ISSN 2349-7904

Volume 5 • Supplement 1 • June 2022

The Journal of The International Society of Physical and Rehabilitation Medicine

www.jisprm.org

ISPRM
International Society of Physical and Rehabilitation Medicine

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The Journal of the International Society of Physical and Rehabilitation Medicine

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The Journal of The Journal of the International Society of Physical and Rehabilitation Medicine is a peer-reviewed, open-access journal published quarterly on behalf of the Beijing U-Health Medical Institute with the mission of the Journal of *The International Society of Physical and Rehabilitation Medicine (JISPRM)* is to advance the field of physical and rehabilitation medicine (PRM), promote optimal functioning and health-related quality of life, strengthen rehabilitation research, and minimize disabilities by providing an online colloquium for communication of discoveries, established evidence and contemporary practice of PRM across the globe. The JISPRM will also encourage cross-fertilization among basic, translational and clinical researchers, and practitioners of PRM.

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Published by
Wolters Kluwer India Private Limited.
A-202, 2nd Floor, The Qube,
C.T.S. No.1498A/2 Village Marol,
Andheri (East), Mumbai - 400 059, India.
Phone: 91-22-66491818
Website: www.wolterskluwer.com

ISSN: 2349-7904

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Volume 5 ¦ Supplement 1 ¦ June 2022

CONTENTS

Comprehensive Curriculum on Spasticity Assessment and Management

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Introduction

ToxNET is a global educational initiative that aims to improve the quality of care for people with spasticity. The ToxNET group comprises 19 neurological rehabilitation specialists (clinicians and scientists) with a combined experience of more than 250 years in treating poststroke spasticity. The mission of ToxNET is to raise awareness of the best clinical practice for patients with spasticity and – by providing readily accessible tools for all clinicians who treat spasticity – improve patient outcomes.

In 2020, the group published a Consensus Paper: A Practical Guide to Optimizing the Benefits of Post-Stroke Spasticity Interventions with Botulinum Toxin A: an International Group Consensus. (J Rehabil Med, 2021;53:jrm00134. doi: 10.2340/16501977-2753.)

Following this paper, this curriculum now aims to provide a blueprint, comprehensive training course covering the management of spasticity. The four different modules cover:

- **Module 1: Pathophysiology and Assessment; Goal Setting.** Covering the underlying pathophysiology of spasticity and identifying the muscles involved and the extent of that involvement. The importance of patient involvement and goal setting is considered as well as the best tools for patient assessment
- **Module 2: Nonsurgical Management.** Covering the most commonly used drugs and interventions. The optimal use of baclofen or botulinum toxin A (BoNT-A) and suitable adjunctive therapies are included in detail
- **Module 3: Surgical Management**. Covering patient selection for surgery and the appropriate surgical techniques to employ
- **Module 4: Optimizing Outcomes.** A helpful troubleshooting guide, which provides practical algorithms for assessing the reasons behind suboptimal with treatment oral drugs, alcohol/phenol, intrathecal baclofen, or BoNT-A.

The entire group was divided into four subgroups, with each focusing on one particular module. However, all members of the group made contributions based on their clinical experience across the whole curriculum. The modules were refined by each subgroup and then circulated to everyone for approval. Illustrative case histories are provided; in some instances, videos allow the reader to fully appreciate the movement disorder caused by the spasticity of different muscles. Competency assessments allow the reader to test how well they have assimilated the information in each module.

We hope that this Curriculum will be widely used and will contribute to improving outcomes for patients requiring treatment and rehabilitation for spasticity.

This supplement comprises an introduction and four modules covering different aspects of spasticity assessment and management. All authors are listed alphabetically and each module acknowledges the authors responsible for that module. However, all authors were given the opportunity to read and comment on the entire supplement. All authors met the criteria for authorship and each author believes the manuscript represents honest work.

Financial support and sponsorship

The ToxNET group is supported by supported by Merz Therapeutics. Medical writing support was provided by

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Videos available on: www.jisprm.org

Access this article online

Quick Response Code:

Website: www.jisprm.org

DOI: 10.4103/jisprm.JISPRM-000154

How to cite this article: Deltombe T, Francisco GE. Comprehensive curriculum on spasticity assessment and management. J Int Soc Phys Rehabil Med 2022;5:S1-2.

Submitted: 14-Nov-2021; **Revised:** 13-Dec-2021; **Accepted:** 14-Dec-2021; **Published:** 20-Jun-2022

Brenda McCleary and Jan Hawthorn, who were paid from this grant.

Conflicts of interest

The support from Merz covered all meeting expenses. However, the curriculum and all content were developed by the authors independently of the sponsor. No member of the group was paid for contributing to these manuscripts. In addition, the following authors would declare conflicts of interest as follows:

- Dr. Alexander Balbert has attended sponsored meetings and received honoraria from Merz
- Dr. Ganesh Bavikatte has attended sponsored meetings, participated in research activities, and received honararia from Merz, Allergan, and Ipsen
- Dr. Djamel Bensmail is a Consultant for MERZ, Medtronic, IPSEN and Allergan.
- Dr. Francesca Bianchi has no other conflicts of interest
- Dr. Stefano Carda has received travel reimbursements and educational grants from Merz, AbbVie. Medtronic and Almirall.
- Prof. Thierry Deltombe has served as investigator, speaker, and advisor for Allergan, Merz, and Ipsen
- Dr. Nathalie Draulans has attended sponsored meetings from Merz, Ipsen and Allergan
- Dr. Steven Escaldi has received a consulting honorarium from Merz
- Prof. Gerard Franciso is a consultant to Abbvie, Ekso, Flowonix, Merz, and Sword Health and has received research grants from AbbVie, Merz, Microtransponder, Ottobock, Parker Hannifin, ReWalk, and Revance Therapeutics. He is the Editor-in-Chief of the Journal of ISPRM
- Dr. Raphaël Gross receives financial support by Merz, Allergan, and Ipsen for educational activities
- Dr. Jorge Jacinto Has received honoraria for consulting, scientific advisory, lecturing, peer training, and clinical research, from Allergan/Abbvie, Ipsen, and Merz.
- Dr. Nicholas Ketchum is a consultant for Merz, Allergan, Ipsen, and Medtronic
- Dr. Franco Molteni has no other conflicts of interest
- Dr. Susana Moraleda has attended sponsored meetings and has received honoraria from Allergan, Ipsen, and Merz
- Dr. Michael W O'Dell receives research grants from Merz and Ipsen
- Dr. Rajiv Reebye has received honoraria, educational, and research grants from Allergan, Abbvie, Merz, Ipsen
- Dr. Patrik Säterö has performed lectures and training in spasticity treatment for Allergan, Ipsen, and Merz since 2005
- Dr. Monica Verduzco-Gutierrez has been a consultant for Allergan, Merz, Ipsen, and Piramal
- Dr. Heather Walker has attended sponsored meetings, participated in research activities, and received honoraria from Merz and Ipsen
- Prof. Jörg Wissel is a Consultant and Speaker for Abbvie-Allergan, Merz, Medtronic, Ipsen, Shionogi
- Máximo Zimerman has no other conflicts of interest.

Module 1: Pathophysiology and Assessment of Spasticity; Goal Setting

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Abstract

This module discusses the pathophysiology of spasticity and the lesions underlying the condition. It considers the clinical presentation of spasticity and outlines the relevant clinical history that should be documented. The positive and negative signs of spasticity are explained. Clinical presentations of spasticity are discussed, and an illustrated table of spastic limb postures details how the muscles involved in each individual's condition may be identified. The main systems for assessing the severity of the condition, the Ashworth Scale, the modified Ashworth scale, and the Tardieu Scale, are explained. The likelihood of spasticity developing following a stroke and the probable long-term outcomes are considered. The value of involving patients in their own treatment regimens, by defining and setting goals, using the SMARTER system is explained, and the need to continually assess and refine treatment with time as the condition progresses is also discussed.

Keywords: Spasticity, pathophysiology, assessment

Learning Objectives

On completion of this module, the learner will be able to:

1. Describe the pathophysiology giving rise to spasticity based on disease, condition, and the location of the underlying lesions
2. Compare and contrast the positive and negative signs of spasticity and predict likely occurrence of spasticity
3. Verbalize key elements in the assessment of a patient's history and current condition
4. Explain different presentations and various spastic limb postures and identify the specific muscles involved in postural abnormalities
5. List the impact of spasticity on patients' quality of life
6. Outline the steps in performing the modified Ashworth scale (MAS) or modified Tardieu scales
7. Demonstrate treatment goal setting with the patient using goal attainment scaling (GAS).

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DOI: 10.4103/2349-7904.347807

Pathophysiology

Pathophysiology of spasticity based on disease condition and location of the lesion

The development of muscle over-activity, or hypertonia, is a well-known consequence, resulting from a lesion to the upper motor neuron (or motoneuron) (UMN) pathway. There are various types and clinically distinct presentations of hypertonia. The clinical pattern of motor over-activity is primarily (along with other factors to be discussed) determined by the location and extent of the lesion to the UMN.

An understanding of the basic neuroanatomy and pathophysiology pertaining to the UMN will assist clinicians in providing the most effective treatment options. The focus of this learning objective is one particular positive sign of UMN injury: spasticity.

Over the years, the term "spasticity" has been attributed to a number of signs and symptoms seen as part of the UMN syndrome (UMNS). Its definition has been debated and discussed repeatedly over the past 40 years. The debate has centered on a definition where a precise description is based solely on physiology versus one that is more aligned with the clinical presentations and residual sequelae. Examples of the most commonly accepted definitions are:

How to cite this article: Escaldi S, Bianchi F, Bavikatte G, Molteni F, Moraleda S, Deltombe T, *et al*. Module 1: Pathophysiology and assessment of spasticity; Goal setting. J Int Soc Phys Rehabil Med 2022;5:S3-22.

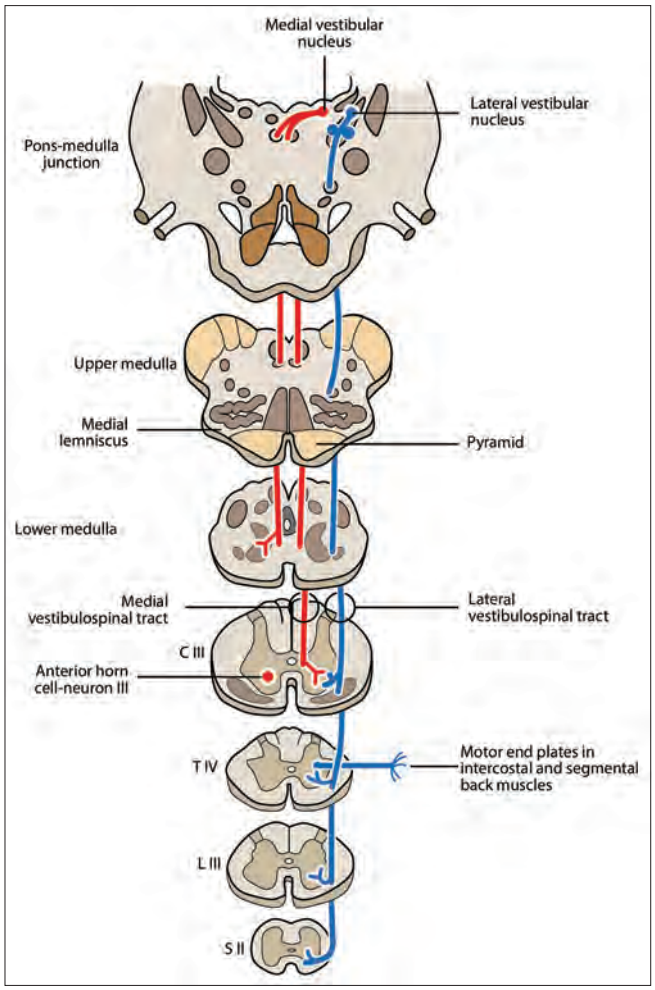


Figure 1: Vestibulospinal and reticulospinal tracts

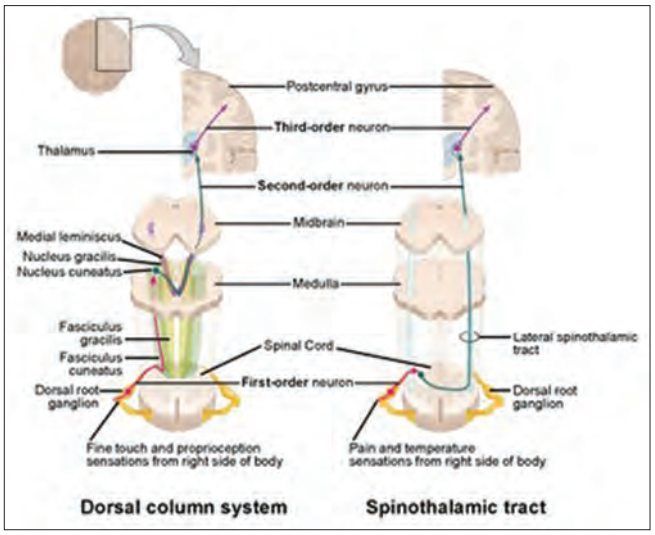


Figure 2: The dorsal column system and spinothalamic tract. This figure is taken from Open Stax Leaning. Download for free at http://cnx.org/content/col11496/latest/

1. A motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the UMNS[1]
2. Enhanced excitability of velocity-dependent responses to phasic stretch at rest[2]
3. A disordered sensorimotor control, resulting from an UMN lesion, presenting as intermittent or sustained involuntary activation of the muscles. SPASM project, 2005 – the Support Program for Assembly of a database for Spasticity Measurement.[3]

Being the final motor pathway, the UMN plays an important role in the control of muscle tone and activity. It receives descending supraspinal inhibitory and excitatory fibers that exert a balanced control on spinal reflex activity. "An UMN lesion disturbs the balance of supraspinal inhibitory and excitatory inputs, producing a state of net disinhibition of the spinal reflexes."[4] Spasticity results from this net hyperexcitability of the stretch reflex.

Muscle tone is maintained by a controlled balance on the stretch reflex arc by the inhibitory influence of corticospinal tract (CST) and dorsal reticulospinal tract (RST), and a facilitatory influence (on extensor tone) by the medial RST and, to a lesser extent in humans, by the vestibulospinal tract (VST).

The four descending pathways that are important in spastic paretic syndrome are arranged as follows in the spinal cord: lateral funiculus contains CST and dorsal RST, while anterior funiculus contains VST (that has lesser role in human spasticity)[5] and medial RST (in proximity with medial longitudinal fasciculus).[6]

The positive features of UMNS are probably more related to damage to the parapyramidal motor pathways with brainstem origin than to the pyramidal tracts.[5]

Spasticity occurs due to a hyperexcitability of the stretch reflex. Hyperexcitability occurs from an imbalance of descending inhibitory signals from the dorsal RST and the excitatory signals from the medial RST and VST. Spinal stretch reflexes are mediated by Ia afferents and involve muscle spindles whose excitability is controlled by the gamma efferents. No evidence of muscle spindle hypersensitivity due to increased gamma efferent drive has been found; however, altered intraspinal processing and peripheral muscular changes can also contribute to spasticity [Figures 1 and 2].[6]

Positive and negative signs and symptoms of the upper motor neuron syndrome

The functional impairments seen in patients with spasticity occur due to three main processes: weakness, biomechanical changes (soft tissue stiffness, muscle shortening, tendon contracture), and muscle over-activity through hyperexcitability or loss of inhibition. These can be grouped as positive and negative signs and symptoms [Table 1].

Spasticity is characterized by velocity-dependent increase in stretch reflexes along with exaggerated tendon jerk responses and increased muscle resistance to passive stretch. These become more pronounced as the speed of the applied stretch increases.

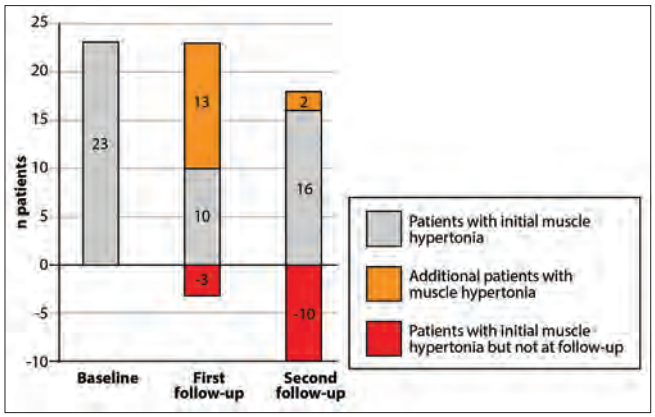


Figure 3: Development of muscle hypertonia during follow-up[8]

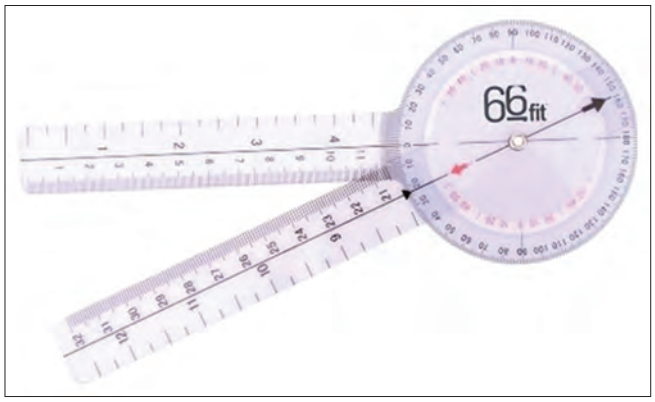


Figure 5: A goniometer

Table 1: Positive and negative signs of functional spasticity

Positive signs (abnormal behaviors)	Negative signs (performance deficits)
Spasticity	Weakness
Spastic dystonia	Paralysis/paresis
Co-contraction	Decreased dexterity
Clonus	Fatigability
Hyper-reflexia	
Release of primitive reflexes	
Dystonia	
Increased cutaneous reflexes	
Associated reactions	

Spastic dystonia displays tonic muscle contraction at rest and is present in the absence of passive stretch, spinal reflex activation, or voluntary effort. Spastic dystonia is sensitive to stretch and length of muscle (although not dependent on stretch reflex), as described by Denny-Brown.[7] It provides a significant contribution to limb deformities, muscle shortening, and disfigurement.

Co-contraction is due to simultaneous activation of agonist and antagonist muscle groups during voluntary movement. It results from the failure of reciprocal inhibition at the level of either the spinal cord or the cortex.

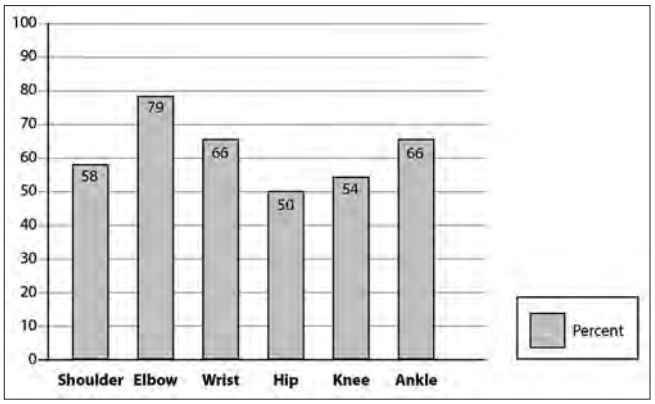


Figure 4: Localization of spasticity 6 weeks poststroke[8]

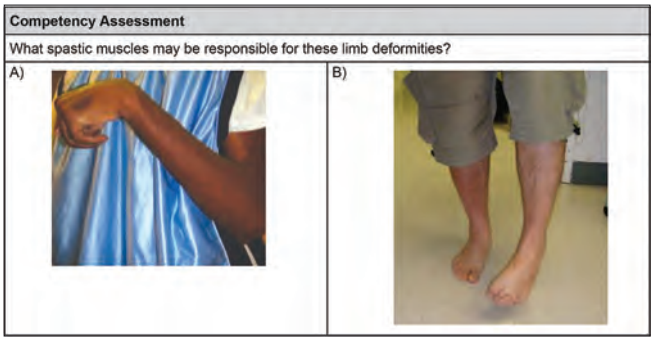


Figure 6: Patient images for Competency Assessment 2, question 1

Clonus is a low-frequency (6–8 Hz) rhythmic oscillation generated as a result of a rapid stretch of a muscle, which may also be triggered by cutaneous stimuli or voluntary effort.

Mass synergy patterns are primitive movements that dominate reflex and voluntary effort and interfere with coordinated voluntary movements, for example, flexion of the upper limb and extension of the lower limb in a stroke patient.

Associated reactions include involuntary activity in one limb that is associated with a voluntary movement effort made by other limbs. Associated reactions may be due to disinhibited spread of voluntary motor activity into a limb affected by a UMN lesion.

- Examples
  - Progressive flexion of the hemiplegic elbow seen as a stroke patient walks
  - Action-induced spastic dystonia: an overflow phenomenon associated with voluntary movements, for example, knee extension and ankle plantar flexion seen on the hemiparetic side in a stroke patient which occurs upon standing from a seated position or with walking, although this posture is not present at rest
  - Imitation synkinesis: a motor response performed in the unaffected extremity will elicit the same motor response in the hemiparetic limb
  - Flexor synergy of a hemiparetic arm during yawning.

Flexor and extensor spasms are caused by abnormal sensorimotor reflexes where a decreased inhibitory stimulus

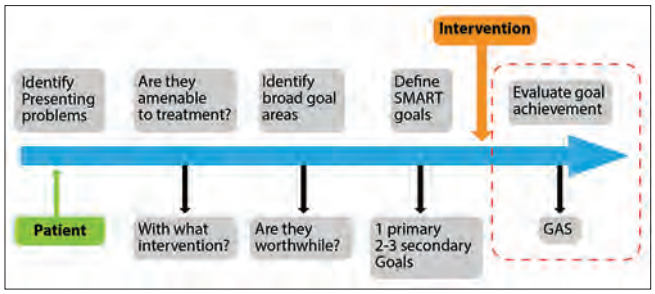


Figure 7: The goal attainment scaling model

results in a disinhibited reflex with increased afferent stimulation. For example, flexor spasms seen after spinal cord lesions result from the disinhibited flexor reflex with flexor muscle contraction across multiple joints. It is also termed "release of flexor reflex afferents."

Prediction of occurrence of spasticity within the first few months after injury or disease onset

Being able to predict the development of spasticity may help clinicians to be more vigilant of complications that need to be assessed and managed in order that further complications can be avoided. It can also assist in long-term planning and resource allocation. Given individual patient and disease variability, a universal prediction model does not exist. Perhaps, the evolution of spasticity is best described in the months subsequent to a stroke. Wissel *et al*. conducted a prospective, observational study in two stroke units and one rehabilitation facility in and around Berlin. A total of 103 stroke survivors were observed. Spasticity, defined as a MAS score of 1 or more, was assessed at 6 days, 6 weeks, and 16 weeks poststroke. They reported a prevalence of spasticity in 24.5% (23 of 94 survivors) at 6 days, 26.7% (23 of 86 survivors) at 6 weeks, and 21.7% (18 of 83 survivors) at 16 weeks.[8]

There were 13 stroke survivors who had spasticity at 6 days but not at 6 weeks. During the same timeframe, three who did not have spasticity initially were found to have spasticity at 6 weeks. At the 16-week follow-up, there were two who did not have spasticity initially but had the condition and 10 whose initial spasticity resolved. It appeared that, in 98% of subjects with poststroke spasticity (PSS), hypertonia emerged about 6 weeks poststroke [Figures 3 and 4].[8]

In considering the factors predictive of PSS, the strongest predictor of moderate-to-severe spasticity (defined as Ashworth >2) is severe proximal and distal limb weakness on acute hospital admission. Reduced sensorimotor function was the most important predictor both for any and severe spasticity 12 months poststroke.

A best predictor model suggests that any spasticity can be predicted by 10 days poststroke and that spasticity 4 weeks poststroke is a significant predictor of severe spasticity.

Factors predictive of PSS are summarized in Table 2.[8-12]

When instigating early treatment, clinicians should consider the nature of the spasticity and the likelihood that it will resolve or be a long-term problematic condition. Decisions should always take into consideration the evolution of spasticity.

Competency Assessment 1

The answers to these questions can be found at the end of this module before the references.

1. What are the three main processes that lead to functional impairments seen in an UMN injury?
2. A patient had a left subcortical stroke 4 weeks ago and is now ready for discharge. He has spasticity of the right elbow flexors and plantar flexors (both scored as "3" in the MAS) and is nonambulatory. Hemiplegia has persisted. His spouse asks you what will happen to the elbow and ankle spasticity in the near future.
3. Describe the clinical features being exhibited by this patient.
4. A 75-year-old male presents for rehabilitation 2 weeks after sustaining an ischemic right middle cerebral artery (MCA) artery cerebrovascular accident (CVA) with left hemiparesis. His examination is noted as having left arm movement at the elbow limited to a flexor synergy pattern and hyper-reflexia at the biceps tendon. His tone using the Modified ashworth scale (MAS) in the left arm is significant for a 2 for the elbow flexors and 1+ each for the wrist and finger flexors. As you are formulating a treatment plan, what other signs of the UMNS do you anticipate to encounter which may interfere with functional improvements as motor recovery progresses?
5. A stroke patient reports that every time, he yawns his hemiparetic elbow is able to flex, although he is unable to flex the elbow on command. The patient is describing what phenomenon?
    1. Spastic dystonia
    2. Associated reaction
    3. Spasticity
    4. Mass synergy pattern.

Assessment

Historical and medical information specific to spasticity across diagnoses

Evaluation of the patient with spasticity should start with a full history.[13] The items to be covered should include:

- History of present illness
    - Detailed description of symptoms of spasticity, such as characteristic posture, temporal nature, triggering and relieving factors, and significance and severity as measured by its impact on mobility and activities of daily living (ADLS)
    - Spasticity onset and progression[14]
    - Associated symptoms, such as pain.
- Review of systems and medical history
    - In addition to obtaining information on medical comorbidities, other important elements that may affect assessment and treatment include, but are not limited to, the following:

Table 2: Factors predictive of poststroke spasticity

Risk factor	Time of onset	Time and degree of spasticity development
Severe arm paresis[9]	Baseline (2-10 days poststroke)	Spasticity by 1 month
Increased muscle tone (MAS >1)[8,10]	Baseline (1-14 days poststroke)	Spasticity by 12-24 weeks poststroke
Low BI score[11,8]	Baseline (1-4 days poststroke)	Severe spasticity (MAS >3) by 12-24 weeks poststroke
Moderately increased muscle tone (MAS >2)[8]	Baseline to 6 weeks poststroke	Severe spasticity by 12–24 weeks poststroke
Hemihypesthesia[11]	Baseline (1-5 days poststroke)	Spasticity by 6 months
Severe paresis[11]	Baseline (1-5 days poststroke)	Spasticity by 6 months
Low EQ-5D score	Baseline (1-5 days poststroke)	Spasticity by 6 months
Paresis[8,11]	Any time point poststroke	Spasticity by 6 months
Low day 7 BI score with early arm or leg weakness[12]	Baseline (7 days poststroke)	Spasticity by 12 months
Low day 7 BI score with left-sided weakness and positive smoking status[12]	Baseline (7 days poststroke)	Severe spasticity by 12 months
Hemispasticity[12]	4-12 weeks poststroke	Permanent spasticity

MAS: Modified Ashworth scale, BI: Barthel index, EQ-5D: Standardized instrument for health-related quality of life

- Cognition (i.e., cognitive impairment)
- Mood disorder
- Liver disease
- Bowel disorders, such as constipation
- Bladder continence
- Coagulopathy.[15]

- Functional limitations influenced by spasticity
  - Relevant family history
    - A history of neurological disease, such as hereditary spastic paraplegia
  - Relevant general information
    - Residence (domicile, facility-based long-term care services including assisted living, nursing homes, and continuing care community)
    - Patient's family support (i. e., caregivers)
    - Economic status
    - Health insurance.

