Disclosure

- Sofia Tilton has no relevant financial relationships with commercial interests
- During the course of this lecture, Sofia may mention the use of medications for both FDA-approved and non-approved indications

2

Role of Speech-Language Therapist in Multidisciplinary Treatment of Spasticity

- Central role in diagnosis, assessment, and treatment of persons with
  - Dysarthria
  - Dysphagia
- Settings: acute, inpatient rehab, outpatient, home, private practice
- Cases show significant benefits of BoNT injections + speech and swallowing therapy for patients with spasticity, regardless of time since onset
- Other BoNT patient referrals related to speech therapy
  - Spasmodic dysphonia
  - Vocal fold paralysis
  - Cricopharyngeal dysfunction

3

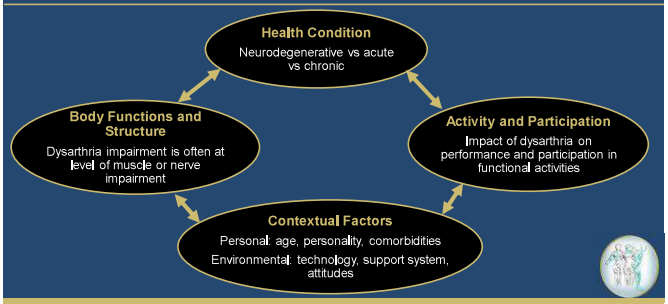
Muscle Tone in the Orofacial System

- Abnormal muscle tone is presumed to underlie certain types of dysarthria[1] and dysphagia[2]
- Tone disruption may manifest differently in the orofacial musculature vs the limbs
- Jaw-closing musculature is the only muscle group in the orofacial system with high density of muscle spindles, and which exhibits clear stretch reflexes[3]

1. Duffy JR. *Motor Speech Disorders*. 2nd ed. St. Louis, MO: Mosby; 2005. 2. Bahr DC, et al. *Oral Motor Assessment and Treatment: Ages and Stages*, Boston, MA: Allyn & Bacon; 2001. 3. Neilson PD, et al. *Brain Res*. 1979;178(2-3):311-27.3

4

Decision-Making Based on ICF Framework



ICF=International Classification of Functioning, Disability, and Health. World Health Organization.2001.

5

Psychosocial Impact of BoNT in Oromandibular Dystonia

Semi-structured, face-to-face interview with 8 individuals treated with BoNT for oromandibular dystonia (OMD)[1]

- Study Goals
  - Explore psychosocial impact of BoNT in OMD
  - Gain understanding of how participants judged treatment success
- Results
  - BoNT had variable impact on quality of life (QoL), satisfaction with therapy, speech production, and communicative participation[1]
  - All participants reported changes to their speech production and some degree of benefit from BoNT[1]

1. Page AD, et al. *Am J Speech Lang Pathol*. 2021:1-15. 2. Bhattacharyya N, Tarsy D. *Arch Otolaryngol Head Neck Surg*. 2001; 127(4):389-392.

6

Speech Intervention After Neurotoxin Injections

- Behavioral management of tone
  - Stretch/massage for spasticity in jaw
- Strength training targeting respiratory and phonatory support
- Training specificity: greatest gains in strength will be observed in movements that match that exercise
  - Working on *tongue elevation* for production of lingual-alveolar phonemes (eg, /d/ and /l/)
  - Improving *labial closure* for production of bilabial phonemes (eg, /m/, /p/, /b/)
  - Improve *mouth opening* for vowel production

7

Swallowing Interventions After Neurotoxin Injections

- Oral-Motor Exercises
- Traditional swallowing exercise
- Neuromuscular Electrical Stimulation (NMES)
  - Research emerging on NMES in combination with swallowing therapy
- Postural/Positioning: redirect the movement of the bolus in the oral cavity and pharynx (eg, chin-down, head rotation to side, head tilt)
- Sensory stimulation

8

BoNT Injection of Salivary Glands

Goals

- Decrease oral secretions *and:*
  - Improve management of oral secretions at rest
  - Improve speech intelligibility
  - Decrease coughing and choking on secretions
  - Reduce burden of family and caregivers
  - Relieve embarrassment and increase communication participation
  - Increase participation in activities of daily living
  - Increase participation in other therapies, such as physical therapy

Jost WH, et al. *Neurol Ther*. 2019; 8(2): 273–288.

9

BoNT Injection of Masseters and Pterygoid Muscles

Goals

- Improve oral hygiene by decreasing dry mouth
- Decrease or eliminate anterior loss of secretions or bolus
- Improve liquid or solid bolus acceptance
- Improve timing of the swallow with adequate labial/jaw closure
- Improve vocalizations and verbalizations
- Decrease burden of care of family and caregivers

10

BoNT Injection of Masseters, Pterygoid, and Temporalis Muscles

Goals

- Provide oral care
- Facilitate participation in dental cleaning/dental work
- Enable participation in dysphagia treatment
- Increase vocalizations and verbalizations
- Enable participation in respiratory support exercises
- Increase PO intake

11

Combination of BoNT, Speech Therapy, and Dysphagia Therapy Beneficial in Spasticity Management

Provides functional and psychosocial benefits:

- Improved oral hygiene
- Participation in dysphagia treatment
- Improved PO intake
- Improved speech production
- Increase in communication participation
- Improved quality of life

Page AD, et al. *Am J Speech Lang Pathol*. 2021:1-15.

12