The radiological features of the lesions leading to spasticity must be documented since a better understanding of the relationship between the brain lesion profile (lesion location and volume) and the presence and severity of spasticity may help early identification of those patients with higher risk of developing spasticity and those who may particularly benefit from preventative and therapeutic strategies.

Brain lesion characteristics correlate with poststroke functional outcome, motor recovery,[16,17] and gait.[18] Damage to the corona radiata and internal capsule has been associated with poor recovery, whereas recovery was linked with lesions sparing the motor cortex.[16,19]

Different studies have reported an association between poststroke upper limb spasticity and lesions involving subcortical structures.[20,21] Injuries to the insula, thalamus, basal ganglia, and white-matter tracts (i.e., internal capsule, corona radiata, external capsule, and superior longitudinal fasciculus) were found to be significantly associated with severe spasticity.[20,21] Lesion volume was found to be positively correlated with spasticity severity.[21]

Damage to the basal ganglia might contribute to spastic dystonia,[17] while Bertoni *et al*. showed that subjects with multiple sclerosis (MS) developing spasticity have three main lesion patterns: small lesions in the genu or posterior limb in the internal capsule, lesions in the rostral brainstem, or extensive lesions in the callosal radiation.[22]

Previous or current treatments for spasticity should be considered, including:

- Rehabilitation interventions – stretching: passive, active, static/dynamic splinting, serial casting;[23] vibrotactile stimulation: whole-body vibration technique,[24] segmental or focal vibration;[25] electrical stimulation: transcutaneous electrical nerve stimulation,[26,27] functional electrical stimulation,[28] extracorporeal shock wave therapy[29]
- Medications – oral medications, botulinum toxin (BoNT), chemical neurolytic agents, and intrathecal drugs
- Surgical treatments (orthopedic procedures: e.g., tendon transfers, muscle/tendon lengthening, tenotomy, joint stabilization; neurosurgical techniques: e.g., rhizotomy, peripheral neurotomy).

  For patients in whom spasticity is worsening, it is important to look for the triggers that can increase spasticity [Table 3].

Differences in clinical presentations of spasticity of cerebral versus spinal origin

Clinical presentation

Clinically, spasticity may be of different types due to involvement of descending pathways.[30] There are clinical differences between spasticity of supraspinal (or cerebral) and spinal origin, most of which can be understood by the location and the extension of the UMN lesion. It is the mixing and matching of lesions that leads to a variety of clinical syndromes.[4]

The problem is made difficult by the fact that individual patients have lesions affecting different pathways to different extents and that the subsequent adaptations in the spinal networks may vary considerably. It is likely that spasticity is not caused by a single mechanism, but rather by an intricate chain of alterations in different interdependent networks.[30]

Table 3: Triggers that can increase spasticity

Physiological	Psychological	Environmental	Pathological	Iatrogenic
Pregnancy, posture, circadian rhythm, menstrual cycle	Mental and emotional stress	Cold weather	Disease progression (e.g., MS or development of traumatic syringomyelia after spinal cord injury)	Removal of antispasticity medications
		Tight clothing or braces	Bladder-related issues (i.e., urinary tract infections or calculi), bowel-related issues (e.g., constipation), hemorrhoids, deep vein thrombosis, fever, skin conditions (i.e., pressure ulcers or skin infections) or chest infections	Failure of intrathecal baclofen pump
			A new disease process that may present initially with spasticity	
			Other example – heterotrophic ossifications and painful joints	

MS: Multiple sclerosis

Spasticity of cerebral origin

In cortical and internal capsular lesions, the controlling drive (corticoreticular pathway) on the inhibitory center in the medullary brainstem (ventromedial bulbar reticular formation) is lost and so, in the absence of the inhibitory influence of the dorsal RST originating from this center, facilitatory action of medial RST becomes unopposed. This results in spastic hemiplegia with antigravity posturing, but flexor spasms are unusual.[30]

Damage to the basal ganglia might contribute to the spastic dystonia component, which is common in patients with hemispheric lesions. The basal ganglia play an important role in motor control: they have bidirectional connections with the primary motor cortex, premotor areas, and supplementary motor areas through basal ganglia–thalamocortical circuits.[20]

Spasticity of spinal origin

Incomplete (partial) myelopathy involving lateral funiculus (e.g., early MS)[31] may affect CST only to produce paresis, hypotonia, hyporeflexia, and loss of cutaneous reflexes. If dorsal RST is involved, in addition, unopposed medial RST activity then results in hyper-reflexia and spasticity (similar to cortical or capsular lesions), the latter being marked in antigravity muscles to produce paraplegia in extension. Extensor and flexor spasms may occur (due to hyperexcitability or disinhibition of flexor withdrawal reflex and extensor reflex, respectively), the former being more common.[30] Paraplegia in flexion is also possible if flexor reflex afferents get stimulated by factors such as pressure sores.

Severe myelopathy with involvement of all the four descending pathways produces less marked spasticity compared to isolated lateral cord lesion because of lack of unopposed excitatory influences of medial RST and VST. The latter factor is also responsible for lack of extensor hypertonia, and in the presence of release of flexor reflexes by dorsal RST lesion, it helps to produce paraplegia in flexion.[30]

Isolated dorsal RST involvement with CST sparing (proved pathologically and electrophysiologically)[32,33] may explain marked spasticity and spasms with little weakness in many cases of spastic paraparesis.

Isolated anterior cord lesions may produce hyper-reflexia with normal tone.

In patients with chronic motor complete spinal cord injury, significant relationships were noted between spasticity and variables of body composition and metabolic profile. This suggests that spasticity may play a role in the defense against deterioration in these variables years after injury; however, the exact mechanism is yet to be determined.[34] Both types of spasticity may be treated with intrathecal baclofen. One study showed that cortical spasticity and spinal spasticity appear to parallel each other with no significant differences in daily dosing, dosing changes, and mode of delivery of intrathecal baclofen. The significant difference noted within groups for daily dosing over the first 3 years challenges the notion of stable dosing over time.

Focal injections of BoNT/phenol in the upper extremities are an important adjunct therapy for patients with cortical spasticity, even after the placement of an intrathecal baclofen pump.[35]

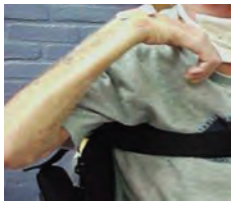
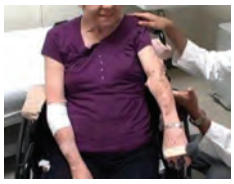
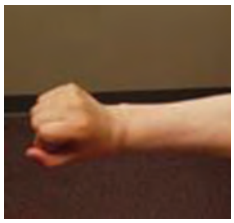
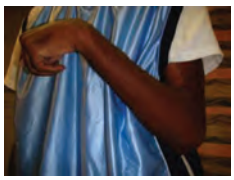
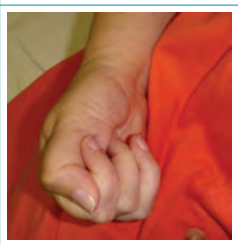
Different clinical presentations and various limb spastic postures

It is important for clinicians to be knowledgeable of functional anatomy to make the best decision regarding which spastic muscles are responsible for common postural abnormalities of the limbs. While instrumented analysis provides more conclusive data, only a few clinicians have access to these sophisticated devices. Hence, the clinician has to assess using examination skills with a foundation of knowledge of functional anatomy. Because several muscles cross limb joints, typically more than one muscle is responsible for a postural abnormality of a limb. Table 4 lists muscles potentially responsible for postural abnormalities.[36]

Muscles involved in various limb spastic postures

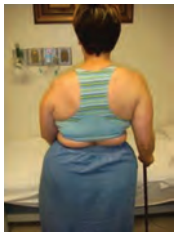
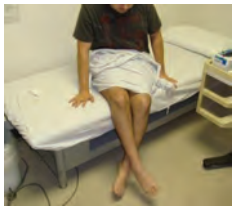
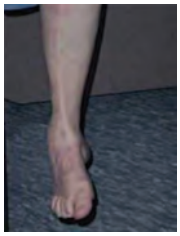
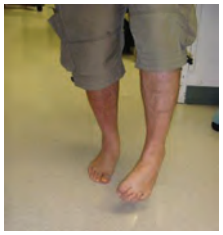
Identifying the muscles involved in any spastic limb posture is crucial to planning treatment. It is important to differentiate between spasticity and weakness since, although they both cause limb deformity, their treatment vary considerably.[37] Spasticity usually involves several muscles and may occur in common postural patterns, whereas weakness may be more generalized.

Table 4: Muscles potentially responsible for postural abnormalities Photographs taken from Francesco and Li 2015.[36]

Postural abnormality		Muscles potentially involved	Benefits of correcting postural abnormality
Shoulder adduction		Pectoralis major Latissimus dorsi Coracobrachialis (especially when shoulder is forward flexed)	Sitting posture Ease of dressing Axillary hygiene Improve balance and symmetry of gait and can sometimes help to reduce unwanted spasticity in the elbow and hand
Shoulder internal rotation		Subscapularis Teres major Pectoralis major and minor	
Elbow flexion		Brachialis Biceps Brachioradialis Pronator teres	Improve flexion deformity Improve reach/retrieve
Elbow extension		Triceps Anconeus	Improve extension deformity Improve ability flex elbow and bring hand close to body axis
Forearm pronation		Pronator teres Pronator quadratus	Improve ability to supinate the forearm Improved functional use of arm and hand
Wrist extension		Extensor carpi radialis Extensor carpi ulnaris	Improve wrist flexion Prevent worsening of finger flexion (tenodesis phenomenon)
Wrist flexion		Flexor carpi radialis Flexor carpi ulnaris Palmaris longus	Maintain palmar skin hygiene
Metacarpophalangeal (knuckle) flexion		Lumbrical	Maintain palmar skin hygiene Improve grasp and release
Finger flexion		Flexor digitorum superficialis (proximal phalanx) Flexor digitorum profundus (distal phalanx)	Maintain palmar skin hygiene Improve grasp and release
Thumb flexion Thumb adduction		Flexor pollicis brevis (proximal) Flexor pollicis longus (distal phalanx) Adductor pollicis	Maintain palmar skin hygiene Improve grasp and release

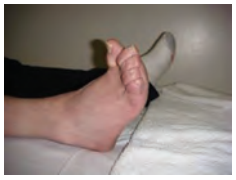
Contd...

Table 4: Contd...

Postural abnormality		Muscles potentially involved	Benefits of correcting postural abnormality
Trunk flexion, lateral		Quadratus lumborum Latissimus dorsi	Improve trunk position and comfort decrease trunk asymmetry during gait
Hip flexion		Psoas Iliacus Rectus femoris	Improve weight bearing Improve gait pattern and seating posture
Hip extension		Gluteus maximus Semitendinosus, semimembranosus, bicep femoris	Increase pelvic mobility and facilitate hip advancement (flexion) during gait
Hip adduction		Adductor magnus Adductor longus Adductor brevis Sartorius Gracilis	Improve “scissor gait” Ease of perineal hygiene and urinary catheterization Easier sexual intercourse
Knee extension		Recturs femoris Vastus medialis Vastuc intermedius Vastus lateralis Gastrocnemius (at certain phases of gait)	Improve knee flexion ability Increase knee flexion during gait Decrease genu recurvatum and associated pain and overloading of knee joint
Knee flexion		Semimembranosus Semitendinosus Bicep femoris Gracilis Gastrocnemius Tensor fascia lata	Seating posture (note potential to worsen sit and stand and standing) Improve knee extension Improved knee stability during stance
Ankle plantar flexion		Gastrocnemius Soleus Tibialis posterior Flexor hallucis longus Flexor digitorum longus	Correct equinus deformity, and foot inversion to allow heel strike Improve fit and comfort of AFO and shoes
Ankle inversion		Tibialis posterior Tibialis anterior Extensor hallucis longus Flexor hallucis longus Flexor digitorum longus	Correct varus deformity, and foot inversion to allow heel strike Improve fit and comfort of AFO and shoes

Contd...

Table 4: Contd...

Postural abnormality		Muscles potentially involved	Benefits of correcting postural abnormality
Small toe flexion		Flexor digitorum brevis (proximal) Flexor digitorum longus (distal)	Decrease pain during toe off phase of gait cycle (brevis and longus) and secondarily decrease foot inversion (longus) Improve fit and comfort of AFO and shoes
Great toe hyperextension		Extensor hallucis longus	Ease of donning footwear and comfort

AFO: Ankle–foot orthosis

Table 5: Aims in treating spasticity

Aims	Examples
Relieve symptoms or reduce impairments	Pain/spasm reduction
	Reducing sleep disturbances
	Reducing disfigurement and improving body image
	Prevention of contracture
	Prevention of subluxation
	Pressure sore reduction
	Increased tolerance for orthotics/shoes/splints
	Reduce abnormal bone growth in children
Improve passive function	ADLs: LE dressing, hygiene, bathing
	Toileting and perineal care
	Wheelchair and bed positioning
	Transfers
	Application of splints, orthoses, and footwear
	Promotion of physical and occupational therapy programs
Improve active function	Mobility (transfers, improved gait pattern)
	Improved balance
	Energy demand reduction
	Wheelchair management and mobility
	ADLs: LE dressing, hygiene, bathing, toileting
	Use of UEs

ADL: Activities of daily living, LE: Lower extremity, UE: Upper extremity

It is important to consider the predominant active muscles in relation to the intended goals of treatment.

Detailed descriptions of the location, origin, and insertion of these muscles are given in "Spasticity Early and Ongoing Management" by Bavikatte *et al*.[38]

The impact of spasticity on quality of life

The disadvantages of spasticity include:

- Body
  - Painful spasms
  - Impeded ambulation
  - Contractures or dislocations
  - Abnormal bone growth
  - Skin breakdown
  - Impairment of respiratory function.
- Activities
  - Interference with ADLS
  - Masked volitional movement.
- Social/societal
  - Sexual dysfunction
  - Fatigue/depression
  - Social isolation
  - Decreased productivity.

It is important that patients and physicians also consider other factors that may be contributing to or exacerbating the spasticity. These include urinary tract infection, kidney stones, menses, bowel impaction or gas, deep vein thrombosis (DVT), pneumonia, wounds or infections, progression of disease, stress, ingrown nails, restrictive clothing, fatigue, psychological factors, and change in temperature or humidity.

The benefits of treating spasticity include an increased stability in sitting or standing, assisting with transfers, prevention of edema, prevention of DVTs, awareness of noxious stimuli, improvement in cough strength, and improvement in venous return.

Effective spasticity treatment relies on contributions from a multidisciplinary team. The patient and family/carers are central to management strategy. Physician input should be provided by a physiatrist, neurologist, neurosurgeon, and orthopedic surgeon. Nurse/nurse practitioners, social workers, physical therapists, occupational therapists, speech/language pathologists, dieticians, and psychologists can all make valuable contributions to the patient outcome.

An important step in planning treatment is goal setting (see the section on "Goal Setting" below) where the patient and the team define the aims of treatment and goals to be achieved.

Some examples of aims are given in Table 5.

Comprehensive spasticity management involves rehabilitation treatments, reduced nociceptive input, focal/segmental treatments (nerve/motor point blocks, tendon transfer/lengthening), and generalized treatments (oral/intrathecal medications, rhizotomy).

Performing the Ashworth or modified Ashworth scale

History

The Ashworth Scale (AS) was originally described by Ashworth in 1964[39] in assessment of carisoprodol in MS. It

consisted of an assessment of resistance to passive stretch. In 1987, Bohannon and Smith[40] developed the MAS which is performed by testing functional muscle groups starting from a shortened position to a lengthened position. They used the scale to assess interrater reliability of assessment of elbow flexor spasticity, testing muscle groups by moving through a range of motion (ROM, from flexion to extension) over approximately 1 s. The scale is given in Table 6.[41]

Table 6: The Ashworth and modified Ashworth scales

Score	AS	MAS
0	No increase in tone	No increase in muscle tone
1	Slight increase in tone giving a catch when the limb was moved in flexion or extension	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part (s) is moved in flexion or extension
1+		Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2	More marked increase in tone but limb easily flexed	More marked increase in tone through most of the ROM, but affected parts easily moved
3	Considerable increase in tone, passive movement difficult	Considerable increase in tone, passive movement difficult
4	Limb rigid in flexion or extension	Affected part (s) rigid in flexion or extension

Taken from.[41] ROM: Range of movement, AS: Ashworth scale, MAS: Modified Ashworth scale

Table 7: Tardieu scale

- Tardieu scale principles
  - Muscle assessment always performed
    - On a muscle at rest before the stretch maneuver
    - At a reproducible velocity of stretch
    - At the same time of day
    - In a consistent body position for a given limb (seated vs. supine)
    - Other joints, particularly the neck, must also remain in a consistent position during the assessment
  - Velocity of stretch
    - V1 - As slow as possible (slower than the rate of natural drop of the limb under gravity)
    - V2 - The speed with which the limb falls under gravity
    - V3 - As fast as possible (faster than the natural drop of a limb with gravity)
  - X=spasticity angle (threshold)
    - End angle at slow speed X_{v1} minus angle of catch at fast speed Y_{v3}
  - Y=Spasticity grade (gain)
    - 0 - No resistance throughout passive movement
    - 1 - Slight resistance throughout passive movement
    - 2 - Clear catch at a precise angle, followed by a release
    - 3 - Fatigable clonus (<10 s) occurring at a precise angle followed by release
    - 4 - Unfatigable clonus (>10 s) occurring at a precise angle
      - Catch without release: Graded 0 if $X_{v1}=X_{v3}$
      - Catch with "minimal" release: Graded 2 if X_{v3} is consistent and consistently less than X_{v1}
      - Angle 0°=Position of minimal stretch of the tested muscle
      - For Grades 0 and 1, spasticity angle X=0° by definition

From[47]

Several studies have investigated the interrater reliability of the AS and MAS. Meseguer-Henarejos *et al*.[42] performed a systematic review of the MAS and demonstrated that upper extremities had good-to-moderate interrater reliability while the lower extremities had fair-to-moderate interrater reliability.

Looking at specific populations, the AS has shown good reliability in poststroke upper limb spasticity.[43] However, the MAS only demonstrated moderate reliability in hemiplegic patients – both upper and lower extremities.[44]

In spinal cord injury patients, there was fair-to-moderate agreement for AS and generally fair agreement for MAS when assessing the lower extremities.[45] However, moderate-to-substantial interrater reliability of the MAS was shown in the elbow flexors of stroke patients; this was better than seen in assessments of the ankle plantar flexors in these patients.

A drawback of the AS and MAS is that these scales to not account for differences in velocity. They describe resistance to passive stretch of a joint but do not differentiate spasticity from soft tissue or joint changes.[46]

The American Spinal Injury Association has developed a Spasticity Assessment Training e-Program that includes a module designed to educate treaters on how to examine and score a patient's spasticity using the AS and Tardieu method, based on a consensus panel convened and surveyed in 2013. This course can be accessed at: https://asia-spinalinjury.org/learning/.

Performing Tardieu assessment

In 1954, Tardieu *et al*. described the spastic reaction of the limb, which was velocity dependent based on the speed at which the limb was moved. In 2010, Gracies *et al*. translated and compiled Tardieu's work describing the four basic principles of Tardieu.[47]

The first principle is ensuring that the muscle that is being assessed is completely relaxed. This is thought to be theoretically obvious, however, commonly not maintained in practice.

Second was the principle of maintaining a constant position of proximal segments, especially on testing of two joint muscles. As an example, this is important while testing the gastrocnemius at the ankle, ensuring a constant length of the muscle by maintaining a constant angle of the knee, which it also crosses.

The third principle is to identify the angle where passive stretch is arrested, followed by the fourth principle which is to use this angle to differentiate between spasticity and contracture.

The Tardieu scale is described in Table 7.

Table 8: Performing a Modified Ashworth Scale assessment or Tardieu assessment

Principal muscles	Patient positioning	Examiner positioning	Examiner action	Range of motion
Shoulder adductors				
Latissimus dorsi, pectoralis major Secondary movers: Subscapularis, teres minor, infraspinatus, triceps brachii, coracobrachialis	0° of shoulder flexion, extension and abduction, forearm and hand in a neutral, relaxed position	Glenohumeral joint stabilized while grasping the arm just above the elbow	Abduct the shoulder while maintaining 0° of shoulder flexion	90°
Shoulder internal rotators				
Subscapularis, teres major, latissimus dorsi, pectoralis major Secondary movers: Deltoid	0° of shoulder abduction, minimal flexion and full internal rotation	Stabilize elbow in mid-flexion while grasping the forearm at the wrist	Externally rotate shoulder while maintaining elbow mid-flexion and shoulder abduction at 0°	80°
Elbow flexors				
Biceps brachii, brachialis, brachioradialis Secondary movers: Pronator teres, extensor carpi radialis longus, flexor carpi radialis, flexor carpi ulnaris	0° shoulder abduction and flexion, elbowed fully flexed Forearm in full supination to isolate the biceps brachii Forearm in neutral to isolate the brachialis Forearm in full pronation to isolate the brachioradialis	Stabilize patient's anterior shoulder while grasping the arm at the elbow	Fully extend the elbow	150°
Elbow extensors				
Triceps brachii (all 3 heads) and anconeus	0° shoulder abduction, enough shoulder flexion to be able to fully extend the elbow	Stabilize the elbow while grasping the forearm at the wrist	Fully flex elbow	150°
Forearm supinators				
Biceps brachii (long and short heads), supinator	0° shoulder abduction, flexion, and neutral rotation, 45°–90° of elbow flexion and full pronation	Stabilize the arm just above the elbow while grasping the hand	Full elbow supination	80°
Forearm pronators				
Pronator quadratus (humeral and ulnar heads) pronator teres muscle Secondary movers: Flexor carpi radialis	0° shoulder abduction, flexion, and neutral rotation, 45°–90° of elbow flexion and full pronation Elbow fully flexed to isolate the pronator quadratus	Stabilize the arm at the elbow while grasping the hand	Full supination of the forearm	80°
Wrist extensors				
Extensor carpi radialis (brevis and longus), extensor carpi ulnaris (both heads) Secondary movers: Extensor digitorum, extensor digiti minimi, extensor indicis	0° shoulder flexion, abduction and rotation, forearm in in full supination, wrist in full extension	Stabilize elbow while grasping the hand	Full wrist flexion	70°
Wrist flexors				
Flexor carpi radialis, flexor carpi ulnaris (both heads) Secondary movers: Palmaris longus, flexor digitorum superficialis, flexor digitorum profundus, abductor pollicis longus, flexor pollicis longus	0° shoulder flexion, abduction and internal rotation, forearm in in full pronation, wrist in full flexion	Stabilize elbow while grasping the hand	Full wrist extension	80°
Finger flexors (interphalangeal joints)				
Flexor digitorum superficialis, flexor digitorum profundus	90° elbow flexion, forearm in pronation, wrist in neutral/20° extension, all finger joints in full flexion	Stabilize wrist while grasping index, long, ring, and small fingers	Stabilize wrist while grasping index, long, ring, and small fingers	135°

Contd...

Table 8: Contd...

Principal muscles	Patient positioning	Examiner positioning	Examiner action	Range of motion
Finger flexors (MCP joints)				
Lumbrical, dorsal, and palmar interossei Secondary movers: Flexor digitorum superficialis, flexor digitorum profundus, flexor digiti minimi brevis, opponens digiti minimi	90° elbow flexion, forearm in pronation, wrist in full extension, MCP joints at 90° flexion, full extension at interphalangeal joints	Stabilize wrist while grasping index, long, ring, small fingers just distal to the MCP joint	Full MCP extension	90°
Thumb adductors				
Adductor pollicis (both heads) Secondary movers: 1st dorsal interosseous	90° wrist flexion, forearm pronation, thumb in full adduction	Stabilize hand while grasping the thumb	Full thumb abduction	70°
Thumb flexors				
Flexor pollicis brevis and flexor pollicis longus	90° elbow flexion, neutral forearm rotation, full thumb flexion at interphalangeal joints	Stabilize wrist and hand while grasping the thumb distal to the distal interphalangeal joint	Full thumb extension	130°
Hip extensors (isolating gluteus medius)				
Gluteus maximus muscle, long head of biceps femoris, Semimembranosus muscle, Semitendinosus muscle Secondary movers: Adductor magnus, gluteus medius	Patient on side, 0° hip abduction, hip in full extension, knee flexed	Stabilize patient and pelvis while grasping the thigh above the knee	Hip flexion	120°
Hip extensors				
Gluteus maximus muscle, long head of biceps femoris, Semimembranosus muscle, Semitendinosus muscle Secondary movers: Adductor magnus, gluteus medius	Patient on side, 0° hip abduction, hip in full extension, knee extended	Stabilize patient and pelvis while grasping the leg below the knee	Hip flexion	120°
Hip flexors				
Psoas major, iliacus Secondary movers: Rectus femoris, sartorius, tensor fascia lata, pectineus, adductor brevis, adductor longus, adductor magnus, gluteus medius	Patient on side, 0° hip abduction, hip in full flexion, knee flexed	Stabilize patient and pelvis while grasping the thigh above the knee	Hip extension	120°
Hip adductors				
Adductor longus, adductor brevis, adductor magnus, pectineus, gracilis	Supine, 0° hip flexion and abduction, knee in neutral	Grasp foot of lower extremity being tested and stabilize below knee on contralateral lower extremity	Abduct hip	45°
Knee extensors				
Rectus femoris, vastus intermedius, vastus lateralis, vastus medialis	Lying on side with neutral hip and knee in full extension	Grasp foot while supporting thigh under knee	Full knee flexion	135°
Knee flexors				
Biceps femoris, semimembranosus, semitendinosus Secondary movers: Gastrocnemius, gracilis, sartorius	Supine, 90° hip flexion, knee in full flexion	Grasp foot while stabilizing thigh slightly above the knee	Full knee extension	135°

Contd...

Table 8: Contd...

Principal muscles	Patient positioning	Examiner positioning	Examiner action	Range of motion
Ankle plantar flexors (isolating soleus)				
Gastrocnemius, soleus Secondary movers: Plantaris, flexor hallucis longus, flexor digitorum longus, tibialis posterior, fibularis longus, fibularis brevis	Supine, flex hip and knee 90°, ankle in full ankle plantar flexion	Grasp foot while stabilizing leg at the knee	Full ankle dorsiflexion	70°
Ankle plantar flexors				
Gastrocnemius, soleus Secondary movers: Plantaris, flexor hallucis longus, flexor digitorum longus, tibialis posterior, fibularis longus, fibularis brevis	Supine, hip and knee in neutral, ankle in full ankle plantar flexion	Grasp foot while stabilizing leg at the knee	Full ankle dorsiflexion	70°
Ankle invertors				
Tibialis anterior, tibialis posterior Secondary movers: Peroneus tertius, extensor digitorum longus and extensor hallucis longus	Supine, 0° hip, knee, ankle flexion, foot inverted	Grasp distal foot and stabilize leg at the ankle	Full foot eversion	40°

MCP: Metacarpophalangeal

Table 9: Recording GAS without numbers (GAS-light)

	Verbal Rating			Numerical conversion	
At baseline	With respect to this goal do they have?	Some function	☐	-1	
		No function (as bad as they could be)	☐		-2
At Outcome Was the goal achieved?	**Yes**	A lot more	☐	+2	+2
		A little more	☐	+1	+1
		As expected	☐	0	0
	No	Partially achieved	☐	-1	-1
		No change	☐	-1	-2
		Got worse	☐	-2	

Table 10: Goal attainment scaling recoding before treatment

Goal	Category	Subcategory	Baseline	Expected
1ary	Symptoms	Pain	9/10	6/10
2ary	Passive function	Dressing	7/10	3-4/10
2ary	Passive function	Hygiene	7/10	3-4/10
2ary	Passive function	Use of orthosis	1.0 h daily	1.5-3.0 h daily

The advantages of the Tardieu scale over the MAS are that the Tardieu:

- May be able to identify the presence of spasticity better than AS
- May be able to differentiate spasticity from contracture, whereas the AS does not.

In assessing the interrater reliability of the Tardieu scale in cerebral palsy (CP), good-to-excellent agreement between inexperienced and experienced raters across all joints.[47] It was also noted that a 1-day training session substantially improved reliability and there was high agreement between goniometric and visual angle assessments, suggesting that it can be reliably administered without a goniometer.

In spinal cord injury patients, excellent interrater reliability was found for the R1–R2 (spasticity angle) for all muscles tested. This group also found that the assessment of R1 was excellent in terms of interrater reliability in the hip adductors, hip extensors, knee flexors, and knee extensors. However, only fair interrater reliability was seen when assessing at the ankle plantar flexors.[48]

The limitations of the Tardieu are that the spasticity grade (Y) describes a quantifiable reaction of muscle, not necessarily increasing severity of spasticity. The data are nominal rather than ordinal and it is not as extensively studied as the AS and MAS.[49]

Performing the modified Ashworth or Tardieu assessment

Although the two scales rate the patient's spasticity in slightly different ways, the physical examination by the clinician is the same for both.

A summary of important information on performing the AS or Tardieu assessments for different muscle groups is given in Table 8.

Video

Please view this video for more information on performing the MAS measurement. Available on: https://www.dropbox.com/sh/jl6xudc3evrkkvc/AADvQht-SxMvV1IrxDzKwgcma/Part_2.mp4?dl=0.

ACTIVE RANGE OF OPTION

Perform goniometric measurement of limb spasticity

Goniometers are simple plastic devices that allow measurement of joint angles. By having two rulers joined in way that the angle between them can be altered and measured allows the two ruler scales to be aligned with a joint and the angle formed by the bones determined. By moving the joint and repeated measurements, the ROM may be determined.

Goniometric measurements are frequently used for joints such as elbow, shoulder, and hip [Figure 5].

To perform a goniometric assessment, the clinician should follow this protocol:

- Position the joint in zero position and stabilize the proximal joint component
- The joint should be moved to the end of the ROM (to assess quality of movement)
- The end-feel at the limit of the ROM should be sought and the joint rested at this angle
- The bony landmarks should be palpated
- The goniometer should be aligned with bony landmarks while holding joint at the end of range
- The goniometer reading should be taken and the measurement recorded.

Classically, a standard goniometer for measuring joint ROM is the gold standard in clinical settings because it is portable and relatively inexpensive. However, it has several limitations, making it difficult for clinicians to use. Clinicians need both hands to use a goniometer, making limb stabilization difficult. Thus, the risk of a high measurement error increases.[50]

Video

Please view this video for more information on how to perform goniometric measurements.

https://www.dropbox.com/sh/jl6xudc3evrkkvc/AADuTF7whVT0t96_IDBbwR0Za/Part_1.mp4?dl=0.

Describing the role of diagnostic nerve block in assessing spasticity versus contracture

A nerve block is the application of a chemical substance to a nerve that will interfere temporarily or permanently with conduction along the nerve.[51] There are two types of nerve blocks: diagnostic nerve block (DNB) with anesthetics and therapeutic nerve block with alcohol or phenol. The technique of injection is the same while the drugs injected and the indications are different.

Therapeutic nerve blocks are considered in more detail in Module 2.

The DNB is performed with anesthetics[52] which allows evaluation of how much the lack of ROM, joint and muscle tightness, and joint deformity can be attributed to spasticity instead of muscle or soft tissue rheologic changes. Consequently, DNB can also assist the clinician in diagnosing contractures (that will not respond to chemodenervation or neurolysis) on top of underlying spasticity, identifying potentially undesirable outcomes (e.g., excessive muscle weakness), and appreciating the beneficial effects of pain reduction and improved limb posture on function and hygiene.

The benefits of anesthetic blocks in the evaluation of spastic patients are that they allow differentiation between muscular hyperactivity and contractures and facilitate evaluation of the antagonists in terms of strength, dystonia, and co-contractions. It allows the muscles involved in motor problems to be identified, thus helping identify the muscles to be targeted for treatment with BoNT-A. An anesthetic nerve block can provide information on the likely outcome of treatments such as BoNT-A or selective neurotomy.

Performing a diagnostic nerve block

The DNB procedure consists of injecting a local anesthetic (usually lidocaine 1%–2%) on a motor nerve innervating a spastic muscle. It is performed using a disposable needle for conduction anesthesia coupled to an electromyography (EMG) apparatus or an electrical stimulator. Once the needle is inserted, the nerve is located according to anatomic landmarks, electrical stimulation, or by ultrasonography.[52,53]

When a clinical muscular contraction is still obtained with a low stimulation intensity (1 ms duration and 0.1 mA intensity with a portable stimulator or 0.01 ms duration and 4–10 mA intensity with an EMG apparatus), meaning a close contact of the needle with the nerve, the anesthetics is injected.

A DNB eliminates spasticity after few minutes and lasts for some hours, allowing assessment of the respective contribution of the spastic muscles, the degree of muscle shortening, and the weakness of the antagonistic muscles. It will allow the clinician to determine the potential benefits of performing longer lasting interventions such as chemodenervation or surgery. It also allows the patient to experience the potential benefit of reduced muscular hyperactivity and have a better understanding of what to expect from more definitive procedures.

Sensorimotor (mixed) nerve block (i.e., tibial nerve in case of spastic foot, musculocutaneous nerve in case of elbow flexion, and median and ulnar nerve in case of spastic hand) is the easiest to perform. Due to their size and well-known anatomic location, these nerves are easy to find and target and require a 3 mL dose of anesthetic. However, as such nerves innervate many muscles (i.e., the tibial nerve innervates both soleus, gastrocnemius, tibialis posterior, and flexor digitorum muscles), it does not provide information about the precise spastic muscles that are the most involved in the deformity. Furthermore, the

procedure may induce sensory disturbances (i.e., the tibial nerve includes the sensory fibers innervating the sole of the foot), which may interfere with function and assessment (i.e., after tibial nerve, the induced foot anesthesia interferes with gait and balance). Therefore, such sensorimotor nerve DNB is mainly used to simply differentiate increased muscle tone from fixed contracture. A small volume, e.g., 1–2 mL, can be used to help differentiate between a true contracture and a spastic muscle.

Selective motor nerve blocks (i.e., individual motor branches of the tibial nerve innervating the soleus, gastrocnemius, and tibialis posterior) are more complex to perform due to manifold steps, but of great value in more complicated clinical presentations. Considering their small size, they are more difficult to find but require smaller dose of anesthetics (0.5–1.5 mL). However, such selective DNB allows the spastic muscle(s) involved in the deformity to be identified (e.g., soleus muscle is usually responsible for the triceps clonus; disappearance of the clonus after selective DNB of the soleus motor nerve branch confirms it) and avoids sensory disturbances (as motor nerves branches are separated from the sensory nerves). Several selective DNB (e.g., soleus motor branch followed by gastrocnemius motor branch) can be performed during the same session.

Interestingly, DNB can be used as a valuable screening tool before surgery such as neurotomy. The spasticity reduction and gait kinematics improvement obtained after DNB is consistent with the one obtained after surgery.[54] At last, DNB is a safe technique with clinical guidelines devoted to increase the security was recently published.[55]

To summarize the procedure:

First, prepare the appropriate material and equipment for the procedure:

- Needle of 1”–2” length
- Syringe (3cc or 5cc)
- Gel electrodes
- Internal ± external nerve stimulator
- Gauze and alcohol or betadine
- Desired medication for injecting
- Draw needle.

The procedure and goals of treatment must be explained to the patient who must give informed consent to proceed. The patient must be positioned appropriately depending on the nerve or motor point to be treated (e.g., for treating a tibial nerve, then patient should be prone with knee extended).

The injection site can be selected based on anatomical landmarks. Gel electrodes should be applied and the stimulator turned on to observe contractions; the site can then be marked. Potential anatomical pitfalls should be identified.

The technique for administering the injection can be summarized as:

- Clean site with chlorhexidine, alcohol, or betadine
- Draw up injectant
- Attach syringe to needle
- Connect electrode
- Insert special device needle for conduction anesthesia into site and adjust output of stimulator for maximum contraction </=1.0 mA
- Aspirate syringe prior to injection to look for blood return
- Inject as needed monitoring for loss of contraction (up to 3cc)
- Ultrasound can be used for localization of injection needle and for nerve stimulator for muscle contraction.

Aftercare must be explained to the patient, the site monitored for redness, pain, or sensory complaints. Ice should be applied as required and if any excessive adverse changes occur the physician should be contacted. The response to the injection should be evaluated in terms of tone and ROM. Future plans and follow-up schedules should be discussed with the patient.

Competency Assessment 2

The answers to these questions can be found at the end of this module before the references.

1. What spastic muscles may be responsible for these limb deformities?
2. A 65-year-old patient admitted following the right MCA stroke. On 5th day following the stroke, examination findings demonstrated cognitive deficits, visual inattention to the left side, MAS 2 around his left wrist and elbow, and muscle power of 1/5. What are the features that indicate higher risk of developing spasticity in this patient?
3. What scales would you consider for measuring the outcome of treatment?
4. An 80-year gentleman admitted following brain injury. On examination, he has no power on his right side with spasticity (MAS 3 over his right wrist and elbow flexors). He also was diagnosed with a urinary tract infection 2 days ago and on treatment. He has an indwelling catheter and blood was found in the urine bag. He appears agitated and restless. He shouts out when touched. He has ingrown toenails. What are the aggravating factors (triggers) of spasticity in this patient?

Management

Goal setting

Most human behavior is arguably goal directed; people generally act for a reason even if it is nebulous or unconsidered. Hence, a goal is an end or result toward which behavior is consciously or unconsciously directed. In the context of spasticity, a goal may be defined as the intended consequence of actions undertaken by the patient and rehabilitation team.[56]

Goal setting may be defined as the process during which patient and clinical members of the multidisciplinary team make a collective decision, following an informed discussion, of how and when to carry out rehabilitation activities. The goal setting process should lead to the explicit and comprehensive identification of the reasons for all actions to be taken.[56]

The importance of treatment goal setting

Adequate goal setting should derive a set of goals that motivates patients, caregivers, and the team, ensuring that the same goals are desired, important actions are not overlooked, and there is adequate monitoring of change and quick cessation of ineffective actions.[56]

Setting goals for a person increases their behavior changes, presumably through increasing their motivation. The team effort in goal setting should facilitate both the efficiency and effectiveness of rehabilitation and allow the rehabilitation process to be monitored objectively. In this context, it is very important that actions which are clearly ineffective should be stopped as soon as their lack of desired effect is apparent and an alternative way of achieving the goal can then be started in a timely fashion.

When setting goals, it is important that the team do not make assumptions about the wishes and expectations of individual patients in any situation; even when they seem obvious. Primary goal setting should take into account the patient's wishes. If the patient is unable to decide on their own, then the wishes and expectations of other important parties, such as family, caregivers, peers, funding bodies, and the rehabilitation team, may also be considered. Goals should be recorded using "patient-friendly" wording wherever possible.

Despite setting common goals, patient and clinician's evaluations of benefit of an intervention are not always aligned. In a study of BoNT-A injections, treatment effect was rated as excellent or good by 76% of neurologists but only by 52% of patients.[57]

Treatment satisfaction may change over the course of their treatment. In a study assessing patient satisfaction at different intervals after BoNT-A treatment, it was shown that satisfaction dropped significantly with time after the peak effect of the toxin.[58] It is important to emphasize the need to make attainable, patient-centric goals and manage the patient's expectations.

An algorithm for developing an individual strategy is provided by Turner-Stokes.[59]

SMARTER goals are goals identified on an individual basis:
- **S**pecific
- **M**easurable
- **A**chievable
- **R**ealistic
- **T**imed
- **E**thical
- **R**ecorded.

It is recommended that one primary and several secondary goals (about 3–4) are defined[59] with a defined expected outcome and the time frame in which this is potentially achievable; the combination of the objective goal and action plan is important for success.

Goal attainment scaling

GAS is a method of assessing the degree of achievement in reaching established rehabilitation goals. Each person has their own measure for each goal expected outcome. It allows the achievement to be scored in a standardized way, ascribing a numerical value which can then be used for statistical analysis.

The most frequent goal categories are divided into functional activities, such as active function, passive function and mobility, and symptoms of impairment, such as joint ROM, pain, discomfort, involuntary movements, and associated reactions. One parameter should be chosen for each goal, and after identification of 3–4 goals, a primary goal should be identified.

GAS may be used to monitor an individual patient over consecutive treatment cycles and also to compare different patients or groups of patients or different treatment strategies.

Goal attainment is scored by giving points to the outcome where the goal achievement is:
- Much better than expected: 2
- A little better than expected: 1
- As expected: 0
- Only partial: −1
- No change: −1
- Worse: −2.

The GAS can be calculated via a formula or downloadable Excel spreadsheet from https://www.kcl.ac.uk/cicelysaunders/resources/tools/gas.

The formula is:

$$GAS = 50 + \frac{10 \sum (w_i x_i)}{\left[(1 - \rho) \sum w_i^2 + \rho (\sum w_i)^2\right]^{½}}$$

Where w_i = goal weight, X_i = result (−2 to +2), and ρ = expected correlation for goal scales (ρ = 0.3).

Goal attainment scaling-light

GAS-light is a simplified version of GAS designed to be used in routine clinical practice. It provides a verbal rating scale for clinicians who prefer verbal descriptors to numbers.

Clinicians often think in terms of change from baseline. A problem with the five-point GAS score is that it does not allow "partial achievement" of a goal to be recorded if the baseline score was −1. On the other hand, if all baseline scores are recorded at −2, this does not allow for worsening.

The following algorithm allows clinicians to record goal attainment without reference to the numeric scores and so avoids the perceived negative connotations of zero and minus scores.

Clinical Case Example

The patient was a 58-year old man who had suffered a stroke 6 months ago. He had a right spastic hemiplegia (muscular strength 0/5; global MAS score 3). He did not have any spasms or clonus. Because of spasticity, he had difficulty to put on his wrist–hand orthosis.

The main problem of the patient was pain, both at rest and during passive movement. He also had difficulty with dressing and hygiene. The patient and clinician agreed that the main goal of treatment was to decrease pain from 9 to 6 (visual analog scale), mainly in the shoulder (he also had axillary candidiasis).

Other objectives were to decrease spasticity in the elbow (to facilitate dressing) and in the hand (to facilitate palmar hygiene). A treatment program consisting of BoNT-A injection, followed by physical therapy (1 hour a day, from Monday to Friday) was planned. In addition, a wrist–hand orthosis (splint) to maintain the expected spasticity reduction in the hand was contemplated. The target is to achieve the goals in 6 weeks.

Pretreatment video

The video shows how painful passive movement in the upper limb was, mainly in the shoulder.

It was difficult to examine the range of movement in each joint because of the spasticity and the associated pain. BoNT-A (Incobotulinum toxin A) was injected into the following muscles:

- Pectoralis major 100 U (2 points)
- Subscapularis 50 U
- Brachioradialis 50 U
- Brachialis 50 U
- Flexor digitorum superficialis 50 U
- Interossei 40 U
- Opponens pollicis 10 U.
- Total dose: 350 U.

Posttreatment video

The pain decreased more than what was previously expected. The video shows that physical examination was easier to perform. Passive mobilization of the shoulder and the other joints of the upper limb was easier than before the injection.

The GAS-eous tool is a system for using GAS in the **E**valuation of **O**utcome for **U**pper limb **S**pasticity. It consists of a semi-structured framework for goal setting and outcome measurement. It is divided into two domains: symptom/impairment and activities/function. There are with six main goal areas: pain/discomfort, involuntary movements, ROM/contracture prevention (domain 1); and passive function (care tasks), active function, mobility (domain 2) with additional goals of cosmesis/body image and therapy facilitation.

It is important to note that there may be cultural and geographic variations in the meaning of the terms Cosmesis and Esthetic. In the current context, the term "cosmesis" is referring to the preservation, restoration, or bestowing of physical beauty to the human body, whereas "esthetic" is concerned with the idea of beauty or appreciation of beauty.

A worksheet for using GAS-eous is available online at: tools-gaseous-gaseous-tool.pdf (kcl.ac.uk).

Table 12 summarizes the Gas-eous system.

Table 11: Goal attainment scaling recording after treatment

Goal	Category	Subcategory	G. parameter	Baseline	Expected	Achieved	GAS
1ary	Symptoms	Pain	VAS	9	5-6	4	+1 (a little more than expected)
2ary	Passive function	Dressing	VAS	7	3-4	3	0 (as expected)
2ary	Passive function	Hygiene	ROM (ease, less pain)	90°, painful 7/10	90°, less pain 4/10	4	0 (as expected)
2ary	Passive function	Use of orthosis	Time (hours)	1.0 h	1.5-3.0 h	2.0 h	0 (as expected)

P=0.3. GAS: Goal attainment scaling, ROM: Range of motion, VAS: Visual analog scale

Table 12: The GAS-eous system

Domain 1	**Symptoms/impairment**	**Parameter**
Pain/discomfort (b280)	Spasticity-related pain or discomfort	Pain rating/10
Involuntary movements (b735, b765)	Unwanted involuntary movements during use of other limbs (spasms/associated reactions)	Carry angle (spasm frequency)
Range of movement/contracture prevention (b710, b735)	Range of movement, or splint tolerance prevention of contractures/deformity	Percentage joint range
Domain 2	**Activities/function**	**Parameter**
Passive function (care tasks) (d520)	Ease of caring for the affected limb	Ease of care rating/10
Active function (d440, d445)	Using the affected limb in some active motor tasks	Able to do defined task (time taken/control)
Mobility (d450)	Improved mobility - Transfers/standing/walking	Confidence rating/10 (gait speed//endurance)
	Other	
Cosmesis/body image	Patient's perception of body image, aesthetic appearance	Rating/10
Therapy facilitation	Team's perception of interference with therapy	Team rating/10

Modified from: Turner-Stokes *et al*. The GAS-eous tool Goal Attainment Scaling – Evaluation of outcomes for upper limb spasticity version 1.1. 30.12.13. http//www.csi.kcl.ac.uk/Gaseous_tool3 pdf. The Domains are mapped onto the WHO ICF, disability and health, ICF, disability and health ICF (who.int). GAS: Goal attainment scaling, ICF: International Classification of Functioning

Free tools are available on the internet for calculating GAS, GAS-light, and GAS-eous. A good selection of tools is available from King's College UK in: https://www.kcl.ac.uk/cicelysaunders/resources/tools/gas.

Competency Assessment 3

The answers to these questions can be found at the end of this module before the references.

1. Attributes of SMARTER goals are:
   a. Specific, measurable, realistic, timed
   b. Specific, measurable, aspirational, realistic
   c. Specific, achievable, elusive, realistic
   d. Specific, ambiguous, realistic, timed.
2. According to the GAS, when a outcome of an intervention is "a little better than expected," the score assigned is:
   a. −2
   b. −1
   c. 1
   d. 2.
3. Domains in the GAS-eous tool in the evaluation of outcome for upper limb spasticity include:
   a. Pain, agraphia, care tasks, cosmesis
   b. Pain, involuntary movement, mobility, cosmesis
   c. Discomfort, dystonia, mobility, cosmesis
   d. Involuntary movements, contracture prevention, motivation, therapy facilitation.
4. Spasm frequency is a parameter for what GAS-light system domain?
   a. Pain
   b. Passive function
   c. Involuntary movement
   d. Cosmesis.

Competency Assessment Answers

Competency Assessment 1 Answers

1. What are the three main processes that lead to functional impairments seen in an UMN injury?
   Expected content of answer
   The functional impairments seen in patients with spasticity occur due to three main processes: weakness, biomechanical changes (soft tissue stiffness, muscle shortening, tendon contracture), and muscle over-activity through hyperexcitability or loss of inhibition.
2. A patient had a left subcortical stroke 4 weeks ago and is now ready for discharge. He has spasticity of the right elbow flexors and plantar flexors (both scored as "3" in the MAS) and is nonambulatory. Hemiplegia has persisted. His spouse asks you what will happen to the elbow and ankle spasticity in the near future.
   Expected content of answer
   In some people with a stroke, spasticity may disappear after about 4 months (16 weeks), but in others, it may persist. Your husband is at high risk of having persistent and severe spasticity because continues to have no movement at all on his right side. Therefore, it is important that he will be followed up to manage the limb tightness.
3. What clinical features was the patient exhibiting?
   Expected content of answer
   This video displays an example of finger muscle co-contraction. Co-contraction is the simultaneous activation of agonist and antagonist muscles groups during voluntary movement. It results from failure of reciprocal inhibition at either the spinal cord or cortical level. In this video, the patient's finger flexors are co-contracting while the patient is attempting to extend the fingers.
4. A 75-year-old male presents for rehabilitation 2 weeks after sustaining an ischemic right MCA artery CVA with left hemiparesis. His examination is noted as having left arm movement at the elbow limited to a flexor synergy pattern and hyper-reflexia at the biceps tendon. His tone using the MAS in the left arm is significant for a 2 for the elbow flexors and 1+ each for the wrist and finger flexors. As you are formulating a treatment plan, what other signs of the UMNS do you anticipate encountering which may interfere with functional improvements as motor recovery progresses.
   Expected content of answer
   Using the models of motor recovery described by Twitchell and Brunnstrom, it is expected that the spasticity will increase over the next few weeks. The patient may also develop other positive signs associated with the UMNS including increased reflex activity, clonus, co-contraction, and dystonia. It is important to minimize the impact these findings will have on the early motor recovery. In addition, efforts to maintain the normal elastic properties of the muscle and tendons are important since the combination of the above postures and resistance to stretch will lead to muscle stiffness and fibrosis.
5. A stroke patient reports that every time he yawns his hemiparetic elbow is able to flex, although he is unable to flex the elbow on command. The patient is describing what phenomenon?
   1. Spastic dystonia
   2. Associated reaction
   3. Spasticity
   4. Mass synergy pattern.

   Expected content of answer
   Associated reaction. Associated reactions may be due to disinhibited spread of motor activity into a limb affected by a UMN lesion.

Competency Assessment 2 Answers

1. What spastic muscles may be responsible for these limb deformities?
   Expected content of answer

Figure A

Elbow flexion – Biceps, brachialis, brachioradialis
Forearm pronation – Pronator teres and quadratus
Wrist flexion – Flexor carpi radialis and ulnaris
Proximal finger flexion – Flexor digitorum

superficialis and profundus (because it crosses the proximal interphalangeal joint).

Figure B

Equinovarus – Tibialis posterior, triceps surae, flexor hallucis longus, flexor digitorum longus

Toe flexion – Flexor hallucis longus, flexor digitorum longus, and brevis.

2. A 65-year-old patient admitted following the right MCA stroke. On 5th day following the stroke, examination findings demonstrated cognitive deficits, visual inattention to the left side, MAS 2 around his left wrist and elbow, and muscle power of 1/5. What are the features that indicate higher risk of developing spasticity in this patient?

   Expected content of answer

   Cognitive deficits, visual inattention, reduced motor power, and already present high tone across 2 joints.
3. What scales would you consider for measuring the outcome of treatment?

   Expected content of answer

   GAS, MAS, Tardieu scale, goniometer (improved range of movement), patient/caregiver satisfaction rates, improved walking speed.
4. An 80-year-old gentleman admitted following brain injury. On examination he has no power on his right side with spasticity (MAS 3 over his right wrist and elbow flexors). He also was diagnosed with urinary tract infections 2 days ago and on treatment. He has an indwelling catheter and blood was found on the urine bag. He appears agitated and restless. He shouts out when touched. He has growing toe nails. What are the aggravating (triggers) factors of spasticity in this patient?

   Expected content of answer

   Urinary tract infection, possible trauma from catheter, ingrown toenail, and pain.

Competency Assessment 3 Answers

1. Attributes of SMARTER goals are:
   a. **Specific, measurable, realistic, timed**
   b. Specific, measurable, aspirational, realistic
   c. Specific, achievable, elusive, realistic
   d. Specific, ambiguous, realistic, timed.
2. According to the GAS, when a outcome of an intervention is "a little better than expected," the score assigned is:
   a. −2
   b. −1
   c. 1
   d. 2.
3. Domains in the GAS-eous tool in the evaluation of outcome for upper limb spasticity include:
   a. Pain, agraphia, care tasks, cosmesis
   b. **Pain, involuntary movement, mobility, cosmesis**
   c. Discomfort, dystonia, mobility, cosmesis
   d. Involuntary movements, contracture prevention, motivation, therapy facilitation.
4. Spasm frequency is a parameter for what GAS-light system domain?
   a. Pain
   b. Passive function
   c. **Involuntary movement**
   d. Cosmesis.

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Module 2: Nonsurgical Management of Spasticity

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Abstract

Spasticity management should be part of a well-coordinated and comprehensive rehabilitation program that is patient-centric and goal-specific. There are a variety of options available for the treatment of spasticity. A usual approach is starting with the least invasive treatment modalities initially and gradually increasing to more complex interventions as this is required. This curriculum considers oral antispasticity drugs in terms of mechanism of action, clinical use, efficacy, and adverse events. It also presents other treatment options, such as chemical neurolysis using phenol and alcohol and chemodenervation using botulinum toxin A (BoNT-A). Therapeutic intramuscular injections of BoNT-A require sound patient selection, accurate muscle selection, and precise localization. The common methods for achieving these are described. The importance of physiotherapy is explained, along with the necessity to combine treatment modalities to address spasticity and the various components of the upper motor neuron syndrome. Recognizing differences in various health-care systems across countries and regions, the authors aim to present various treatment options. While this section of the curriculum highlights the importance of an interdisciplinary effort in managing spasticity, it is understandable that not all treatment options are available uniformly. The challenge to clinicians is to make the most of the management options on hand to optimize outcomes.

Keywords: Spasticity-non-surgical treatment-antispasticity drugs-BoNT-A-nerve blocks

Learning Objectives

On completion of this module, the learner will be able to:

1. List nonsurgical treatment options in spasticity
2. Elucidate the mode of action, dosages, and side effects or oral antispasticity drugs
3. Explain when intrathecal or intramuscular drugs may be more appropriate
4. Describe how physical and pharmacological treatments should be combined for optimal outcome
5. Explain the use of nerve blocks in spasticity and to be able to compare phenol and BoNT-A nerve blocks
6. Spell out the main techniques of identifying muscles for injection and be able to demonstrate muscle identification
7. Define adjunctive therapies post-BoNT-A and understand the evidence base behind treatment regimens
8. Demonstrate BoNT-A injection techniques
9. Identify the health-care professionals who are needed to provide the combined skills for appropriate nonsurgical management of spasticity.

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Website: www.jisprm.org

DOI: 10.4103/2349-7904.347808

Spasticity Treatment Options

Many therapeutic interventions are used either alone or in combination in the management of spasticity. This Curriculum described nonsurgical treatments and provides an overview of physical and nonpharmacological modalities as well as pharmacological treatment modalities.

Nonsurgical treatment(s) should form the basis of management, although not all of these options may be available in all treatment centers.

Nonpharmacological and nonsurgical/nonorthopedic treatment should be the starting point of spasticity management and not disregarded, even if progression to pharmacological or surgical interventions follows [Figure 1].

Stand-alone pharmacological and surgical management is often not recommended; treatments should be used in combination with other therapeutic modalities encompassing an interdisciplinary rehabilitation approach.[2]

Spasticity management should be part of a wider rehabilitation program that is patient-centric and goal-specific. It should comprise multimodal treatment delivered as both generalized and focal interventions, and importantly, it should be remembered that spasticity treatment is a

How to cite this article: Reebye R, Balbert A, Bensmail D, Walker H, Wissel J, Deltombe T, Francisco GE. Module 2: Nonsurgical management of spasticity. J Int Soc Phys Rehabil Med 2022;5:S23-37.

dynamic process requiring constant re-evaluation and updating.

Physical and other nonpharmacological modalities

The role of physical and other nonpharmacological modalities in managing spasticity

Appropriate physiotherapy is central to the management of patients with spasticity, and the physiotherapy team should be an integral part of treatment planning from an early stage.

The role of physiotherapy includes, but is not limited to, early intervention to maintain muscle length, maintenance of joint alignment, prevention of secondary complications, strengthening of antagonist muscles, strengthening of proximal and axial muscles to improve central stability, and task-specific training.[3]

Despite its central role in rehabilitation (and possibly because it has been a long-standing treatment modality), there is actually a paucity of clinical trial data underpinning the use of physiotherapy. Similarly, a recent systematic review has concluded that there is a lack of high-quality evidence for many modalities. There is "moderate" evidence for electro-neuromuscular stimulation and acupuncture as an adjunct therapy to conventional care in stroke patients. Only "low-"quality evidence exists for rehabilitation programs targeting spasticity (e.g., induced movement therapy, stretching, dynamic elbow-splinting, occupational therapy) in stroke and other neurological conditions.[2] These authors concluded that further research is needed to judge the effect of nonpharmacological interventions with appropriate study designs, timing and intensity of modalities, and associate costs of these interventions. Yet, it should be noted that absence of strong research-based evidence does not mean that these treatment approaches do not contribute to the overall outcome of spasticity interventions.

Self-rehabilitation

Self-rehabilitation is a system of encouraging patients to be involved in their own rehabilitation by recording activities including daily self-care, use of devices and equipment, and socializing along with exercises and activities recommended by the health-care team.[4] Involvement can help patients feel that they still have some control over their own situation. A systematic and meta-analysis of randomized trials[5] showed similar results for Barthel index, Berg balance, and Fugl–Meyer scoring in home-based rehabilitation versus conventional rehabilitation, but the studies lacked spasticity outcome measures.

Another study,[6] considering home-based tele-supervising rehabilitation on physical function in stroke survivors, suggested that it could play a role in improving functional recovery in stroke survivors. To date, there has not been any published randomized control trials of BoNT-A + self-rehabilitation versus BoNT-A alone.

Splinting/taping/casting

Casting/taping/splinting all rely on elongation of the muscle.

Providing a prolonged stretch decreases motor neuron activity in spastic limbs and can decrease spasticity since the stretch leads to increased muscle fiber tension and length through an increase in the number of serial sarcomeres.[7]

Using this maintained low-load stretch, muscle tissues unfold and collagen fibers within the connective tissues undergo temporary re-alignment of which stimulates growth of the muscle.[8-10]

However, in muscles with increased tone, the shortening of muscles and connective tissues recurs unless the muscle length and stretch is maintained.[10]

Casting may be inhibitive or serial. Inhibitive casting consists of one application of a cast post injection, which is removed within 2 weeks to help decrease tone.[11]

Serial casting uses a series of progressive casts to increase muscle length using low load prolonged stretch to soft tissue.[7-9,12]

Casts can remain in place for between 5 and 10 days each and may be repeated 3–4 times in succession. If 15° from the neutral position of a joint is reached, then the casting can be stopped and an orthotic brace used to help keep the range of motion.

The spasticity patterns amenable to serial casting in the upper limb are flexed elbow, pronated forearm, and flexed wrist. In the lower limb, equinus foot and equinovarus foot may be treated. Casting has also been applied to knee flexion spasticity.

Transcutaneous electrical stimulation

The hypotheses for transcutaneous electrical stimulation (TENS) in reducing spasticity include:

- Modulation of excessive alpha motor neuron activity through dynorphin release
- Reduced corticomotor excitability – plasticity
- Modulation of reciprocal inhibition via 1a
- Increase in presynaptic inhibition via 1b

Of 6506 articles identified, 10 studies with 360 subjects were included in the systematic review by Marcolino *et al*.[13] In this review, it was shown that six studies demonstrated that TENS alone or as additional therapy was superior to placebo to reduce poststroke spasticity assessed by the modified Ashworth scale, especially in lower limbs (−0.58 [−0.82 to − 0.34] $P < 0.0001$, 5 studies); low-frequency TENS showed a slightly larger improvement than high-frequency, but without significant difference between subgroups.[13]

Extracorporeal shock wave therapy

The mechanism behind extracorporeal shock wave therapy (ECSWT) is unknown, but it does not seem to be related to a decrease in spinal excitability.[14] Several theories have been proposed to explain ECSWT:

- Nitrous oxide produced in response to ECSWT may have an effect on synaptic plasticity, and formation of neuromuscular junctions in the peripheral nervous system (PNS)
- Effects on neurotransmission at the neuromuscular junction
- Modulation of muscle rheology.

The effects last up to 12–16 weeks (but no study with longer follow-up has been conducted). When used alone, ECSWT can reduce spasticity in forearm and triceps following stroke.[15-17] Three sessions provided a longer effect (16 vs. 8–12 weeks) and better hand function–wrist control than one session.[16]

When used with BoNT-A, ECSWT compared with BoNT-A plus ES showed results in favor of ECSWT for MAS, spasm frequency scale, and pain (using a visual analog scale).[18]

Noninvasive neuromodulation

Two narrative reviews of repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation as spasticity treatment have recently been published.[19,20] They reported that low-frequency rTMS over the unaffected hemispheres could be effective in the reduction of spasticity when applied with alone or with conventional therapies. The need for uniform, large, multicenter trials to confirm these findings was highlighted by the authors.

Robotics

Little evidence exists concerning the use of robotics in spasticity. A review of electro-mechanical and robot-assisted arm training has concluded that the quality of evidence is very low and studies show too much heterogeneity in intensity, duration, amount of training, type of treatment, and participant characteristics to make meaningful conclusions.[21]

Oral medications

Mechanism of action, indications, benefits, and potential adverse effects of oral spasmolytics

Generalized spasticity can be addressed with a variety of oral medications with differing mechanisms of action. The most commonly used oral agents include baclofen, tizanidine, benzodiazepines, and dantrolene sodium [Table 1].[22-24]

Baclofen is one of the more commonly used agents to treat generalized spasticity. It is a gamma-aminobutyric acid (GABA) analog that binds presynaptically to GABA-B receptors in the brain and spinal cord, thereby decreasing monosynaptic and polysynaptic reflex activity. The half-life is typically 2–6 h, and initial doses generally start at 5 mg BID to TID with slow uptitration as required and tolerated. The maximal daily dose is 80 mg/day; however, higher doses have been effective and well tolerated in certain populations including individuals with spinal cord injury.[25] Common side effects include sedation, ataxia, and muscle weakness. Abrupt withdrawal of this medication should be avoided as this can result in delirium, seizures, and hallucinations. Overdose of baclofen can cause altered mental status, respiratory distress, coma, and death.

Benzodiazepines may also be useful in the management of generalized spasticity and particularly spasticity with painful spasms. The most commonly used benzodiazepine is diazepam. It binds near the GABA-A receptor to assist the binding of GABA to the GABA-A receptor, thereby increasing presynaptic inhibition. Its half-life is 20–80 h. The typical starting doses are 2 mg twice daily or 5 mg if initially dosing at bedtime to assist with management of nocturnal symptoms. Doses can be uptitrated to maximize efficacy, with usual doses between 2 and 10 mg divided three to four times daily, up to a maximum of 30 mg per day. Higher doses may be used in individuals with spasticity due to spinal cord injury.

Common side effects include sedation, impaired cognition, weakness/incoordination, and respiratory depression/coma in overdose. The risk of addiction and dependence must be considered in those receiving high doses over a long period of time. Caution must be exercised when using diazepam in individuals with hepatic dysfunction as it is metabolized by the liver. This medication cannot be discontinued abruptly due to risk of withdrawal, which presents with symptoms such as anxiety, agitation, nausea, seizures, and death.[26] Other benzodiazepines such as clonazepam and ketazolam may be effective in certain populations.

Alpha blocking agents such as tizanidine and clonidine may also be effective in managing generalized spasticity. Tizanidine is a central alpha-2 receptor agonist which binds to alpha-2 receptors and prevents the presynaptic release of excitatory neurotransmitters; it may also enhance the release of inhibitory neurotransmitters. The half-life of tizanidine is 2–4 h, and starting doses are 2–4 mg doses initially administered at bedtime with gradual uptitration to twice or thrice daily dosing. Maximal daily dose is 36 mg/day. Common side effects include sedation, dizziness, hypotension, and dry mouth. It is important to note that tizanidine is available in capsule and/or tablet forms which are both equally absorbed on an empty stomach. However, when taken after a meal, the tablet is absorbed much faster, which may increase side effects or cause them to manifest quickly. Clonidine is another alpha-2 agonist that may be used to treat spasticity; however, it has a much greater effect on blood pressure and may result in more significant hypotension.

Dantrolene sodium is the only agent that acts peripherally at the level of the muscle to decrease spasticity. It blocks the release of calcium from the sarcoplasmic reticulum within the muscle, thereby decreasing the force of muscular contraction. The half-life is 15 h, and doses typically are started at 25–50 mg daily with gradual uptitration as needed to a maximal daily dose of 400 mg/day divided TID to QID. Common side effects include nausea, diarrhea, and weakness. Although less of an issue compared with the centrally acting spasticity agents, dantrolene can also cause cognitive side effects. Dantrolene may be hepatotoxic, particularly at high doses; therefore, liver function tests (LFTs) must be monitored.

Other options are also being investigated for the management of spasticity. Cannabis has gained popularity in recent years for the management of multiple medical issues including spasticity. D9-tetrahydrocannbinol (THC) and cannabidiol (CBD) are the active ingredients in marijuana. THC is a partial agonist to the CB1 and CB2 receptors in the central nervous system (CNS) and periphery which can provide analgesia, nausea, and muscle

Table 1: Oral antispasticity drugs

Mode of action	Dosing	Side effects
Baclofen		
Baclofen is a GABA analog that binds to presynaptic GABA-B receptors in the brain and spinal cord to decreased monosynaptic and polysnaptic reflexes Binding causes an influx of calcium into presynaptic terminals which decreases the release of excitatory neurotransmitters leading to decreased reflex activity Binding of baclofen to GABA-B receptors may also decrease gamma motor neuron activity, thereby decreasing muscle spindle activity	Half-life is 2-6 h Starting dose 5 mg BID to TID increase dose slowly with dose titration Package insert states maximal daily dose 80 mg/day, but higher doses are used in other neurological disorders (SCI)	Sedation, ataxia, altered mental status, hypotonia, constipation and muscle weakness are common side effects Abrupt cessation can cause withdrawal reactions resulting in seizures, hallucinations and potentially death
Benzodiazepines		
Diazepam (the most commonly used benzodiazepine) binds near the GABA-A receptor to potentiate GABA binding to the receptor, increasing presynaptic inhibition Other long-acting benzodiazepines such as clonazepam and ketazolam have also been used in treatment of spasticity	Diazepam: Half-life 20-80 h Starting dose 2 mg to 5 mg if given at bedtime, 2 mg if given during daytime to limit sedation Dose can be gradually titrated upward to a maximum dose of 40-60 mg/day	Sedation, impaired memory and attention, impaired motor coordination Overdose may cause respiratory depression
Tizanidine		
Tizanidine is a central alpha-2 receptor agonist Binding to alpha-2 receptors prevents the presynaptic release of the excitatory neurotransmitters glutamate and aspartate It may also enhance the release of the inhibitory neurotransmitter glycine	Half-life is 2-4 h Starting dose is 2-4 mg given initially daily at bedtime (QHS), with gradual increase by 2-4 mg every 2-4 days Maximal daily dose 36 mg/day	Sedation, dizziness, hypotension, dry mouth May cause elevated liver function tests. Patients should be monitored at baseline and 1, 3, 6 months Tizanidine is available in capsule or tablet, with equal absorption on empty stomach; however, when taken after a meal, the tablet is absorbed much faster which may increase side effect profile
Dantrolene		
Dantrolene is the only antispasticity agent that acts peripherally at the muscle to decrease spasticity by inhibiting ryanodine receptors It decreases the release of calcium from the sarcoplasmic reticulum within the muscle which decreases muscle contraction force	Half-life is 15 h Starting dose 25 mg per day with gradual upward titration every 5-q7 days to maximal dosage of 100 mg QID	Nausea, vomiting, diarrhea, dizziness, weakness. Fewer cognitive side effects than centrally acting spasticity medications May cause hepatotoxicity, particularly in high doses. Monitor liver function at baseline and intermittently
Less commonly used agent for non-CVA spasticity		
Clonidine		
Clonidine is an alpha-2 agonist	Dose: 0.05-0.2 mg BID orally, or 0.1-0.3 mg transdermally	Orthostasis, bradycardia, constipation, edema, drowsiness Clonidine has a more significant effect on blood pressure than tizanidine
Cyproheptadine		
Cyproheptadine is a histamine and serotonin antagonist Its antispasticity effects are thought to be due to neutralization of serotonergic excitatory input at spinal/supraspinal levels	Starting dose 4 mg QHS with dose increases of 4 mg every 3-4 days. Most common effective doses 16-24 mg/day	Sedation, dry mouth. May also stimulate appetite and cause weight gain
4-Aminopyridine		
4-Aminopyridine is a potassium channel blocker which restores conduction along focally damage axons by prolonging the duration of action potential along demyelinated axons	Half-life 3.5 h Maximal dose 10 mg BID	Dizziness, headaches, paresthesias, insomnia, nausea
Cannabinoids		
D9-THC and CBD are active ingredients in marijuana THC is partial agonist to the CB1 and CB2 receptors in CNS and periphery They provide analgesia, muscle relaxation, decrease nausea and stimulate appetite They have been shown to improve spasticity in MS models Synthetic formulations include pharmaceutically derived cannabinoids (nabilone and nabiximols)	Clinical use limited by availability, physician comfort with prescribing, and limited evidence for use in stroke population Potential concern that use of cannabis may increase risk for stroke[23]	Adverse psychological effects including anxiety, psychosis and panic attacks. Also noted to impair motor coordination and executive function, with long-lasting cognitive effects in chronic users[24]

Contd...

Table 1: Contd...

Mode of action	Dosing	Side effects
Canadian clinical practice guidelines recommend use of nabilone or nabiximols in individuals with spasticity due to MS or SCI that is refractory to standard treatments[22]		

THC: Tetrahydrocannabinol, CBD: Cannabidiol, GABA: Gamma-aminobutyric acid, CNS: Central nervous system, SCI: Spinal cord injury, QHS: Bedtime, QID: Four times a day, CVA: Cardiovascular accident, MS: Multiple sclerosis, BID: twice a day

relaxation and may improve spasticity in some individuals such as those with multiple sclerosis. The exact mechanism of action is not well understood; however, it is thought that binding of the cannabinoids to the CB-1 receptors may inhibit release of excitatory neurotransmitters such as glutamate and enhance the effects of the inhibitory neurotransmitter, GABA. In terms of dosing and administration, no specific recommended dosing regimen in the USA is available currently. In Europe, THC/CBD is available in an oromucosal spray Sativex® (approved and marketed in Germany, Italy, Spain, Belgium, Luxembourg, Norway, Denmark, Sweden, Iceland, Portugal, Poland, Austria, and Switzerland. Not yet available in France, Republic of Ireland, Finland, Czech Republic, Slovakia, and The Netherlands. For further information see: Our products gwpharm.co.uk). The recommendation is to identify responders with an initial 4-week trial with a subsequent 14-day self-titration phase to optimize dosage.[27] Adverse effects of cannabinoid use include anxiety, psychosis, and pain attacks. It may also impair motor function/coordination and have a negative impact on cognitive function.[24]

Less commonly used agents include cyproheptadine (histamine and serotonin antagonist); phenytoin, oxcarbazepine, levetiracetam, and lamotrigine (sodium channel blockers); gabapentin and pregabalin (calcium channel blockers); tolperisone and eperisone (combined sodium and calcium channel blockers); and 4-aminopyridine (potassium channel blocker). Further discussion of these agents is beyond the scope of this curriculum; however, it is important to recognize that these agents may be used for spasticity management in some situations.

Competency Assessment 1

The answers to the competency assessments can be found at the end of the module before the references.

1. What is an important role of physiotherapy in spasticity management?
   a. Immobilization to protect spastic muscles
   b. Teaching energy conservation techniques
   c. Strengthening distal muscles to improve core (spinal) stability
   d. Early intervention to maintain muscle length.
2. A common side effect of diazepam and other benzodiazepines is:
   a. Tachycardia
   b. Insomnia
   c. Cognitive dysfunction
   d. Urinary retention.
3. To minimize the risk of sedation and impaired cognition in a person with poststroke spasticity, what oral spasmolytic agent will be the best choice?
   a. Diazepam
   b. Dantrolene
   c. Baclofen
   d. Tizanidine.
4. Regarding the use of serial casting for spasticity, what is the indication to discontinue?
   a. The cast has been in place for 3 days
   b. Additional 10° from the neutral position of a joint was reached
   c. Severe and persistent pain in the casted limb
   d. Failure to gain additional 5° range of motion after maintaining the cast for 7 days on two consecutive applications.
5. The likely mechanism of action of cannabinoids in decreasing spasticity is:
   a. Inhibit release of GABA
   b. Inhibit release of glutamate
   c. Promote release of glutamate
   d. Promote release of serotonin.

Mechanism of action, indications, benefits, and potential adverse effects of botulinum toxins

BoNT blocks acetylcholine release at the motor endplate level and therefore exerts a paralyzing effect on muscles, so it will affect velocity-dependent increase in muscle tone, spasticity, clonus, spastic dystonia, and associated reactions and weakens residual voluntary muscle contraction (spastic paresis). Different subtypes of BoNT may vary in their exact mechanism of action. BoNT-A – the most commonly used in spasticity– once taken up into the presynaptic neuromuscular junction cleaves synaptosome-associated protein 25 required for fusion of neurotransmitter vesicles and thus transmitter release. BoNT-B cleaves a vesicle-associated membrane protein. (Since BoNT-B is not utilized as commonly as the other BoNT-A, subsequent discussion will focus on the latter.)

BoNT-A injections into the shorter of the co-contracting muscles will augment stretching activities and allow antagonistic coordination to be trained by repetitive training activities in the therapeutic window of BoNT-A action.

BoNTs are the treatment of choice for focal and multifocal symptoms of spastic movement disorder (positive symptoms of the upper motor neuron syndrome [UMNS]) as part of a multimodal approach to management. BoNT significantly decreases muscle tone, spastic dystonia, clonus, and spasms

from UMNS and improves passive functions such as reducing spasticity-associated pain, improves hygiene and passive motility of involved limbs, and reduces disfigurement and associated reactions. A single spastic muscle is rarely treated in isolation, and it is important that the individual spastic pattern of muscle under- and over-activity, at rest and while moving, is correctly understood by the evaluating physician and therapist so that all relevant muscles can be treated appropriately by the injector.

BoNT is very much a long-term and individualized treatment. By modifying the target muscles, the BoNT dose (per session, per muscle, and/or per injection site), the interval between treatments, and the number of target sites, focal and segmental BoNT treatment can be tailored to individual patient's symptoms. However, muscle selection and dosing are based on the clinical experience of the treating physician.[28]

Clinically detectable reduction in muscle tone or of voluntary muscle force is evident after 24–72 h, and maximal effect occurs within 10 days to 4 weeks and can last for up to 12–24 weeks and these timelines must be recognized and included in the management plan.

Differences between different botulinum toxin products

The available BoNT-A drugs are different and not interchangeable. The most important difference in BoNT drugs available refers to the serotype used. So far, only BoNT-A and BoNT-B are commercially available, whereas BoNT-C and BoNT-F have been tried in humans in studies in dystonia only.

All BoNT-A products contain the 150-kD neurotoxin with or without nontoxic accessory proteins (NAPs). BoNT-B product contains the toxin (molecular weight not reported) with NAPs. Comparing different toxin formulations is extremely difficult, since a number of variables will affect performance (including serotype, strain of *Clostridium botulinum*, diluent, mouse strain used to standardize the toxin content, protein content, and the ratio of active to inactive toxin).

Differences in potency depend mainly on the amount of active toxin available in each vial (which depends on the manufacturing process). This means that the amount toxin in a vial does not reflect the real potency. Moreover, the potency differences demonstrated in mice may not be directly translated to humans and to clinical practice.

The commonly used formulations of BoNT are onabotulinum toxin A (Botox® Allergan); abobotulinum toxin A (Dysport® Ipsen); incobotulinum toxin A (Xeomin® Merz); and rimabotulinum toxin B (Myobloc® Solstice neurosciences) [Table 2].[29]

In addition, there are other formulations that are licensed but not in use worldwide: neuronox/botulax/regenox (letibotulinum toxin A, Hugel Pharma, South Korea) and BTX-A/prosigne/lantox (Lanxhou Institute of Biological Products, China).

Dose equivalence

Dosages of the BoNT-A drugs that are licensed in European and North American countries for the treatment of spasticity are given in the Summary of Product Characteristics of each drug; however, the doses and muscles licensed for each drug vary between different countries.

Various studies have investigated the dosing equivalence between onabotulinum toxin A and incobotulinum toxin A. Results show a 1:1 equivalence in rodents[30] in healthy volunteers[31] and in blepharospasm.[32-34]

However, the conversion ratio of onabotulinum toxin A and abobotulinum toxin A is far more variable, ranging from 1:3 to 1:11. Most authors consider that 1:3 or lower is an appropriate ratio to use, although some of these studies were in cervical dystonia[35,36] or blepharospasm. The 1:3 ratio has been demonstrated in cervical dystonia[37] and in cerebral palsy.[38]

A randomized controlled trial suggests the dosing equivalence of onabotulinum toxin A and letibotulinum toxin A to be 1:1 in upper limb spasticity.[39]

Due to differences in properties of individual toxins and lack of supporting evidence, a definitive conversion ratio cannot be feasibly recommended.

Differences in diffusions between the products

The diffusion potential of BoNT is complex and not well understood. Generally, intramuscular BoNT has a small diffusion potential in humans; however, this could be a potential source of side effects. *In vitro* studies have shown no differences between onabotulinum toxin A, incobotulinum toxin A, and abobotulinum toxin A.[40] Animal studies have demonstrated some spread in adjacent muscles[41] and spread has also been noted in hemifacial spasm.[42] Rimabotulinum toxin B shows less spread than onabotulinum toxin A.[43]

Side effects: differences between products

All products licensed for spasticity treatment are well tolerated and associated with few adverse events across all regions injected for spasticity treatment. Local adverse effects (AEs) are caused by local diffusion of BoNT-A from the target muscle into adjacent muscles or tissues. Systemic AEs occur in tissues distant from the injection site and based upon BoNT-A transport within the lymphatic or blood circulation. Those symptoms would include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties.

The AEs associated with all BoNT-A preparations occur with a typical latency about 1 week after injection of the toxin. Severity and duration of local and systemic AEs depend on the local or total dose of the different products applied.

Most cases of generalized weakness (botulism-like syndrome) have been reported with abobotulinum toxin A.[44-46] These data have been confirmed by analyzing the FDA Adverse Event System Reporting Database.[47]

High doses

Clinical experience has shown that using higher doses than those recommended in the package insert can be beneficial for some patients.

Table 2: Summary of botulinum toxins formulations

	Botox®	Dysport®	Xeomin®	Botulax®	Myobloc®
Generic name	Onabotulinum toxin A	Abobotulinum toxin A	Incobotulinum toxin A	Leitobotulinum toxin A	Rimabotulinum toxin A
C. botulinum strain	Hall A-hyper	Hall A	Hall A (ATCC 3502)	CBCFC26	Bean
Toxin type	A1	A1	A1	A1	B1
MW (progenitor toxin complexes)	900 kD complex (yes)	MW not reported (yes)	150 kDa None	900 kDa complex (yes)	MW not reported (yes)
Pharmaceutical form	Vacuum-dried powder for reconstitution	Freeze-dried powder for reconstitution	Freeze-dried powder for reconstitution	Freeze-dried powder for reconstitution	Ready-to-use solution
Shelf life	2°C–8°C 36 months	2°C–8°C 24 months	Room temperature 36 months	2°C–8°C 24 months	2°C-8°C 24 months
pH	7.4	7.4	7.4	6.5±0.5	5.6
Excipients	In 100 U vial HAS 500 µg NaCl (09 mg/vial)	In 500 U vial HAS 125 µg Lactose (2.5 mg/vial)	In 100 U vial HAS 1000 µg Sucrose (4.7 mg/vial)	In 100 U vial HAS 500 µg NaCl 0.9 mg	HAS 500 µg Succinate 10 mM NaCl 100 mM
Unit/vial	100 U or 200 U	300 U or 500 U	50 U, 100 U or 200 U	50 U, 100 U or 200 U	2500 U/0.5 mL 5000 U/1 mL 10,000 U/2 mL
Protein load/vial	5 ng/100 U	4.35 ng/500 U	0.44 ng/100 U*	<5 ng/100 U	55 ng/2500 U
Clinical activity compared to Botox®	1	1:2i1:3	1	1	1:40-1:50

*Neurotoxin concentration measured by ELISA. Units are manufacturer specific and not interchangeable. ®Hugel Pharma website. HAS: Human serum albumin, ELISA: Enzyme-linked immunosorbent assay

Reports have considered higher doses using abobotulinum toxin A in 6 patients treated with 2000 IU;[48] using onabotulinum toxin A in 84 patients described in 3 case reports using up to 800 IU[49] and 2 case series using 700 IU and 900 IU; and using incobotulinum toxin A in 284 patients in 6 case series using up to 1200 IU[49] and one prospective trial using 800 IU.[50]

A recent review of high-dose use of BoNT-A[51] has concluded that while evidence is still insufficient to recommend high-dose use in clinic practice, for some patients, the benefits may be clinically acceptable.

Immunogenicity

There may be differences between toxins in the immunogenic potential. Antibodies can be produced that are against the NAPs or against the neurotoxin (mainly against the heavy chain). Antibodies directed against the NAPs do not prevent the neurotoxin's biological activity while antibodies directed against the neurotoxin may or may not prevent biological activity (neutralizing or nonneutralizing antibodies). The incidence of anti-BoNT antibodies is 0%–3% for BoNT-A and 10%–44% for BoNT B.[52-54]

Performing botulinum toxin chemodenervation

It is recommended that injection guidance is used to inject BoNT-A in the target muscles, especially in small and deep-seated muscles. Recommended injection guidance techniques include ultrasound, electrical stimulation, or electromyographic (EMG) guidance methods.

To induce an optimal uptake of the toxin following injection within muscles with diffuse endplate distribution, injected volume per muscle should be distributed in more injection sites and this is particularly important in larger muscles. However, in muscles with discrete endplate bands, the dose of toxin should be divided across this defined endplate region at one or two sites.

To optimize the uptake rate of BoNT-A, the injected muscles should be activated following injection, e.g., by electrical stimulation or by procedures such as stretching of the spastic muscles, to enhance SV2-receptor exposure and therefore the binding and consecutive uptake of the BoNT injected.

With respect to combination of different treatment approaches, BoNT-A could be used to open a so called "window of opportunity" or "therapeutic window" with less spastic muscle tone and less positive signs of the UMNS, allowing a better combination of neurorehabilitative treatment approaches and better re-establishment of antagonistic co-ordination. Reversibility of BoNT-A effects may lead to repeated treatment in postacute and chronic spastic paresis with muscle tone increase, muscle over-activity, spastic dystonia, and disturbed reciprocal inhibition but may perhaps modify the course of muscle over-activity in early poststroke intervention.

Adjunctive therapies when using toxins

Controlled studies in the postacute phase of stroke rehabilitation (less than 3 month following stroke) have shown that BoNT-A injected before spasticity becomes chronic facilitates lower doses; also, improvements in impairment and passive function level tend to be more pronounced and longer lasting.[55]

Three review articles consider the evidence for adjunctive treatments[56-58] and show that adjunctive therapies can be effective, although the evidence is not robust, since there is considerable heterogeneity in study design and low patient numbers.[56-58]

The adjunctive therapies evaluated in the Mills review include electrical stimulation (ES) (n = 8); taping (n = 4); casting (n = 2); stretching (n = 2), ECSWT (n = 1); physiotherapy

($n = 1$); segmental muscle vibration ($n = 1$); dynamic splinting ($n = 1$); modified constraint-induced movement therapy ($n = 1$); and motorized arm ergonometer ($n = 1$). The authors conclude that while there is a high level of evidence to suggest that adjunctive therapies may improve outcome, no results have been confirmed by independent replication and all interventions would benefit from further study.[57]

Comparisons between BoNT-A plus different adjunctive mechanisms[57] show that there is Level 1 evidence for casting being superior to taping and taping being superior to ES and stretching. Extra corporeal shock wave therapy (ESWT) is also superior to ES. Level 2 evidence suggests that immediate ES is superior to delayed ES and low-dose BoNT plus ES is equivalent to high-dose BoNT. Casting was also considered superior to taping by Picelli *et al*., but consensus about their most appropriate timing, duration, target, and material is lacking.[58] There is high-quality evidence that stretching does not have clinically important effects on joint mobility in people (with or without neurological conditions) if performed for less than 7 months.[58]

A study comparing BoNT-A treatment plus serial casting, taping, or stretching[59] in spastic equinus foot has shown that the modified Ashworth scale was improved more with casting than with stretching or taping. Similarly, ankle patient-reported outcome measures (PROM) showed superiority for casting over stretching at all time points and over taping at 90 days. The 6-min walk distance increased for casting and taping but not stretching.

It has been shown that ES increases synaptic activity which leads to increased BoNT uptake and increased mechanical spread of toxin in the short term.[60] Direct effects of ES on spasticity have been observed in both the short- and long-term. ES increases strength in antagonist muscles and BoNT-A decreases the tone in agonist muscles in the long term. However, the best protocol has not been defined.[58]

There is Level 1 evidence that ECSWT is better than ES for some postinjection outcomes including spasticity and pain.[58]

The evidence and a consensus statement for the use of adjunctive treatment are summarized in Table 3.

Case Study Mr. L

- A right-handed 59-year-old artist
- 2010: carotid dissection and subsequent stroke → left-sided hemiplegia
- Left upper > lower limb affected
- Flexor synergy upper limbs
- Extensor synergy lower limbs
- Left flexed elbow
- Left pronated forearm
- Left flexed wrist.

Patient goals and physician goals

1. To help decrease left forearm pronation and reduce left elbow flexion attitude to help his activities of daily living
2. To help with better arm position when walking
3. To help improve his walking speed and overall gait pattern
4. To enhance cosmetic appearance of arm position
5. To prevent contractures.

Case: injection of incobotulinum toxin A

- Incobotulinum A 200 U
  - Ultrasound-guided injection
- 60 units into pronator teres (PT), 40 units into pronator quadratus, 100 units into brachialis
  - Casting 10 days postinjection
  - Home stretching program 5 min per day
  - At 1 month, decrease in pronation spasticity
  - At 1 month, improvement of elbow extension
  - At 1 and 3 months, improvement in functional gait parameters as left arm less flexed at elbow [Figure 2].

Serial cast application

- 10 days postinjection
- Cast stretched to maximum stretch V1 value: 143°
- Arm was supinated in casting process
- Should perceive stretch but no pain
- Bony prominences are padded internally [Figure 3].

Gait videos

Pre- and post-casting videos

Competency Assessment 2

The answers to the competency assessments are given at the end of this module before the references. Each question has only one correct answer.

1. What is the mechanism of BoNT action?
   a. Increases acetylcholine release
   b. Blocks acetylcholine release
   c. Binds GABA-A receptors
   d. Binds α-2 receptors.
2. What are the indications for BoNT administration?
   a. Muscle weakness
   b. Muscle hyperactivity
   c. Muscle contractures
   d. Muscle rigidity.
3. When does the maximal effect of BoNT occur?
   a. After 24–72 h
   b. After 3–7 days
   c. Within 10 days to 4 weeks
   d. Within 2 months.
4. What are the most common side effects?
   a. Muscle weakness
   b. Muscle spasm
   c. Rash
   d. Nausea and vomiting.
5. What is a known beneficial effect of casting/taping/splinting?
   a. Decreases muscle synergy
   b. Increases spasticity
   c. Elongates the muscles
   d. Shortens the muscles.

Table 3: Summary of evidence and consensus statements for adjunctive treatment

Summary of evidence	Consensus statement
Casting/splinting/taping	
Selective groups of stroke survivors have benefited from casting/splinting/taping as an adjunctive therapy post-BoNT-A Current evidence lacks robust controlled research designs, large sample sizes for power calculation and sensitive outcome measures Critical need for high-evidence research on effect of casting/splinting/taping post-BoNT-A and long-term benefits in this population	Consider casting/splinting/taping as adjunctive therapy Main barriers to implementation: Access to casting, funding, experience, clinical time to monitor patient postcasting
ES	
Likely that ES provides some degree of additional effect physiological, and possibly, clinical benefit in conjunction with BoNT-A The ideal ES settings and protocol are also unclear (Hz, best time after injection to initiate stimulation, length and frequency of sessions), distinguish adjunct versus therapeutic The mandate for further research in this area is fairly high given the cost of BoNT-A and the intervention and the potential to augment the effect with an alternative, inexpensive and readily available modality	Consider ES as adjunctive therapy Main barriers to use: Lack of experience, availability of device, time constraints
ECSWT	
There is a need to establish the effects of repeated sessions, the mechanism of action, the muscle changes with ECSWT and the optimal sites and intensity for ECSWT use	Consider ECSWT as an adjunctive therapy to BoNT-A injections but practically difficult to implement Main barriers to implementation are cost, availability of device, lack of experience
Self-rehabilitation	
There is some evidence in the lower limb where repetitive task-oriented exercise focusing on balance control, transfers, gait, strengthening and stretching has been shown to be useful in improving gait in stroke Extrapolation of results from lower limb studies to upper limb may not always be appropriate	Recommend that patients are trained to follow a self-rehabilitation program for spasticity and poststroke recovery to supplement their clinician-administered physiotherapy
CIMT	
There is good evidence for the use of CIMT in poststroke rehabilitation	Good evidence for post stroke rehabilitation with CIMT Use for post stroke rehabilitation but studies lacking regards its use as adjunctive therapy to BoNT-A
Repetitive transcranial magnetic stimulation and transcranial direct current stimulation	
No evidence for BoNT-A + transcranial magnetic and transcranial direct current stimulation	Cannot recommend as adjunctive therapy post BoNT-A in PSS
Robotics	
No evidence for BoNT-A + robotics	Cannot recommend as adjunctive therapy post BoNT-A in PSS

CIMT: Constraint-induced movement therapy, ECSWT: Extracorporeal shock wave treatment, ES: Electrical stimulation, BoNT-A: Botulinum toxin A, PSS: Poststroke spasticity

Nerve blocks/chemoneurolysis

A nerve block is the application of a chemical substance to a nerve that will interfere temporarily or permanently with conduction along the nerve.

The use of nerve blocks for diagnosis and assessment purposes has been covered in Module 1 of this Supplement.

Mechanisms of action, indications, benefits, and potential adverse effects of phenol or alcohol nerve blocks

The therapeutic nerve block (TNB) consists of injection of a neurolytic drug (alcohol or phenol) on a motor nerve innervating a spastic muscle. The technique is the same as for the diagnostic nerve block (see Module 1 in this Supplement).

Phenol, alcohol, and local anesthetics are the most commonly used agents. Nerve blocks are intended to treat spasticity, hypertonicity, and other aspects of the UMN. Alcohol or ethanol at 50%–100% is commonly used for chemical neurolysis as well.

At concentrations of 4%–5%, phenol denatures the proteins in the myelin sheath and nerve axons. This is followed by an inflammatory reaction and Wallerian degeneration, but nerve regeneration can subsequently occur. Higher concentrations (~7%) can cause permanent nerve damage. The literature shows extreme variability in the duration of action of phenol, but this is partially due to the measurement tools used for assessment, the percent and volume of phenol, and the individual injector's technique.[61] However, onset of action is usually always relatively rapid (<1 h).

Although systemic doses of 8.5 g of phenol are lethal (from cardiovascular failure and central nervous system dysfunction

such as seizures), the doses used for neurolysis are way below this level (e.g., 20 mL of a 5% solution contains 1 g of phenol).

There are differing targets for alcohol or phenol nerve blocks. The site of the injection and the agents used can determine whether a nerve block is complete or affects only motor or sensory nerves. A phenol injection for a peripheral nerve block into a mixed nerve causes a total nerve block for 2–12 months (injection of a local anesthetic stops nerve conduction for a few hours). A motor point or end-plate block is injected into the motor branch of the nerve as it penetrates the muscle. The determination of whether to do a peripheral nerve versus motor point blocks is patient specific. If a patient has more global and severe spasticity, there may be need for a more longer lasting total nerve block. To minimize side effects of a total nerve block, such as painful dysesthesia, or when a patient has more functional movement, then a motor point block should be considered.

The injection site is determined by the number of muscles to be treated, the tolerance of the patient for a needle search, and the risk of needle search in different areas and dysesthesia if targeting mixed sensory and motor nerves (0.4%–32%; general consensus 15% for adults and 5% for children).[62,63]

The target of a nerve block injection is determined by the primary posture of the patient. For a patient with their shoulder in internal rotation, the physician would target the medial and lateral pectoral nerves. For a patient with a flexed elbow pattern, the musculocutaneous nerve would be the major target. For a spastic clenched hand, primarily, the median nerve would be targeted, though the ulnar is another consideration depending on the posture. For an adducted hip, the main targets would be the obturator nerve and the sciatic branch to the posterior adductor magnus. When a patient has an equinovarus foot, the tibial nerve would be the major target. Of the nerves listed above, there should be caution with the median and tibial nerves, as there is higher risk for dysesthesia in these sensory nerves.

The main clinical indications and target can be summarized as follows:

- Shoulder internal rotation — Pectoral major nerve
- Flexed elbow — Musculocutaneous nerve
- Spastic hand — Median and ulnar nerve (sensory risk +++)
- Adducted hip — Obturator nerve
- Equinovarus foot — Tibial nerve (sensory risk +++)

Some major comparisons between phenol nerve blocks and BoNT are shown in Table 4. Phenol is injected perineurally or intramuscularly at the motor points, while BoNT is injected intramuscularly. The maximal dosage of each substance is dependent on the clinical scenario. Maximal dosages of phenol would be less than 2 g (20 mL of 5%) and of BoNT would be 400 units within 3 months.

The main risks of phenol are pain of injection, chronic dysesthesia, and, in rare cases, permanent nerve palsy. Possible problems encountered with both phenol and alcohol injections can be bleeding, infection, and compartment syndrome due to the injection. (compartment syndrome occurs where the injection causes increased pressure in a compartment of the arm or leg due to the resistance of the surrounding fascia. This can damage muscle blood vessels or nerves or compromise the blood flow, leading to ischemia or necrosis).

Phenol or alcohol nerve blocks are often used in combination with BoNT-A. The indication for using phenol would be in larger or proximal muscle groups, especially when limited by the amount of BoNT-A in a patient with multiple muscle groups affected by spasticity. An example of this would be obturator nerve blocks to aid with hygiene of a patient who may have adductor tone and need to have diaper changers and fit comfortably in a wheelchair. Furthermore, blocks can be used when you do not have to be concerned with sensory integrity (i.e., complete spinal cord patients). BoNT-A can be injected in affected muscles that are accessible with intramuscular injections. It is also more often used to help with active function. Techniques for injection differ including stimulation of motor points for phenol or alcohol nerve blocks. The cost of the two is very different, with phenol or alcohol being low and BoNT-A being higher.

Nerve blocks can cause over-correction of the spasticity, strains or sprains, tissue atrophy, or temporary loss of useful motor function. Phenol injections can cause pain, temporary sensory loss, dysesthesias, painful nodules, swelling and inflammation, and hypotension.[61,64,65]

Performing alcohol or nerve blocks

A study has shown that obturator neurolysis with 5% aqueous phenol as guided by both ultrasound and electrical stimulation reduced hip adductor spasticity and improved hygiene scores and patient-centered outcomes measured by the GAS.[66] It was a double-blind placebo-controlled trial with a 9-month follow-up period (n = 26). Patients were randomized to two groups that received ultrasound and electrical stimulator-guided obturator nerve block using either 5% phenol in aqueous solution or saline.

In summary, chemodenervation with alcohol or phenol may be regarded as an old technique that provides transient treatment for focal spasticity. Nerve injection is preferred for a better effect, but sensory nerves should be avoided to reduce the risk of neuropathic pain. Chemodenervation can be combined with BoNT-A, especially when the maximal dose of BoNT-A is to be injected. Where a patient is likely to undergo subsequent nerve surgery, then treatment should be restricted to a single injection of alcohol or phenol since fibrosis could interfere with the surgical procedure.

Competency Assessment 3

The answers to these questions can be found at the end of this module before the references. There is only one correct answer for each question.

1. A common side effect of therapeutic nerve block using alcohol or phenol is:

Table 4: Comparison of phenol and botulinum toxin A

	Phenol 5%	BoNT-A
Mechanism	Tissue destruction	Presynaptic block of ACh
	Circulatory damage	
Site of injection	Perineural or intramuscular damage	Intramuscular
Structure blocked	Sensory and motor nerve	NMJ
	MNJ	
Onset	<1 h	Days
Duration	Up to 36 months	3-6 months
Max dose/concentration	<1 g (10 mL of 5%)	400 IU within 3 months
Main risks	Pain of injection dysesthesia	No major risks but distal spread
	Permanent nerve palsy	
Indications	Proximal/large muscles	Muscles accessible with IM injection
	Sensory integrity not a concern	Sensory integrity indispensable
	Combination with BoNT	Active function
	Hygiene and comfort	
Techniques	Stimulation	Stimulation
	Motor point	End plate targeting
Cost	Low	High

BoNT: Botulinum toxins A, IM: Intramuscular, MNJ: Motor nerve junction, NMJ: neuromuscular junction

a. Sedation
b. Drowsiness
c. Dysesthesia
d. Diarrhea.

2. What is a typical concentration of phenol for spasmolysis?
   a. 1%
   b. 3%
   c. 5%
   d. 7%.

Injection guidance

The role of guidance in identifying muscles and nerves for chemodenervation or neurolysis

BoNT-A injections may be localized using a number of techniques: anatomical localization, EMG guidance, electrical stimulation, or ultrasound. The use of all of these techniques concomitantly with anatomic localization can improve accuracy of muscle localization and may improve clinical outcomes.

Electromyography for injection guidance

An EMG detects the electrical nerve signals (potentials) generated by muscle cells when these cells are electrically or neurologically activated. EMG equipment consists of recording electrodes, preamplifiers (which are normally placed very close to the patient to avoid pick-up of electrical interference), amplifiers to provide the correct gain, calibration, and frequency characteristics, a display system (usually a cathode ray tube), a range of integrators and averagers partly to achieve some data compression (chart records may be very long and difficult to read), and a recording medium, which is often a photographic (fiber-optic) system.

EMG guidance is performed using an EMG machine, a hollow insulated monopolar needle electrode, and ground electrodes. The electrical activity detected by this electrode is displayed on the monitor (and may also be heard audibly through a speaker).

Using bony landmarks and palpation, the location of the target muscles should be established. The area near the motor endplate is targeted using electrode insertion sites as described in standard EMG texts.

Before the injection, the injector should palpate the target muscle and perform passive movement at the appropriate joint to initiate stretch on the target muscle which results in movement of the target muscle. Once the needle is inserted into the target muscle, the passive movement may be repeated, and the physician may observe movement of the needle or feel a tug on the needle.

Anatomical guidance

The accuracy of muscle localization with anatomical guidance was investigated in a cadaver study.[67] The accuracy of 121 physicians' performance in needle insertion into medial or lateral gastrocnemius of 30 cadaver limbs was evaluated. Once the needle was inserted, ink was injected into the target muscle. The limb was subsequently dissected by an orthopedic surgeon and an anatomist. Results showed that 43% of injections were placed appropriately; however, 37% were too deep and nearly 20% were too superficial. No difference in success rates were noted in physicians with >5 years injection experienced compared to novice injectors.

The accuracy of anatomical guidance has also been investigated in comparison with EMG and ES guidance. Molloy *et al*.[68] investigated needle placement with anatomic guidance verified with EMG. Only 37% of needle placement attempts were accurate using solely anatomical guidance.

Picelli *et al*.[69] investigated needle placement with anatomic guidance versus ES guidance verified with US in the medial and lateral gastrocnemius. ES guidance was noted to be superior in lateral gastrocnemius, but no difference was noted between groups for medial gastrocnemius.

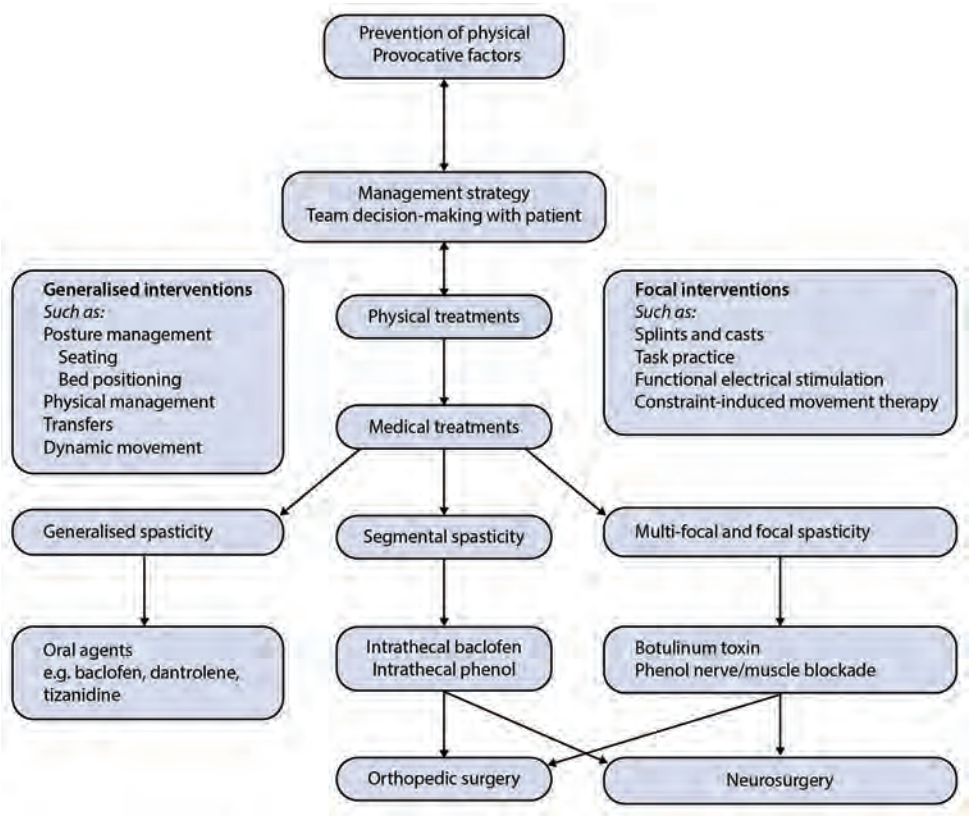

Figure 1: Spasticity treatment options[1]

Clinical outcomes using electromyography and electrical stimulation guidance

Mayer *et al*.[70] evaluated the efficacy of BoNT injections into spastic elbow flexors employing EMG or ES guidance. No significant differences were noted in the Ashworth scale, Tardieu spasticity angle, and surface EMG between groups.

Another study[71] compared the efficacy of BoNT injections in stroke patients with clenched fist or flexed wrist patterns of spasticity using anatomic, ES, or ultrasound (US) guidance. Both the ES and US guidance groups demonstrated improved MAS scores, Tardieu angle, and PROM postinjection compared to anatomic guidance; no significant difference was noted between ES and US guidance groups.

Ultrasonography for injection guidance

Anatomical guidance may be enhanced by the use of US to verify the needle placement before injections are performed.[72] In 41 adult patients with chronic CVA resulting in spastic flexed wrist and clenched fist, injections of BoNT-A were performed into the flexor carpi radialis (FCR), flexor carpi ulnaris, flexor digitorum superficialis (FDS), and flexor digitorum profundus. Once the needle was placed into target muscles, the location accuracy was confirmed with US before the toxin injection. If the needle was not placed into the targeted muscle, it was correctly repositioned under ultrasonographic guidance before injecting BoNT-A.

The overall accuracy of manual needle placement evaluated using ultrasonography was 51.2%. Accuracy was significantly higher for the finger flexors than for the wrist flexors (63.4% vs. 39.0%). The finger flexors were significantly thicker than the wrist flexors (mean 1.58 vs. 0.49 cm).

A similar study used US to evaluate accuracy of anatomical guidance in 18 adult patients with upper limb spasticity from brain injury or cardiovascular accident.[73] Accuracy of anatomic localization of flexor pollicis longus (FPL), FCR, PT, FDS evaluated using US. FDS injections were performed using surface landmark technique described by Bickerton *et al*.;[74] all other muscles used method described by Delagi and Perotto.[75]

The proposed injection site was marked on skin based upon anatomic localization. The optimal target sites then determined using US guidance. Optimal injections sites were found to be significantly different from proposed injections sites for FPL, PT, and FDS to digit 2.

In summary, both EMG and ES guidance are localization techniques that can be easily utilized to improve the accuracy of muscle localization and clinical outcomes of BoNT injections compared to anatomic guidance alone. The equipment was relatively inexpensive and easy to obtain, and EMG/ES guidance both have Current Procedural Terminology (CPT) codes covered by many insurance companies. Inexperienced injectors can often participate in preceptorship programs sponsored by BoNT pharmaceutical companies to gain experience in these techniques

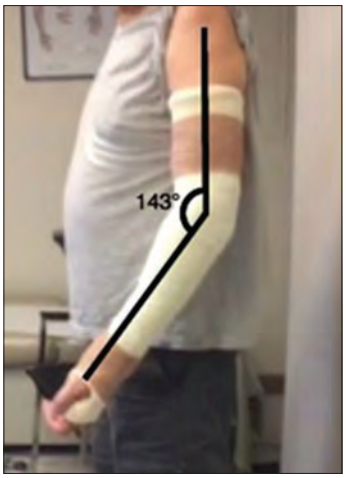

Figure 2: Patient image of serial cast application for Case Study Mr. L

Figure 3: Patient images of preinjection and postserial casting elbow angle for Case Study Mr. L

Competency Assessment 4

The answers to these questions can be found at the end of this module before the references.

1. In a study comparing ES with anatomic localization, in which muscle was ES found to be superior in correct needle placement?
   a. Gastrocnemius, medial head
   b. Gastrocnemius, lateral head
   c. Soleus
   d. Flexor digitorum longus.

Competency Assessment Answers

Competency Assessment 1

1. What is an important role of physiotherapy in spasticity management?
   a. Immobilization to protect spastic muscles
   b. Teaching energy conservation techniques
   c. Strengthening distal muscles to improve core (spinal) stability
   d. Early intervention to maintain muscle length.

The role of physiotherapy includes early intervention to maintain muscle length, maintenance of joint alignment, prevention of secondary complications, strengthening of antagonist muscles, strengthening of proximal muscles to improve central stability, task-specific training.

2. A common side effect of diazepam and other benzodiazepines is:
   a. Tachycardia
   b. Insomnia
   c. Cognitive dysfunction
   d. Urinary retention.

Common side effects of diazepam include sedation, impaired cognition, weakness/incoordination, and respiratory depression/coma in overdose.

3. To minimize the risk of sedation and impaired cognition in a person with post-stroke spasticity, what oral spasmolytic agent will be the best choice:
   a. Diazepam
   b. Dantrolene
   c. Baclofen
   d. Tizanidine.

Dantrolene sodium is the only agent that acts peripherally at the level of the muscle to decrease spasticity. Diazepam, baclofen, and tizanidine are known to cause drowsiness, sedation, and cognitive impairment.

4. Regarding the use of serial casting for spasticity, what is the indication to discontinue?
   a. The cast has been in place for 3 days
   b. Additional 10° from the neutral position of a joint was reached
   c. Severe and persistent pain in the casted limb
   d. Failure to gain additional 5° range of motion after maintaining the cast for 7 days on two consecutive applications.

If the cast causes pain, it should be immediately removed to allow closer inspection of the limb to determine the cause of pain.

5. The likely mechanism of action of cannabinoids in decreasing spasticity is:
   a. Inhibit release of GABA
   b. Inhibit release of glutamate
   c. Promote release of glutamate
   d. Promote release of serotonin.

Although the exact mechanism of action is not well understood; however, it is thought that binding of the cannabinoids to the CB-1 receptors may inhibit release of excitatory neurotransmitters such as glutamate, and enhance the effects of the inhibitory neurotransmitter, GABA. Increasing serotonin levels may increase neuromuscular hyperexcitability.

Competency Assessment 2

1. What is the mechanism of BoNT action?
   a. Increases acetylcholine release
   b. Blocks acetylcholine release
   c. Binds GABA-A receptors

d. Binds α-2 receptors.

2. What are the indications for BoNT administration?
   a. Muscle weakness
   b. Muscle hyperactivity
   c. Muscle contractures
   d. Muscle rigidity.
3. When does the maximal effect of BoNT occur?
   a. After 24–72 h
   b. After 3–7 days
   c. Within 10 days to 4 weeks
   d. Within 2 months.
4. What are the most common side effects?
   a. Muscle weakness
   b. Muscle spasm
   c. Rash
   d. Nausea and vomiting.
5. What is a known beneficial effect of casting/taping/splinting?
   a. Decreases muscle synergy
   b. Increases spasticity
   c. Elongates the muscles
   d. Shortens the muscles.

Competency Assessment 3

1. A common side effect of therapeutic nerve block using alcohol or phenol is:
   a. Sedation
   b. Drowsiness
   c. **Dysesthesia**
   d. Diarrhea
2. What is a typical concentration of phenol for spasmolysis?
   a. 1%
   b. 3%
   c. 5%
   d. 7%

Competency Assessment 4

3. In a study comparing ES with anatomic localization, in which muscle was ES found to be superior in correct needle placement?
   a. Gastrocnemius, medial head
   b. Gastrocnemius, lateral head
   c. Soleus
   d. Flexor digitorum longus

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Module 3: Surgical Management of Spasticity

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Abstract

This module outlines the history of the development of surgical interventions for treating spasticity and discusses when surgical intervention is most appropriate for managing spasticity. A range of surgical techniques are considered; intrathecal baclofen, neurotomy, and muscle or tendon lengthening and transfer procedures. The implications and limitations of the surgical techniques are considered. The need for a multidisciplinary team to deliver optimal surgical treatment is also considered.

Keywords: Spasticity- surgical management - indications - intrathecal treatment -multidisciplinary team

Learning Objectives

On completion of this module, the learner will be able to:

1. Evaluate the need for surgical management options as part of the treatment paradigm for patients with spasticity
2. List the indications for surgical management options including intrathecal baclofen (ITB), neurotomy, and muscle/tendon lengthening and transfer procedures
3. Describe the implications and limitations of the surgical techniques
4. Organize a multidisciplinary team to effectively treat patients who need surgical management for spasticity.

Background and History

Deforming spastic paresis is a condition in which muscle imbalance across joints leads to abnormal positioning and tightness. Muscle over-activity (spasticity, spastic dystonia) and muscle contracture of the agonists coexist with paresis of the antagonists, as the paretic component and the spastic component of the upper motor neuron syndrome are not equally distributed to the muscles (see Module 1 in this Supplement). This drives abnormal postures and deformation of the body segments. Well-known examples of such troublesome situations are the spastic equinus (or equinovarus) foot at the lower limb and the clenched fist at the upper limb. Unlike spasticity, which involves muscles, contractures can involve muscles as well as other soft tissues. The term "contracture" refers to shortening and stiffening of muscles, tendons, and other soft tissues, which lead to joint deformities. In extreme cases, the joint capsule can be involved (arthrogenic contracture). Affected limbs typically demonstrate abnormal posture that affects both passive and active functions.

The initial treatment of spasticity includes conservative management, physical therapy and splinting, oral medications (e.g., baclofen and dantrolene), and injectable neurolytic medications (e.g., botulinum toxin [BoNT] and phenol). These techniques have been discussed in detail in Paper 2 in this Supplement. Patient education and goal setting are covered in Curriculum 1 in this Supplement.

Physicians and other members of teams who care for patients with disabling spasticity are well aware of the fact that medical treatment, either general (using oral medications) or focal (using chemodenervating agents, such as BoNT or phenol), might be insufficient to obtain satisfying results in terms of passive or active function and to prevent muscle contractures and joint deformities. In addition, adverse events of general treatments, gamma aminobutyric acid-ergic (GABAergic) agents and calcium-blocking drugs, and risks associated with repeated injections of BoNT or phenol drive medico-surgical teams to consider treatments that provide a permanent reduction of spasticity. In patients with severe, disabling, spasticity, surgical treatment can be considered.

Surgical procedures for the treatment of spasticity have been developed for almost 150 years. The first-known report was made by Lorenz (1854–1946), an Austrian surgeon who, in 1887, described the section of the obturator nerve to treat spastic hip adduction.[1] In 1912, Stoffel reported on tibial

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DOI: 10.4103/2349-7904.347809

How to cite this article: Gross R, Verduzco-Gutierrez M, Draulans N, Zimerman M, Francisco GE, Deltombe T. Module 3: Surgical management of spasticity. J Int Soc Phys Rehabil Med 2022;5:S38-49.

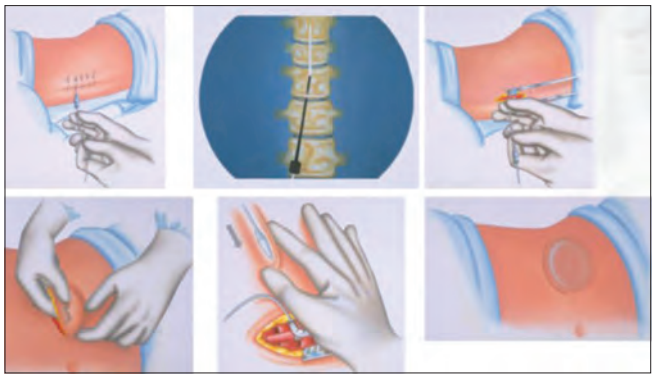

Figure 1: Technique for implantation of the intrathecal catheter and pump. ©Medtronic

nerve neurotomy to treat spastic equinus and median nerve neurotomy for pronation of the forearm and clenched fist.[2] The neurotomy technique spread in Europe and North America, and the first descriptions of surgeries combining neurotomies with muscle lengthening procedures were made shortly after the World War II in the US.[3] Since then, technical improvements were developed by French neurosurgeons such as Gros and Sindou and Mertens to enable selective neurotomies at the nerve fascicle level to be performed. Gros introduced peroperative nerve stimulation to identify the different fascicles among a nerve.[4] Sindou and Mertens used microscopes to perform precise dissections of the nerve fascicles, together with bipolar nerve stimulation.[5] At the same time, in the 1970s/80s, surgical neurotomies in the upper limb were developed, for the treatment of spastic elbow flexion[6] or wrist/finger flexion.[7] There has been a considerable number of descriptions since, about how selective neurotomies can be performed to treat spastic muscle over-activity in muscle groups in the upper and lower limbs, and about their association with orthopedic procedures targeting muscle, tendons, joints, and bones.[8]

Conceptually, selective peripheral neurotomies aim at reducing muscle over-activity of one or several muscles. A first inherent limit is therefore that it does not allow lengthening of a muscle which is already shortened (contracture). Other techniques, aiming at muscle and/or tendon lengthening, have therefore been described. While it is likely that sections of the tendons were already performed in antiquity, the first complete descriptions were made in the early 19th century, in patients with club-foot.[9,10] Many techniques have been described since, to move forward from the simple tendon resection to adjustable tendon lengthening and intramuscular lengthening procedures.[8] The second inherent limit of peripheral neurotomy is its inadequacy when overall spasticity is to be treated, even if several neurotomies can be performed during a single-event surgery. Hence, parallel to peripheral neurotomy, surgical procedures targeting the spinal roots in case of more diffuse spasticity have emerged. Otfrid Foerster, a German neurologist and neurosurgeon, was the first to introduce dorsal root sections (rhizotomy) in human patients, to treat lower limb spasticity. Based on experiments by the famous neurophysiologist Sherrington who, in 1898, showed that muscle over-activity could be reduced by sectioning the dorsal roots of the spinal cord in an animal model of decerebration. Foerster performed in 1908 the first dorsal root resection at the lumbar and sacral levels (from root L1 to root S2) in men.[11] The follow-up of these patients showed that a systematic resection of the dorsal roots L1 to S2 could result in sensory loss as well as functional loss in some patients who were able to walk despite (or thanks to) their spasticity. Foerster also reported that there was variability in the innervation level of the lower limb muscles by the lumbar and sacral roots.[12] This lead followers to improve the selectivity of the resection by performing a mapping of the innervation, using peroperative stimulation of the dorsal roots and observation of the stimulated activation of the muscles.[13] Further developments of the selective dorsal rhizotomy consisted in the application of this technique to the cervical roots to treat the spasticity in the upper limb[14] and in the use of chemical intrathecal radicotomies[15] or percutaneous thermocoagulation of the dorsal roots.[16] In addition, the French team lead by Marc Sindou developed a technique known as DREZotomy, where the spinal afferents from the dorsal root are cut not at the dorsal root level but in the dorsal root entry zone (DREZ) of the spinal cord. The topographical segregation between the reflex and nociceptive fibers (lateral part of the DREZ) and the big sensory fibers that must be spared (medial part) is the anatomic rationale for this surgery, initially developed for chronic refractory pain, and rapidly adapted to focal spasticity of the limbs.

Eventually, the treatment of spasticity by intrathecal infusions of baclofen emerged at the end of the 20th century. Baclofen is known as an agonist of the GABA-B receptors. Its use as an oral drug is hindered by a low risk–benefit ratio, due to cognitive adverse effects, as well as to its low penetration in the cerebrospinal fluid when administered orally. Penn and Kroin were the first to inject baclofen directly in the subarachnoid space by lumbar puncture, to depress spinal reflexes at the lumbar spine (where the density of GABA-B receptors is particularly high).[17] The industrial development of implantable, programmable pumps and catheters allowed ITB therapy to become an adjustable and reversible treatment of spasticity in the 1980–1990s (see specific section below).[18]

Surgical Management

Surgery cannot stand alone in the treatment of spasticity. There needs to be medico-surgical collaborative approach and team of allied specialists. Ideally, rehabilitation physicians will lead the team (including neurosurgeons, orthopedic surgeons, and plastic surgeons, depending on available competencies) and be supported by physiotherapists, occupational therapists, and nursing teams.

The overall principle of surgical treatment is to improve muscle balance by lengthening and/or reducing the activity of muscles that are agonists to the deformity and, if possible, improve the antagonists' mechanical action. This implies the need for surgery for contractures (lengthening procedures) and

for motor over-activity (peripheral neurotomy and selective dorsal rhizotomy being the most common). The release of the short and/or spastic agonists allows potential antagonist muscle activity to be expressed, and specific procedures (tendon transfers) aim at improving the biomechanical action of the antagonists. Joint mobility and stability must be considered and can be affected as side effects of a surgical release. Therefore, stabilization procedures targeting the joints and bones are sometime needed.[8]

Neuro-orthopedic surgery will only be as successful as the preoperative assessment is accurate. The two first key points are that (i) there must be differentiation between deformities that are useful for function and those that are detrimental and that (ii) it is of utmost importance to understand whether muscle hypoextensibility is due to hypertonicity or a fixed contracture. Motor nerve blocks are key to the unraveling of muscle over-activity and contracture in a given muscle or muscle group. Therefore, before surgery, the functional benefit of a spasticity reduction must be assessed by performing a motor nerve block with anesthetics to mimic. This technique has been shown to predict improvement provided by the neurotomy in cases of equinovarus foot.[19]

The third key point in the surgical management of muscle over-activity is the careful attention to the extent of troublesome spasticity in the patient. If it is focal, then localized treatments, such as peripheral neurotomy are indicated. By contrast, diffuse spasticity affecting the entire limb, or even several limbs, requires surgery able to reduce spastic muscle over-activity at multiple levels by one single procedure, such as selective dorsal rhizotomy or ITB therapy through an implantable pump (see below for details about the different techniques).

Mechanisms, Indications, Benefits, and Potential Risks of Intrathecal Baclofen Therapy

Oral baclofen, given for generalized spasticity, has a poor blood–brain barrier penetration. In ITB therapy, baclofen is given directly in the cerebrospinal fluid surrounding the spinal cord, by using an intrathecal catheter and an implantable device consisting of a reservoir and a pump system. Intrathecal administration results in more effect on spasticity with lower serum levels of baclofen and therefore less systemic side effects.

Indication

ITB should be considered in patients with diffuse and significantly refractory spasticity or patients who are experiencing unacceptable side effects or an inadequate response to oral medication or focal treatments. It is appropriate for both adults and children, those with progressive and nonprogressive disease and ambulatory and nonambulatory patients.[20-23] However, ITB therapy must always be undertaken with realistic goals of treatment in mind. Suggested goals for ITB therapy are given in Table 1.[24]

There are no contraindications for patients with ventricular shunts for hydrocephalus, those experiencing seizures, or those on antiplatelet therapy (unless lumbar puncture is required).

Table 1: Goal setting for intrathecal baclofen therapy

Examples of goals potentially achieved with intrathecal baclofen	
Active goals	**Passive goals**
Improved mobility: speed, safety, and quality in the home and community	Improved positioning
	Improved wheelchair tolerance
Increased ability and independence for ADLs: dressing, eating, hygiene	Prevention of complications such has contractures
Decreased time for ADLs	Decreased caregiver burden and time
	Improved quality of sleep
Reduced stretching time during home exercise	Deduced spasticity-related pain
	Discontinuation of oral antispasmodics

Taken from[24] ADLs: Activities of daily living

There is generally no relevant effect of ITB therapy on the unaffected limb in stroke.[25,26] A significant effect of ITB versus conventional medical management (oral medication and physiotherapy) has been demonstrated for both upper and lower limbs in stroke.[22]

Working with ITB requires a dedicated team. Before implantation of the ITB pump and catheter, patients and carers should be well informed about expectations and risks. A trial with bolus or continuous administration of baclofen intrathecally through an external catheter can help in the decision-making process and the realistic goal setting.[27,28] Regular follow-up for titrating the dosage and refill is necessary (usually every 6 months for Synchromed™ pumps and 60 days for Prometa® pumps). If the pump is not refilled, there is a risk of acute withdrawal. Malfunctioning of the baclofen pump and/or incorrect dosing are concerns considered in Curriculum 4 in this Supplement.

Technical procedure

There are basically two types of ITB pumps; those with adjustable flow rate (e.g., Synchromed II™ pump, Medtronic Inc; Prometra II®, Cardiva or Flowonix) and those without adjustable flow rate where changing the concentration in the drug reservoir is necessary to adapt the daily dosage. The technical procedure of implantation is similar. The Prometra® II pump, which can be programmed remotely using a separate hand-held device, was more recently been introduced. Compared to Synchromed II™, Prometra II® has a larger reservoir, more programming options, and longer battery life (>10 years). Unlike the motor-driven Synchromed II™, Prometra II broadly disperses medication into the intrathecal space through its pressure-driven, valve-gated delivery system.

A lumbar incision is used for intrathecal catheter insertion. A pocket is created for the pump using a paraumbilical incision. Subcutaneous tunneling from the pump pocket to the lumbar incision is necessary for connecting the pump with the intrathecal catheter [Figure 1].

In patients with spinal cord injuries, the catheter tip is often positioned at the lesion level. In hemiplegic patients, the tip is often positioned midthoracic.

In ambulatory patients, a trial should be considered. The starting daily dose is usually twice the effective trialing bolus. If no trial was done in nonambulatory patients, starting at 100 mcg/day should be considered.

Adverse effects can include postlumbar puncture headache or meningitis.[27]

Follow-up and maintenance

After pump implantation, patients must be followed up by the multidisciplinary team. It is necessary to evaluate the rehabilitation plan and assess whether any additional therapy is required. Knowledge of different programming modes for programmable pumps is essential, and the team should have experience in troubleshooting. Pumps are fitted with alarm systems in case of malfunction, and it is important that the patient is made aware of the alarms and how to deal with them.

Refills involve emptying the drug reservoir by aspiration and puncturing the membrane of the baclofen reservoir with Port-a-Cath® needle. Consequently, the reservoir is refilled with usually 20cc or 40cc of intrathecal baclofen (e.g., 1000 mcg/mL or 2000 mcg/mL), depending on the capacity of the reservoir.

Treatment can be tailored to the individual's requirement when using programmable pumps. For example, it is possible to give a higher dose at night for comfort or in the morning for ease of care.

Dose-dependent side effects must be a consideration, for example, urinary retention, constipation, drooling, sexual dysfunction, respiratory depression, altered mental status (in overdosing), and loss of trunk balance or ability to walk, if these were due to spastic co-contraction.[22,29]

Every 5–8 years, the pump has to be replaced due to end of life of the battery. If the catheter is still functioning well, it is not replaced.

Costs

ITB therapy is an expensive treatment. However, when the consequent reduction of other spasticity treatments and spasticity-related hospital readmissions, are taken into account it is considered to be cost-effective.[30-33]

Administration of intrathecal phenol by lumbar puncture is a much cheaper way of reducing spasticity, but it also causes problems of incontinence and may provoke major neuropathic pain.

Competency Assessment 1

The answers to these questions can be found at the end of the module before the references.

Are the following statements True or False?

1. Regular refill of the pump reservoir is necessary to avoid potentially dangerous acute withdrawal symptoms that can occur when the drug reservoir is empty
2. ITB therapy cannot be used in hemiplegic patients because it weakens the nonaffected side
3. ITB therapy cannot be combined with BoNT injections because the working mechanism is similar
4. An ITB trial can be useful in helping to identify underlying voluntary strength
5. Sexual dysfunction with disappearance of reflex erection in spinal cord injury patients is a potential side effect of ITB therapy
6. Due to its working mechanism, ITB therapy can resolve fixed contractures in patients with severe spasticity.

Mechanisms, Indications, Benefits, and Potential Risks of Selective Neurotomy

Surgical technique

Selective neurotomy (SN) is a surgical procedure consisting in a partial and selective section of a motor nerve innervating a spastic muscle.[5,34,35] SN is indicated where there is disabling focal spasticity of a muscle innervated by a motor nerve branch that is accessible for surgery and the condition requires permanent treatment.

The SN is ideally performed at the level of a motor nerve branch after it leaves a nerve trunk – for example – soleus, tibialis posterior, and rectus femoris motor nerve branch.

SN can also be performed on a nerve trunk, in which case nerve dissection is necessary to localize and isolate the motor nerve branch – for example – flexor hallucis longus nerve in the tibial nerve and biceps brachialis and brachialis nerves in the musculocutaneous nerve.[36]

The procedure involves general anesthesia without curarization to preserve responses to perioperative nerve stimulation. The motor nerve branches are identified (ideally after nerve trunk dissection under a microscope) with intraoperative electrical stimulation inducing corresponding muscle contraction. The absence of contraction under nerve stimulation identified a sensory nerve branch that must be carefully spared to avoid sensory deficits and/or neuropathic pain. When the motor nerve branches to treat are identified, a partial section over 5–10 mm length is performed under microscope (e.g., the soleus nerve is 2 mm in diameter). The motor nerve branches to treat and the extent of the section (ranging from 50% to 100%) are determined according to the degree of spasticity and the preoperative assessment.

Postoperative care consists of 3 days hospitalization. Casting is not necessary, and the patient should be mobilized (including walking) as soon as possible allowing for scar pain. Rehabilitation should be promoted according to availability and the patient educated to perform a daily stretching program for 2 years. Clinical assessment (including goal attainment) is recommended after 2 months, 1 year, and 2 years. If necessary, SN can be performed in association with tendon surgery (e.g., tibial neurotomy and Achilles tendon lengthening in case of equinovarus foot).

Neurophysiological effects

The mechanism of action underlying neurotomy proposes that sectioning of the Ia, Ib, and II afferent fibers in the nerves, which mediate this myotatic or stretch response, will lead to

a permanent reduction in spasticity and clonus disappearance correlated to the Hmax/Mmax ratio reduction.[37] Such reduction is permanent as Ia fibers sprouting at the level of the muscle spindle are ineffective, explaining the permanent effect on the reflex component of the muscle over-activity, particularly spasticity and clonus. SN also implies a section of the α motor fibers mediating voluntary muscle contraction that leads to a transient muscle weakness. The muscle weakness induced by such α motor fibers explains the reduction of nonreflex muscle over-activity (i.e., dystonia, spastic dystonia, and associated reactions) observed immediately after SN. However, a sprouting process appears, explaining a voluntary muscle strength as well as nonreflex muscle over-activity reappearance after 8–12 months. This suggests that SN is effective on the reflex spastic over-activity (spasticity and spastic component of spastic dystonia) but probably not on the nonreflex over-activity (the dystonic part of the spastic dystonia, associated reactions and dystonia). Indeed, the nonreflex over-activity is immediately reduced after SN in relation to muscle weakness but recurs after 1 year by means of α motor fibers collateral sprouting.[37]

Preoperative assessment

Before considering an SN, making an appropriate determination of the different types of spastic muscle over-activity of the impact of the different muscle's spasticity on the deformity and the presence of a muscle shortening is mandatory. A diagnostic nerve block with anesthetics (see Curriculum 2 in this Supplement) by transiently reducing the spasticity of the muscle(s) innervated by the targeted nerve(s) may address these questions. Interestingly, the diagnostic nerve blocks can predict the decrease in spasticity and the improvement in gait kinematics observed after tibial SN in case of spastic equinovarus foot.[19]

BoNT-A can also be used to predict improvement. It has the advantage of acting for several months, allowing patients time to evaluate the functional benefits in daily living activities, while the diagnostic nerve block only acts for a few hours. Therefore, BoNT-A is frequently performed as an initial treatment after an effective diagnostic nerve block to provide a useful indicator of potential benefits that may be achieved with neurotomy. While BoNT-A is a useful treatment in itself, it is estimated less effective than neurotomy in the case of equinovarus foot).[38-40]

Indications for neurotomy by frequency are given in Table 2.

Therapeutic effects and indications

Studies of the therapeutic effects of selective neurotomy have mainly been conducted in the lower limb. The majority of studies have targeted the tibial nerve in cases of spastic equinovarus foot.[35] In a study compared with BoNT-A, tibial neurotomy induced a higher reduction in ankle stiffness. Both treatments induced a comparable improvement of ankle kinematics during gait, while activity, participation, and quality of life stayed unchanged.[39]

Neurotomy of the rectus femoris in the case of stiff knee gait has been investigated in an observational study in stroke patients, assessed in the short term.[41] Compared with preoperative values, there was a significant increase in maximal walking distance, gait speed, and stride length at 3 months. All kinematic parameters improved, and the average internal early swing phase knee extension moment decreased. The duration of the rectus femoris EMG burst decreased postoperatively.

Small case series on neurotomy of obturator, musculocutaneous, median, and ulnar nerves have been published.[42,43] Recently, tibial cryoneurotomy was described as a novel and safe alternative to open surgery.[44]

Table 2: Indications for selective neurotomy

Condition	Nerve
Equinovarus foot	Tibial nerve and motor branches
Flexed elbow	Musculocutaneous nerve
Adducted hip	Obturator motor branches
Stiff knee gait	Rectus femoris motor branch
Internal shoulder rotation	Pectoralis major motor branch
Wrist–hand	Median–ulnar nerves

Side effects

Reported side effects remained extremely low. Delay in healing due to sweating and maceration, hematoma, and local infections is reported. For lower limb neurotomy, systematic administration of anticoagulant therapy associated with early return to walking and rehabilitation is recommended. The most severe complication is sensory deficit and neuropathic pain when sensory fibers are unexpectedly sectioned.[38] Some sensory fibers are closely related to motor fibers (i.e., tibial nerve: sensory fibers to the sole of the foot and motor nerve branches to the flexor digitorum longus) allowing surgical treatment of such muscle spasticity by means of tendon lengthening instead of SN.

Competency Assessment 2

The answers to these questions can be found at the end of this module before the references.

1. The selective neurotomy surgical procedure requires (1 good answer)
   a. A local anesthesia
   b. Dissection of a nerve trunk in every case
   c. A perioperative electrical stimulation to identify the motor nerve branch.
2. The selective neurotomy induces (1 good answer)
   a. A transient reduction in spasticity
   b. A permanent clonus disappearance correlated to Hmax/Mmax reduction
   c. A permanent reduction in nonreflex muscle over-activity.
3. Neurotomy of the femoral nerve motor branch to the rectus femoris has been found to: (1 good answer)
   a. Decrease gait speed
   b. Increase falls
   c. Increase stride length

Other neurosurgical interventions for spasticity

Selective dorsal rhizotomy

Selective dorsal rhizotomy (SDR) is a well-studied therapy for lower extremity spasticity in children with cerebral palsy (CP) with good selective motor skills, minimal contractures, and good underlying strength.[45-47]

The surgical technique involves single or multilevel laminotomies exposing L2–S2 nerve roots. During SDR, excitatory input from the dorsal roots is attenuated by sectioning (25%–70%) of individual rootlets. Theoretically, this selective sectioning results in improving the balance of the excitatory and inhibitory influences on the alpha motor neurons. EMG-monitoring is used to identify rootlets innervating more clinically abnormal muscle groups.

Some degree of lower limb weakness can be unmasked postoperatively by reducing the spasticity, making intensive physical therapy necessary. Patients must have the cognitive and social capacity for such an invasive intervention and rehabilitation. Long-term complications in children are infrequent and concern sensory dysfunction, bladder and bowel dysfunction, and back pain.[48]

The role of this operation in the treatment of other spasticity causes in adults is less well defined as this procedure has not been systematically studied in contexts outside of CP. Multiple sclerosis and traumatic spinal cord injury are the most commonly reported non-CP diagnoses in patients who have undergone SDR.[49] Although reported results are described satisfactory, no standardized outcome data are available outside of the CP population. Therefore, SDR, as an irreversible neuroablative procedure, should only be performed with great caution and in centers with an experienced multidisciplinary team.

Ventral rhizotomy

Ventral rhizotomies have been performed in individuals with complete spinal cord injury, but the consequent muscle atrophy increases the risk of pressure ulcers.[50]

Microsurgical DREZotomy

Surgery in the DREZ was developed to treat some types of topographically limited pain. Because of its inhibitory side effects on muscular tone, the method is very rarely performed in patients with severe focalized spasticity.[51,52]

Microsurgical DREZotomy (MDT) requires a strong knowledge of spinal cord anatomy. With bipolar coagulation forceps, the small myelinated fibers (considered nociceptive) and the large myelinated myotatic fibers are interrupted, while sparing the large myelinated fibers (considered sensory primary afferents).[51]

MDT can theoretically be considered in hemiplegic patients for the treatment of the paralyzed upper limb when it is affected with severe and sometimes painful hyperspasticity. It could also be considered in severely disabled paraplegic patients, but intrathecal baclofen remains first choice.[51]

Mechanisms and Indications for Tendon Lengthening and Transfer

Shortening of muscles is a frequent occurrence subsequent to neurological damage. Among stroke patients, muscle shortening is often seen accompanied by increased muscle stiffness.[53]

The "deforming spastic paresis" syndrome defines the association between spasticity, weakness, and muscle shortening.[54] Early shortening correlates with poor recovery after stroke[55] and physical therapy or orthosis is only poorly effective at prevention or treatment of this effect.[56] Thus, surgical muscle and/or tendon lengthening may be indicated for restoring joint mobility.[57] The indications for muscle lengthening are summarized in Figure 2.

The indications include muscle shortening that causes active limitation (gait and prehension); passive limitation (comfort, hygiene, dressing, aesthetic considerations, etc.); or pain (excessive foot pressure, claw toes, etc.).

Muscle shortening must be confirmed and differentiated from muscle over-activity by clinical examination and diagnostic nerve block with anesthetics (See Curriculum 1 in this Supplement). It should be resistant to physical therapy and orthoses, and there should be no osteo-articular limitation, for example due to heterotopic ossifications.

Muscle and tendon lengthening/release procedures

The surgical techniques commonly used are:

- Intramuscular lengthening, which allows a maximum of 0–20 mm of lengthening
- Tendon lengthening (section in Z shape + suture), which may be performed to the extent that is required. Postoperative immobilization is necessary
- Tenotomy or tenectomy is a total release of the tendon[58]
- Proximal, gross muscle release (e.g., Page-Scaglietti surgery of the forearm which is a proximal release of the pronator teres and wrist/finger flexors)[59]
- Tendon release procedures, such as described by Braun at the forearm (flexor digitorum superficialis to profundus tendon transfer)[60]
- Whatever the technique, lengthening and release procedures allow for an adjustable gain in passive range of motion, contrary to transverse tenotomy/tenectomy. The actual gain that can be expected depends on the following rule: for each millimeter of lengthening, the joint can be moved 1 more degree. The exact lengthening is often decided during the procedure, depending on the improvement in passive range of motion obtained (see image below).

An alternative to typical surgical procedures described above is the percutaneous tenotomy using a large, sharp needle, through a simple skin puncture, performed under local anesthesia. It is used in case of troublesome deformities of a joint with no

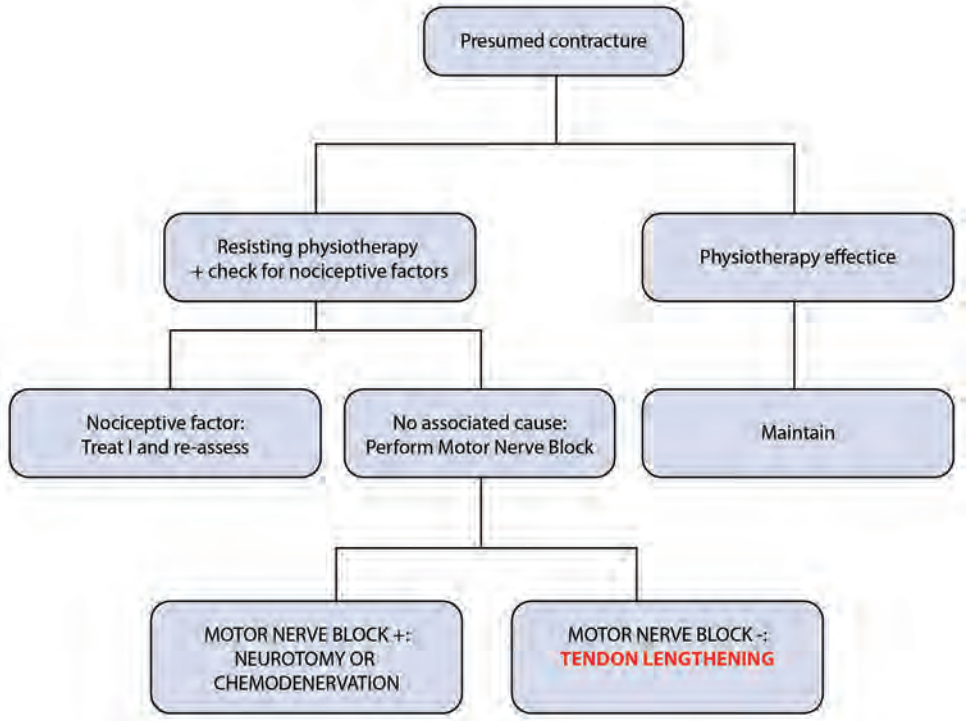

Figure 2: Indications for muscle and tendon lengthening

active function, if general anesthesia is contraindicated.[58,61,62] It does not allow a precise correction but a transverse section of the tendon. It can be performed by nonsurgeons but requires former training on cadavers to allow for a good anatomical targeting.[63]

Tendon transfer procedures

The aim of tendon transfers is to compensate for the paresis of some muscles relative to their over-active antagonists, to rebalance the forces at a joint. There are two main types of transfers: active or passive. In active transfers, the distal part of an active muscle is sectioned and implanted elsewhere so that its action at the joint level is more appropriate. Due to disordered motor control in spastic patients, the strength of the transferred muscle is hardly predictable, as is the integration of the transferred muscle into its new function. In passive transfers (also termed tenodesis), the tendon of a paretic muscle is fixed proximally to a bone or another tendon to increase its tension.

A wide variety of tendon transfers has been described in the literature [Figures 3-7].[8] The most common active transfers, aiming at activating a function in patients with spastic paresis, target the foot and ankle in cases of excessive varus/supination, which is related to imbalance between an overactive tibialis anterior and weak long toe extensors and peronei. The SPLATT (SPLit tibialis Anterior Tendon Transfer) procedure,[64] the tibialis posterior transfer on the dorsal part of the mid-foot or on peroneus brevis,[65] and the tenodesis of the tibialis anterior on the peroneus brevis (Bardot's procedure)[66] are the most well-known techniques.

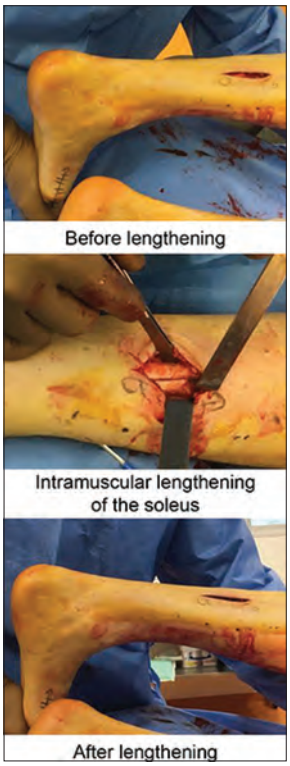

Figure 3: Surgical intramuscular lengthening of the soleus using a Z-lengthening procedure at the emergence of the soleus aponeurosis. This technique allowed a gain of approximately 10° of ankle dorsiflexion in the patient. Courtesy of Dr. G. Gadbled, Nantes University Hospital

Active transfers have also been described at the knee joint, to improve the stiff-knee gait pattern.[67]

Table 3: Surgical techniques in muscle lengthening and transfers

Condition	Involved muscle	Techniques
Equinus	Triceps surae	Intramuscular lengthening of soleus and/or gastrocnemii
		Achilles tendon lengthening
Varus related to muscle shortening	Tibialis posterior	Intramuscular lengthening and/or tenotomy of the tibialis posterior
Varus related to imbalance between tibialis anterior evertors	Tibialis anterior	SPLATT
		Tibialis posterior transfer on peroneus
		Tenodesis of the tibialis anterior on the peroneus brevis
Stiff knee gait	Rectus femoris	Distal release of rectus femoris (tenotomy)
		Distal rectal femoris transfers
Flexed elbow	Brachialis	Tenotomy
	Biceps	Tendon lengthening
	Brachioradialis	Proximal release
Flexed wrist	Wrist flexors	Tenotomy
		Intramuscular lengthening
Pronated forearm	Pronator teres	Intramuscular lengthening
		Proximal release
	Pronator quadratus	Surgical release
Clenched fist	Finger flexors	Tenotomy
		Intramuscular lengthening
	Wrist/finger flexors and pronator teres	Proximal release (Page-Scaglietti procedure)
	Flexor digitorum superficialis	Flexor digitorum superficialis on profundus tendon transfer (Braun's procedure)
	Flexor digitorum profundus	Tenotomy
		Intramuscular lengthening
Thumb-in-palm deformity	Flexor pollicis longus	Intramuscular lengthening of the FPL (flexion of the interphalangeal joint)
		Release of the intrinsic thumb muscles from the metacarpals (adducted thumb)

SPLATT: SPLit tibialis Anterior Tendon Transfer

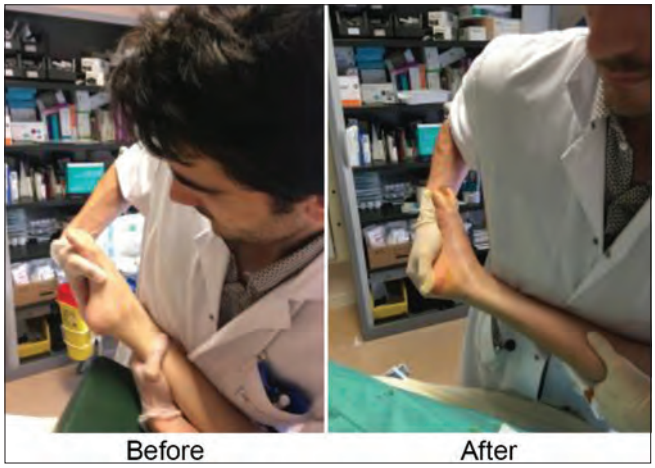

Figure 4: Patient in a minimally responsive state and severe equinus before and after needle tenotomy of the Achilles tendon. Courtesy of Matthieu Gahier, MD and Raphaël Gross, MD, PhD

Active transfers are much less common at the upper limb in adult spastic patients. Tenodesis however can be used to correct a deformity in nonfunctional wrist/hands, such as the shortening tenodesis of the extensor carpi radialis brevis in case of a drop hand.[8]

A summary of the involved muscles and the appropriate surgical techniques is given in Table 3.

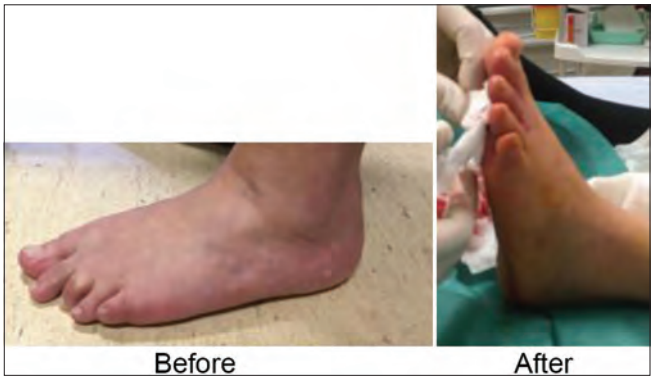

Figure 5: Before/after needle tenotomy of the third long toe flexor in a patient with troublesome claw toe caused by spastic paresis of the lower limb due to a brain tumor. Courtesy of Matthieu Gahier, MD and Raphaël Gross, MD, PhD

Benefits and risks of muscle/tendon lengthening or transfers

Surgical intervention can help overcome the problems of shortened muscles by increasing muscle/tendon length. Consequently, there is decreased resistance to passive motion, making passive movements easier, but decreased voluntary muscle strength (e.g., Achilles tendon lengthening decrease triceps surae muscle strength). Surgery can result in restitution of the physiological range of motion so that it can produce an

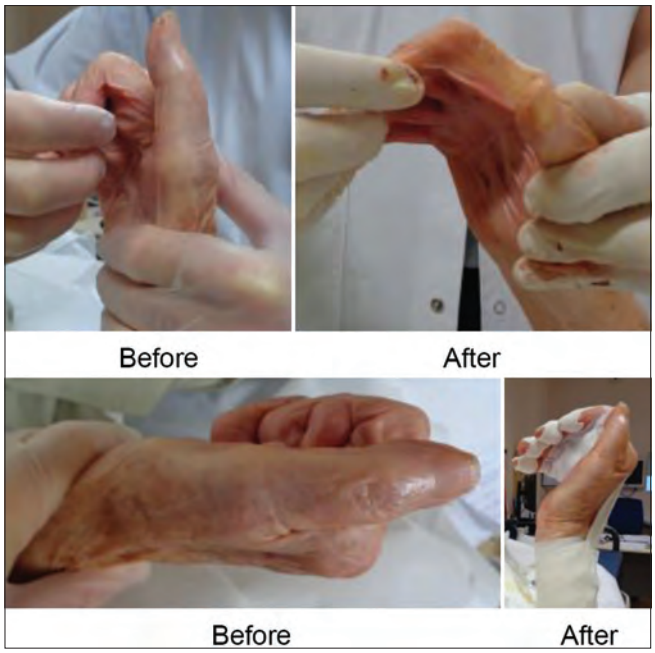

Figure 6: Elderly patient with a clenched fist due to stroke. Pictures before and after tenotomy of the flexor digitorum superficialis and profundis. Courtesy of Matthieu Gahier, MD and Raphaël Gross, MD, PhD

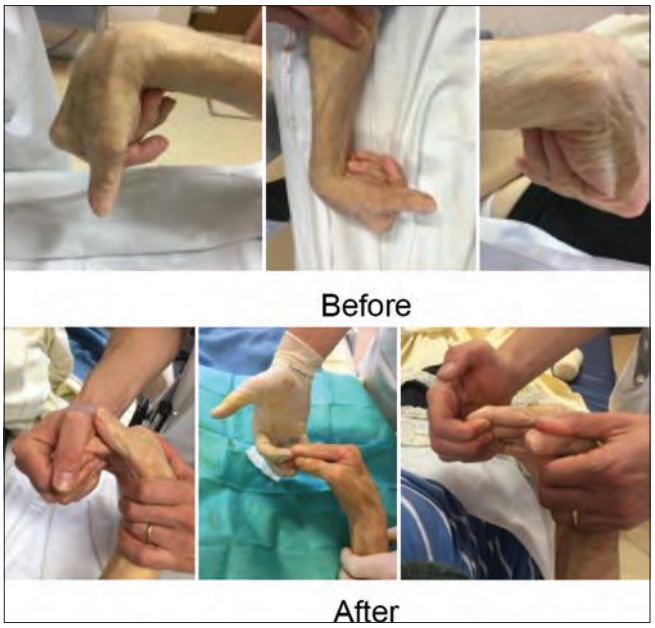

Figure 7: Patient with clenched fist due to shortening of interossei following a stroke. Pictures of before and after needle tenotomy of the intrinsic muscles of the second, third, and fourth intermetacarpal spaces. Courtesy of Matthieu Gahier, MD and Raphaël Gross, MD, PhD

improvement in passive function of the limb and sometimes improvement in active function, for example, as is seen with the Page-Scaglietti intervention. However, the decreased force of the muscle can be either positive or detrimental, and unfortunately, this is not predictable. Unlike for peripheral neurotomy, there is no predictive test for muscle/tendon lengthening procedures. The improvement will depend on the extent of the lengthening and the skill and experience of the surgeon. Besides, most surgical procedures require a period of postoperative immobilization which will impact on the patient's independence. The need for postoperative immobilization and its duration is variable and depends much on the surgeon's habit. In tendon lengthening with sutures, and in large release procedures, immobilization is the rule, lasting from 3 to 8 weeks. In tendon transfers, a firm immobilization is also needed, usually for 6–8 weeks, to protect the tendon suture. On the other hand, intramuscular tendon lengthening without postoperative immobilization is possible.

The risks of surgical intervention include bleeding; nerve injury with sensory loss and neuropathic pain; infection; skin breakdown; tendon rupture; delayed tendon healing; complex regional pain syndrome; overlengthening which can lead to over-correction (for example from pes equinus to pes talus) and a loss of passive or active function; and decompensation of the shortening of the toe flexors when an equinus foot is corrected (giving rise to claw toes to a variable extent).

In conclusion, tendon lengthening or transfer is the most effective way of correcting muscle shortening or imbalance of muscle groups. The problems due to the shortened muscle must be clearly identified and placed within the context of any concomitant issues. Different surgical techniques can produce different ranges of muscle lengthening. A drawback is that there is no predictive tool that will allow assessment of the expected improvement and a variable period of postoperative immobilization is required. Surgical muscle/tendon lengthening may be combined with other interventions, such as BoNT-A or neurotomy, which may improve walking capacities and achieve personal goals over single interventions alone.[68]

Mechanisms, Indications, Benefits, and Potential Risks of Associated Bone Procedures

Associated bone and joint procedures may accompany tendon and muscle procedures. The use of bone procedures has decreased with improvement in early care. Further, soft tissue surgery (involving tendons and muscles, see above) has proved successful in spasticity and contracture treatment, especially when performed early and deformities are mild; it is more easily performed than bone procedures and provides more function and mobility.[69]

Another drawback of bone surgery is that it may also require prolonged immobilization and prevent weightbearing. Patients with vascular disorders such as arteriopathy (e.g., after ischemic stroke) and smokers are at increased risk of bone healing and sepsis.[8] However, bone surgery should not be considered a last resort and should be included in a treatment program where appropriate.

Triple arthrodesis

The most common bony procedure is triple arthrodesis where the talocalcaneonavicular, subtalar, and calcaneocuboid joints are fused. This technique is used to correct severely pronated or supinated feet [Figure 8].

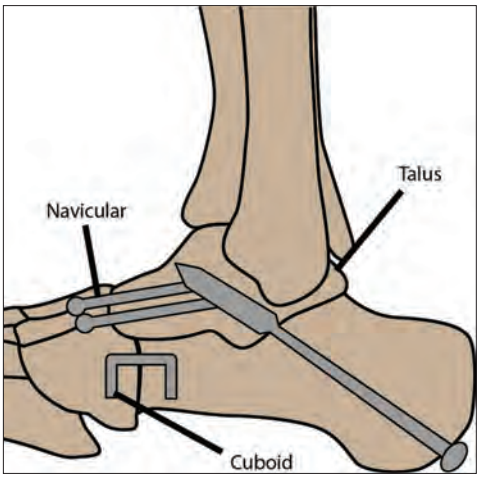

Figure 8: Fusion of the talocalcaneonavicular, subtalar, and calcaneocuboid joints

Long-term walking with an uncorrected triceps surae contracture is a frequent cause of foot pronation, and loss of function in the tibialis posterior can also cause pronation.[8]

Resection of carpal bones and/or arthrodesis of the wrist

Other than heterotropic ossification (HO) resection, bony procedures are less common in the upper limb. However, CP, the most common cause of disability in children, is often accompanied by severe flexion contractures of the wrist and fingers and adduction of the thumb. Hand function is severely affected, maceration may occur in joint creases, and tight finger deformities may occur.[70] When the deformities are not yet fixed, there are a number of treatment options (physiotherapy, BoNT-A, tendon transfers, or soft tissue lengthening); however, when deformities are fixed, resection of the proximal row of the carpal bones and wrist arthrodesis can be a solution.[70] Lengthening of the wrist and extrinsic finger flexors may also be performed. The wrist is immobilized until bony fusion is achieved.[8]

Failures

The success of neuro-orthopedic procedures is very dependent on the preoperative examination. The two main complications are overcorrection, with release of the previously masked dystonia of the antagonist muscle, and the recurrence of the deformity due to transferring a muscle that is too weak or after failure of sutures.[8]

Combined surgery (with botulinum toxin A as complementary treatment)

In most cases of spasticity, it is strongly recommended to begin with preventative techniques. When prevention fails, then the orthopedic options discussed above aid in management of spasticity. BoNT can be used in conjunction with surgical options. Where BoNT aids in reducing spasticity, it cannot change the extracellular matrix, viscosity, or elasticity. BoNT can either be used as a clinical test to differentiate between spasticity and true contracture or to stimulate the effects of reducing muscle activity in a functional muscle.

With surgery, BoNT is best used preoperatively. It can aid in pain management as the surgical procedure can increase spasticity postoperatively. More importantly, preoperative injections can reduce the tension and promote lengthening of a muscle that is being transferred or lengthened.

Competency Assessment 3

The answers to these questions can be found at the end of this module before the references. Each question has one answer.

1. Which technique among the followings is adequate for the treatment of severe foot supination during the swing phase of gait in stroke patients?
   a. Split anterior tendon transfer procedure
   b. Achilles tendon tenotomy
   c. Tibialis anterior tenotomy.
2. What kind of surgical treatment do you suggest for a patient without severe comorbidities who is able to walk and presents a fixed equinus following stroke?
   a. Percutaneous needle tenotomy of the Achilles tendon
   b. BoNT-A injections into the soleus
   c. Intramuscular tendon lengthening of the triceps surae muscles.
3. A known adverse event of neuro-orthopaedic surgery, such as muscle/tendon lengthening, is:
   a. Hypercalcemia
   b. Depressed alkaline phosphatase
   c. Clonus
   d. Overlengthening.

Competency Assessment Answers

Competency Assessment 1

Are the following statements True or False?

1. Regular refill of the pump reservoir is necessary to avoid potentially dangerous acute withdrawal symptoms that can occur when the drug reservoir is empty. (T)
2. ITB therapy cannot be used in hemiplegic patients because it weakens the non-affected side. (F)
3. ITB therapy cannot be combined with BoNT injections because the working mechanism is similar. (F)
4. An ITB trial can be useful in helping to identify underlying voluntary strength. (T)
5. Sexual dysfunction with disappearance of reflex erection in spinal cord injury patients is a potential side effect of ITB therapy. (T)
6. Due to its working mechanism ITB therapy can resolve fixed contractures in patients with severe spasticity. (F)

Competency Assessment 2

1. The selective neurotomy surgical procedure requires (1 good answer)
   a. A local anesthesia
   b. Dissection of a nerve trunk in every case
   c. A perioperative electrical stimulation to identify the motor nerve branch.

2. The selective neurotomy induces (1 good answer)
   a. A transient reduction in spasticity
   b. A permanent clonus disappearance correlated to Hmax/Mmax reduction
   c. A permanent reduction in nonreflex muscle overactivity.
3. Neurotomy of femoral nerve motor branch to the rectus femoris has been found to: (1 good answer)
   a. Decrease gait speed
   b. Increase falls
   c. Increase stride length.

Competency Assessment 3

1. Which technique among the followings is adequate for the treatment of severe foot supination during the swing phase of gait in stroke patients?
   a. Split anterior tendon transfer procedure
   b. Achilles tendon tenotomy
   c. Tibialis anterior tenotomy.
2. What kind of surgical treatment do you suggest for a patient without severe comorbidities who is able to walk and presents a fixed equinus following stroke
   a. Percutaneous needle tenotomy of the Achilles tendon
   b. BoNT-A injections into the soleus
   c. Intramuscular tendon lengthening of the triceps surae muscles.
3. A known adverse event of neuro-orthopaedic surgery, such as muscle/tendon lengthening, is:
   a. Hypercalcemia
   b. Depressed alkaline phosphatase
   c. Clonus
   d. **Overlengthening**

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Module 4: Optimizing Outcomes in Spasticity Treatment

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Abstract

With many recent advancements in spasticity treatment, more patients are surviving critical illness and injury but are left with ongoing disability that needs constant treatment. Such treatment will change as the patient's condition evolves. Constant appraisal of treatment efficacy and patient progress is therefore an important component of spasticity management, and physicians need to be familiar with how to troubleshoot treatment regimens when outcomes of that regimen become suboptimal. This module considers how to optimize the use and outcomes of major treatment modalities and provides drug and device maintenance algorithms to guide the treating team.

Keywords: Troubleshoot- spasticity treatment regimens - suboptimal outcomes - Muscle spasticity - Treatment outcome - Baclofen/adverse effects - Implantable/adverse effects - Botulinum toxins/adverse effects - Muscle relaxants, central/adverse effects

Learning Objectives

Upon completion of this module, the learner will be able to:

1. Identify reasons why botulinum toxin, intrathecal baclofen therapy, oral medications, or phenol/alcohol treatment are producing suboptimal outcomes
2. Discuss the need for constant reappraisal of the patient – goals, progress, and concomitant conditions
3. Enumerate ways to troubleshoot suboptimal outcomes of spasticity treatment.

Addressing Suboptimal Outcomes of Spasticity Interventions

By its very nature, spasticity treatment is not a single, isolated, intervention but continues over months and years. Treatment will also progress over time and different treatment modalities will be employed as the patient's condition changes. It is not unusual for a seemingly effective treatment to start to show decreased efficacy and it is important therefore to be able to troubleshoot why efficacy is waning before making radical alterations to the care plan. Equally, treatments can produce over responses and these must be addressed before plans are changed. Side effects of treatments and other developing neurological conditions can also affect treatment outcomes.

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DOI: 10.4103/2349-7904.347810

Suboptimal outcome following any treatment modality can have multiple etiologies. Concerns that the usual treatment is producing suboptimal outcomes may be raised by the patient, their family and/or carers, or the treating physician.

When a patient is reporting a poorer effect than expected it is important to:

- Listen to their concerns to help identify the problems
- Review previously agreed upon goals
- Ask if they think the treatment did not work at all
- Enquire if the effect wore off too fast
- Establish if the treatment is no longer working after experiencing good effects in previous cycles
- Elicit adverse effects, such as increased weakness
- Consider other side effects related to the treatment, among others.

Listening to patients' concerns expressed in their own terms may provide clues and help point to a real lack of efficacy of the spasticity treatment, or if another problem is impinging on the patient's condition and causing a temporary increase in the spasticity. A good first step is to review the previously agreed upon goals and the treatment objectives should be reviewed and documented. Goals of treatment should be reviewed using the SMARTER goal system (Specific Measurable Achievable Realistic Timely Ethical Recorded) (see Module 1 in this Supplement).

It should be considered whether the goals were appropriate and whether the patient and/or their carer were motivated to achieving these goals. Furthermore, patient expectations may change over time and it is important to assess how the patient views their progress and the future.

How to cite this article: Ketchum N, Carda S, O'Dell MW, Säterö P, Jacinto J, Deltombe T, *et al*. Module 4: Optimizing outcomes in spasticity treatment. J Int Soc Phys Rehabil Med 2022;5:S50-60.

The information previously discussed with the patient about their spasticity and how the treatment acts to address the problem should be re-iterated. It is important to use patient-friendly language and vocabulary; "patient-like wording" instead of medical terminology ensures clearer communication.[1]

It is telling that in a recent international survey of patients living with spasticity, 45% of respondents reported dissatisfaction with the information provided at diagnosis. Of these, 67% wanted more information; 36% felt the clinician used too many technical words or there were problems with communication; and 35% wanted more time with their doctor to better understand their diagnosis and its future consequences. Only 5% were overwhelmed by the information provided.[2]

For treatments that are repeated at regular intervals, such as botulinum toxin injections, it may be an issue of the frequency of treatment schedules. For continuous systems such as baclofen pumps that also rely on properly functioning equipment; there are other considerations.

Treatment Algorithms

Table 1 is a comprehensive listing all the items that need to be considered when assessing under response or over response

Table 1: Items for consideration when troubleshooting spasticity treatment

Item	Considerations
Goals	Unrealistic goals – no spasticity treatment can "undo" what has been done (i.e., neurotoxin cannot reverse the effects a spinal cord injury has on weakness, sensory changes, proprioception changes)
	Misaligned goals – if the treating physician has one set of goals, but the patient/caregiver/family has different goals, even the most successful treatment in the eyes of the physician can appear to be "ineffective"
	Previously met goals – goals can/will change over time. Periodic reassessment of goals is necessary over the course of treatment[3]
Injection technique	Knowledge of anatomy (including muscles, blood vessels, nerves) is key for proper injection technique
	Whenever possible (given local resources), guidance techniques, such as ultrasound, electrical stimulation, and/or electromyography should be used to assist in guidance for injection technique
Muscle selection	Proper knowledge of functional anatomy is essential to properly treat a problematic limb pattern due to spasticity
	For example – for wrist flexion, knowing that the long finger flexors also contribute to wrist flexion in addition to finger flexion is necessary to properly treat some cases of excessive wrist flexion
Not enough muscles	Need to consider all muscles responsible for a particular posture
	For example – when formulating a plan for ankle plantarflexion, you may need to also consider other muscles that cross the ankle and can contribute to plantarflexion such as flexor digitorum longus, flexor hallucis longus[4]
Dosing (per muscle)	Individual muscles may need different doses of toxin in different patients, depending on a number of factors
	Goals – passive functional goals may necessitate greater dose; active functional goals may need smaller doses
	Severity of spasticity
	Muscle size
	Dose ranges are published, but clinical practice falls outside these dosages
	Off-label muscles may not have as many published dose ranges
Disease progression	Majority of spasticity encountered is due to nonprogressive etiology (i.e., stroke, spinal cord injury, acquired brain injury, cerebral palsy), and is static in nature (although things like noxious stimulus can temporarily increase spasticity)
	Upper motor neuron syndromes due to multiple sclerosis or other potentially progressive conditions will lead to spasticity that can change over time due to the progression of the condition itself
Concomitant medical conditions	In most conditions resulting in spasticity, the underlying condition is nonprogressive, thus spasticity should not progress over time (after reorganization)
	Underlying medical conditions may increase spasticity due to the condition acting as a noxious stimulus to the central nervous system (constipation, urinary tract infection, ingrown toenail)
	Underlying medical conditions may increase spasticity such that the apparent effect of the injections is lesser than would be if the underlying condition was treated/not present
	Caution must be taken to account for the presence/absence of concomitant conditions when selecting dosages
Correct handling of the drug	Most neurotoxins require refrigeration
	Improper transportation/handling/storage could potentially lead to decreased effectiveness of the neurotoxin
	Improper reconstitution could lead to incomplete extraction of toxin from vial
Use of adjunctive treatments	Botulinum toxin injections alone may decrease spasticity but may not improve other factors, such as range of motion, goal attainment
	Optimal outcomes are typically seen when botulinum toxin injections are combined with therapy, bracing, ES, etc.
Correct timing for re-evaluation after injection	Evaluating response to botulinum toxin injections is best performed at peak effect of the botulinum toxin response – generally 4-6 weeks
	Doing evaluation prior to this time may be too early to see the magnitude of effect
	Doing evaluation at 12 weeks and beyond will be after effect has waned
	Opportunity for virtual assessment

Contd...

Table 1: Contd...

Item	Considerations
Unmasking weakness	Treating muscles that have spasticity will reduce the excessive activation of muscles
	These muscles frequently are weak in addition to hypertonic
	Some patients utilize the spasticity to substitute for underlying weakness
	This reduction of "useful spasticity" can result in an unmasking of excessive weakness, leading to decreased function
Local side effects	Physical effects
	Hematoma
	Infection
	Nerve injury
	Local effects of medication
	Muscle weakness
Systemic side effects	Neurotoxin side effects
	Distant spread of effect
	Flu-like syndrome
	Oral medication side effects
	Baclofen – sedation, constipation, caution in renal impairment
	Tizanidine – sedation, dizziness, hepatic dysfunction
	Dantrolene – nausea and vomiting, diarrhea, hepatic dysfunction
	Benzodiazepines – sedation, impaired memory and attention, impaired motor coordination
	Gabapentin – sedation, headache, nausea, and vomiting
	Cannabinoids – anxiety, psychosis, panic attacks
	Withdrawal syndromes from oral medications
Dilution	The literature is inconsistent, however, there is some evidence that increased volume can lead to increased diffusion (advantageous) but also increased spread (undesirable)[5–8]
	Can also decrease volume to limit diffusion and spread[9–11]
Spasticity was not the main issue	Contracture, other rheologic changes can contribute to disability. If muscles are appropriately treated and range of motion is unchanged, contracture may be primary issue
	May need to consider surgical intervention to improve range of motion
	Need to still manage spasticity after lengthening for example
	If using spasticity to advantage, weakness can be unmasked, decreasing function
Other neurological diseases (NMJ disease, etc.)	Neuromuscular junction diseases, motor neuron diseases can make patients more sensitive to typical dosages of neurotoxin
New medications	Medication that improves pain may indirectly improve spasticity by decreasing a noxious stimulus which was causing an increase in spasticity
	Medication that has a side effect that is seen as a noxious stimulus may cause a secondary increase in spasticity (constipation caused by opiates can increase spasticity)
	Interaction of medications
	Synergistic effect of aminoglycosides and botulinum toxins
	Inhibition of metabolism of tizanidine with concurrent administration of fluoroquinolones
Choice of the most appropriate toxin	Need to be mindful of noninterchangeability of toxins, no "conversion rates"
	Need to have knowledge of appropriate dosages and titration of each toxin
Change in patient's expectations	Need to continue to assess patient's goals, change goals if prior goals met
	Re-evaluating goals at each visit/periodically realign goals with patients or caregivers and physicians, therapists
Development of antibodies	Neutralizing antibodies can cause a secondary nonresponse to botulinum toxin a in a variety of settings[13] or antibodies against BoNT-A[12]
Change in soft tissue porperties	Contracture, other rheologic changes can contribute to disability. If muscles are appropriately treated and range of motion is unchanged, contracture may be primary issue
	May need to consider surgical intervention to improve range of motion
	Need to still manage spasticity after lengthening for example
Too long an interval between injections	Allowing effect of the injection to wear off completely and have patient get "back to baseline" can lead to excessive "up and down" in function[14]
Individual variability	The duration of effect of botulinum toxin can differ from an individual to another. Even if the mechanisms underlying this phenomenon are not completely known (muscle mass, muscle fibrosis, neutralizing antibodies, genetical variations, muscle activity), this has been reported for several years[15]
Compliance with medication	Inconsistent compliance with oral medications will lead to suboptimal change in spasticity and subsequent perceived treatment failure

Contd...

Table 1: Contd...

Item	Considerations
Changes following reinervation	Phenotype of spasticity may change when reinnervation occurs following neurolysis
	Under response to alcohol/phenol – it may be more difficult to localize the correct injection site after reinnervation since the anatomy may no longer be "typical"
	Over response for alcohol/phenol – neurolysis of more muscles than intended, more difficult to titrate
Pump problem or not	Refer to troubleshooting pump problems algorithm

NMJ: neuromuscular junction, BoNT: Botulinum neurotoxin, ES: Electrical stimulation

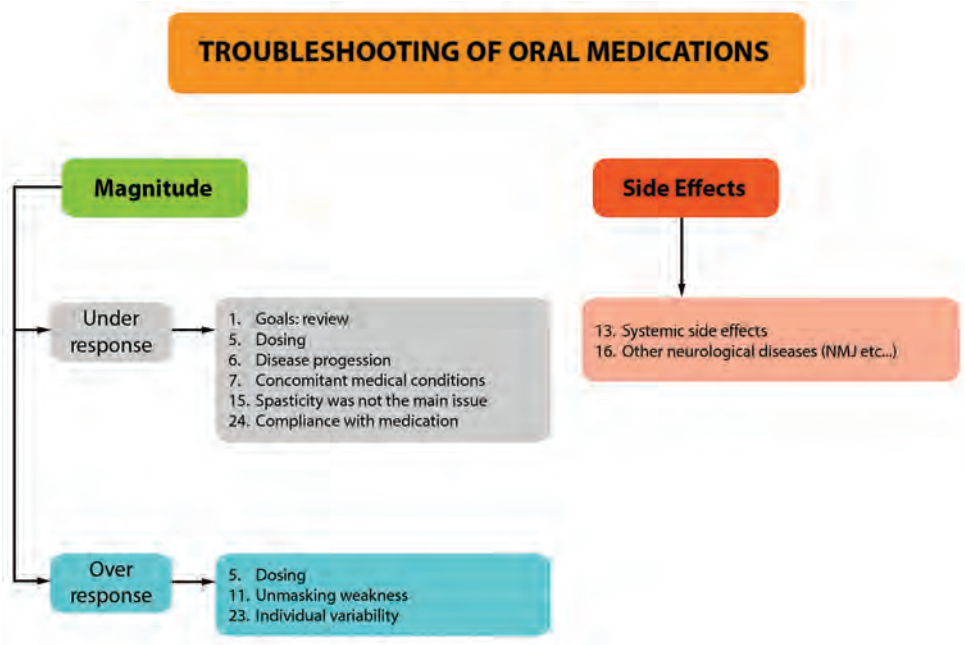

Figure 1: Algorithm for troubleshooting oral medications

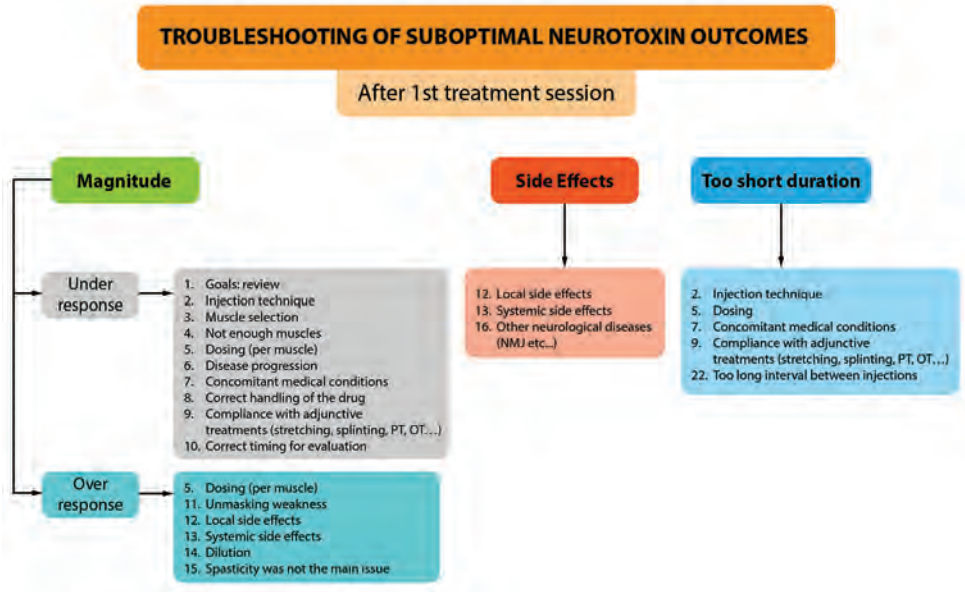

Figure 2: Algorithm for troubleshooting of suboptimal neurotoxin outcomes after the initial treatment session

to spasticity treatments.[3-12] The clinical treatment algorithms Figures 1-4 will provide guidance to which items need to be reviewed under different circumstances – considering both treatment modality and the nature of the problem.

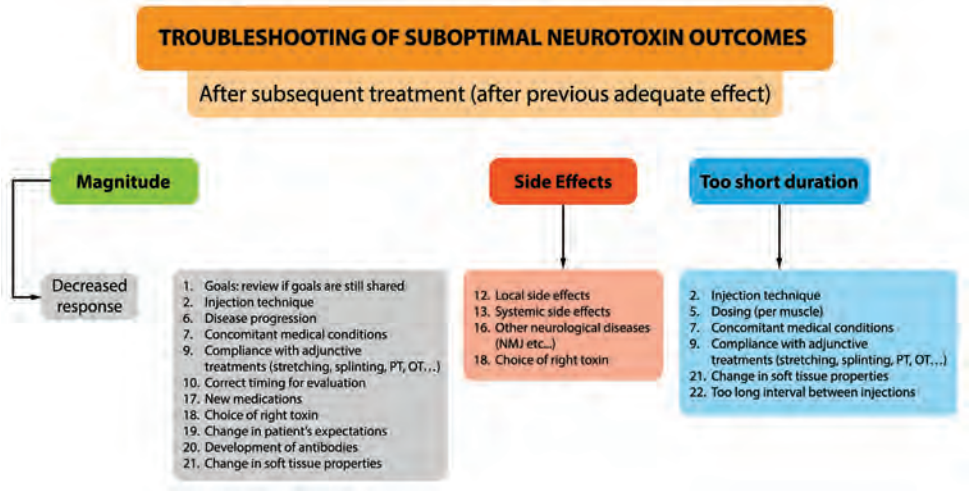

Figure 3: Algorithm for troubleshooting suboptimal neurotoxin outcomes after subsequent treatment sessions

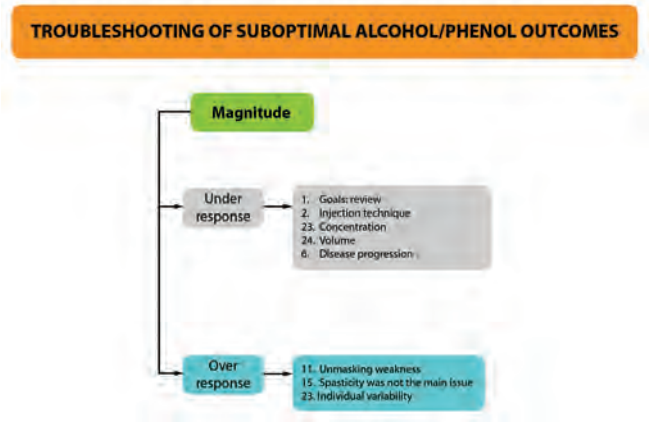

Figure 4: Algorithm for troubleshooting of suboptimal alcohol/phenol outcomes

In addition, there are special considerations for maintaining and troubleshooting intrathecal baclofen pumps and these are considered separately [Figures 5 and 6].

Troubleshooting oral medications

Once the goals have been reviewed, it is necessary, as with any oral regimen, to ensure that the patient is showing compliance with the treatment and taking medication regularly and as prescribed. The dose and timing of the medication should be reviewed.

The patient's overall condition in terms of spasticity progression and other medical comorbidities should be assessed and their spasticity medication adjusted accordingly with referral or additional prescribing for comorbidities.

The algorithm provides guidance on items to review.

Troubleshooting Botulinum Toxin A/Phenol/Ethanol Injections

BoNT-A and neurolytic agents are injected at multiple sites which raise issues such as: Were the muscles targeted correctly related to the goals; was the muscle localization technique adequate; were doses per muscle adequate or underdosed; was the adjunctive therapy carried out; was there any concurrent event that might have influenced a poor outcome?

In cases of suboptimal response to treatment important areas to address include;

- Goals
- Technique
- Concentration
- Volume
- Progression of disease
- Nerve/muscle selection.

Spasticity not the main issue in cases of exaggerated response (e.g., probable overdose), the areas to evaluate include:

- Goals
- Unmasking weakness
- Progression of disease
- Nerve/muscle selection
- Spasticity not the main issue.

The algorithms address troubleshooting after the first treatment session and after subsequent treatment sessions.

Troubleshooting after alcohol/phenol injections follows a similar pathway.

Approach to Troubleshooting Intrathecal Baclofen Systems

Intrathecal baclofen is an effective means of managing severe problematic spasticity in patients. However, these systems can malfunction either acutely or over time. Knowing how to troubleshoot these systems can improve patient outcomes and minimize morbidity in a comprehensive spasticity management practice.

Decreased response, review:

- Pump problem or not?
- Goals

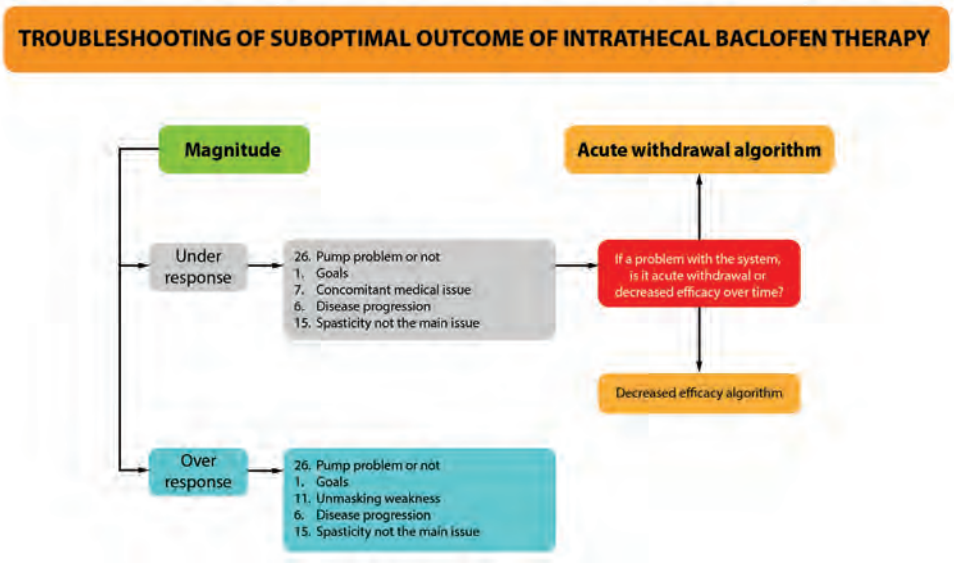

Figure 5: Algorithm for troubleshooting suboptimal outcomes of intrathecal baclofen therapy

- Concomitant medical issue
- Disease Progression
- Spasticity not the main issue.

Excessive response, review:
- Pump problem or not?
- Goals
- Unmasking weakness
- Progression of disease
- Spasticity not the main issue.

In addition:
- Acute withdrawal versus decreased control of spasticity over time.

Assessing Pump Problems

Because of the nature of intrathecal baclofen systems, troubleshooting of these systems necessitates special consideration. Two best practice algorithms for troubleshooting intrathecal baclofen therapy were published in 2016.[16] The first was for loss-of-efficacy and applies to patients with previously well-controlled hypertonia on a stable dosing regimen who have increased spasticity. The second algorithm was for emergent care and describes treatment of overdose or withdrawal, which requires immediate care in a monitored setting and restoration of baclofen delivery. They also address suspected overdose or over-infusion.

These algorithms provide a useful basis for troubleshooting; however, local resources vary and each treatment center or practice will need to develop their own pathway for troubleshooting that uses their own resources to best advantage.

Troubleshooting Intrathecal Baclofen Therapy-related Problems

Three main scenarios when troubleshooting is indicated are:
- When there is suspicion of medication overdose or pump over infusion
- Medication withdrawal or pump under infusion
- Loss of efficacy of the therapy over time.

However, many things can mimic baclofen overdose or underdose. The first step in any trouble setting algorithm is identifying other medical issues which weight may be masquerading as an intrathecal baclofen system malfunction.

Thankfully, baclofen overdose is a rare entity. The etiologies are typically programming error, using the wrong medication concentration, and very rarely, is the phenomenon of device over infusion.

Troubleshooting an intrathecal system is indicated when medication overdose or over-infusion is suspected, when withdrawal or under-infusion is suspected or when efficacy of the medication has decreased over time.[16]

As a first step conditions that mimic incorrect dosing must be eliminated to help confirm that the problem really lies in the pump or catheter delivery. Some conditions can confound identification of the problem as they may produce the same symptoms. For example, withdrawal or increased spasticity may be mimicked by autonomic dysreflexia, serotonin syndrome, noxious stimuli, urinary tract infections (UTIs), or constipation. Overdose or decreased spasticity may be mimicked by multiple sclerosis (MS) exacerbation, a new neurologic event (i.e., stroke), or excessive oral medication.

Overdose

The signs or symptoms of baclofen overdose include dizziness, somnolence, hypotonia, respiratory depression, seizures, and coma. This can arise when the apparatus is programmed incorrectly by the user (e.g., entering 500 mcg/day instead of 50 mcg/day). Errors can also be made in drug concentration

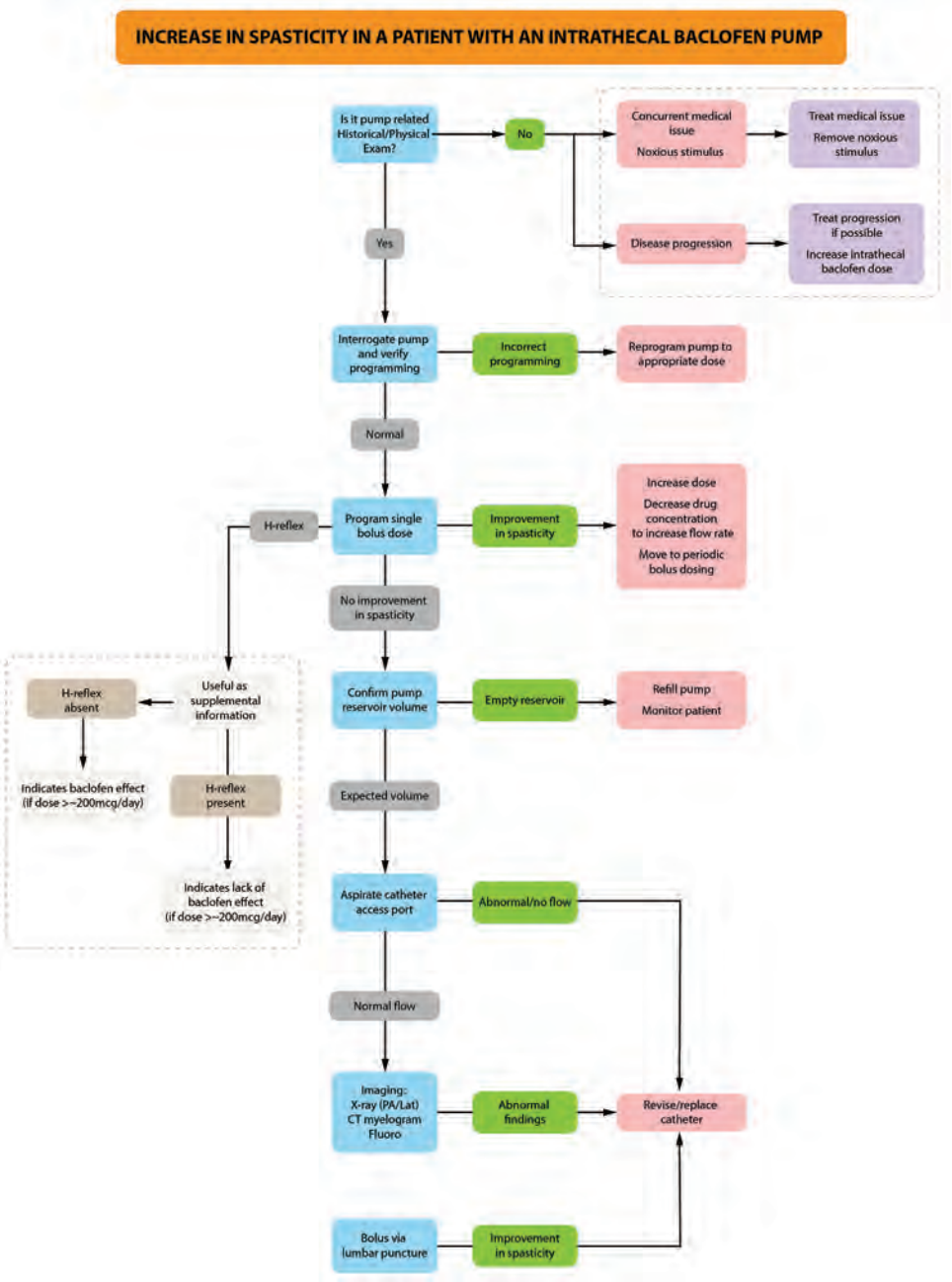

Figure 6: Algorithm for troubleshooting intrathecal baclofen pump malfunction[16]

(e.g., using medication of concentration 2000 mcg/mL rather than 500 mcg/mL). More rarely, the pump may deliver too much medication but this has been reported in < 0.16% of cases (Implantable Systems Performance Registry, August 2003 to July 2015, Medtronic).

The management of baclofen overdose is to maintain airway/breathing/circulation and decrease the intrathecal dose by programming the pump to minimum rate or withdrawal of large volume lumbar puncture (LP)/catheter access port (CAP). It should be noted, following a dramatic ITB dose reduction, the patient must be assessed and treated for symptoms of baclofen withdrawal. However, these symptoms should be self-limited.[16]

Underdose

Withdrawal or under-infusion symptoms include rebound spasticity, pruritis without a rash, mental status changes, fever, or even death.

As with overdosing, a programing error may be responsible for underdosing (e.g., entering 50 mcg/day instead of 500 mcg/day) or errors can be made in the drug concentration (e.g., using medication with 500 mcg/mL concentration instead of 2000 mcg/mL).

If human error is not responsible, the device may have a malfunction (i.e., critical motor stall) or an empty pump

reservoir if the patient or caregiver has missed the alarm date or a refill appointment. The pump may be at the end of its useful service period. Typically, device batteries have a life of approximately 7 years and the device needs to be replaced before the end of battery life. Catheters may also be the source of system malfunction if they become occluded, kinked, or disconnected. One other source of underdosing can result from the so-called "pocket fill." In these cases, the refill needle may become dislodged from or never be properly located in the pump reservoir. When this happens, the medication gets delivered subcutaneously rather than into the pump.

A loss of efficacy may also present slowly as a change over time rather than acute withdrawal. This is seen when the ITB does not give the same effect on spasticity as was achieved with the test dose despite dose escalation. A diminishing effect of the medication on spasticity where there was previous good control can also indicate loss of efficacy.[16]

Apparent loss of efficacy could be due to disease progression or MS exacerbation or other medical issues such as constipation or a deep vein thrombosis.

Baclofen withdrawal or under-infusion should be managed by administering an intrathecal bolus of the medication. Restoring the intrathecal delivery of baclofen is first step if possible, using LP, external indwelling catheter, or pump (if known to be functioning).

Oral or enteral baclofen is another option; if the patient is able to take the medication oral administration is the simplest or, if a percutaneous endoscopic gastroscopy tube is present, this can be utilized. There is no intrathecal to oral conversion; typically, the patient should be given the preimplant dose. If the prior dose not known, 10–20 mg every 6 h should be considered.

Intravenous benzodiazepines are an option but these need cardiac/respiratory monitoring. They can also be prophylactic for seizures. Cyproheptadine may be given at 2–4 mg every 6 h.

Creatine kinase and renal function should be monitored and the patient assessed for rhabdomyolysis.

The "syndromes" associated with catheter malfunction are given in Table 2 and the incidence of catheter malfunction is given in Table 3.

Some of the important points to consider are outlined here.

Firstly, as the data above have shown, most of the time a patient's, caregiver's, or other provider's concern of increased spasticity is NOT a pump or a catheter problem. Hence, patients must be assessed for their recent medical history, paying attention to any illnesses, medication changes, or environmental changes. Compare the spasticity on examination to prior examinations. For many patients, intrathecal baclofen withdrawal is often described as "worse than before getting the pump." The patient should be assessed for changes in mental status and review whether there is a source of noxious stimuli.

While problems with the pump itself are rare, inaccurate programming is often the culprit. It is important to verify the

Table 2: "Syndromes" associated with catheter malfunction

Catheter "syndrome"	Symptoms	Testing	Action	Comment
Microleak	Progressive loss of efficacy	Xray - NL CAP - NL Dye study - NL CT - NL Bolus - + response	Replace catheter/ segment (if segment can be identified)	Bolus doses may mask small leaks
Subdural catheter placement/migration	Vacillating response with alternating overdose and underdose	Xray - NL CAP - NL Dye study - NL CT - Abnormal Bolus - + response	Replace catheter/ segment (if segment can be identified)	Bolus doses may mask
Loculation at catheter tip	Progressive loss of efficacy	Xray - NL CAP - abnormal Dye study - NL CT - abnormal Bolus - + response	Replace catheter	Bolus doses may mask
Catheter migration	Acute loss of efficacy/ withdrawal	Xray - abnormal CAP - abnormal Dye study - abnormal CT - abnormal Bolus - response	Replace catheter	-
VP shunt malfunction	Progressive loss of efficacy	Xray – NL CAP - NL Dye study - NL CT - NL Bolus - + response	Revise shunt	Increase in CSF volume increases baclofen volume of distribution

Taken from.[17] CAP: Catheter access port, CT: Computed tomography, CSF: cerebrospinal fluid, VP: Ventriculo-peritoneal, NL: Normal

Table 3: The incidence of catheter malfunction

Event	Number of events (% of patient with event)
Catheter dislodgement	255 (3.19)
Catheter occlusion	242 (3.24)
Catheter leak	32 (0.45)
Catheter disconnection	39 (0.56)
Pump motor stall	89 (1.18)
Overinfusion	4 (0.16)

Implantable systems performance registry August 2003 to July 2015. Medtronic

actual drug and concentration put in the pump. If the pump alarm is sounding, the pump may be empty, at the end of battery life, or experiencing motor stalling. The pump log should be checked.

The pump volume must be checked since it does not have a "fuel gauge." There may be too little drug in the reservoir due to "pocket fill." If this problem is leading to subcutaneous delivery of baclofen, it would be poorly absorbed and not lead to overdose. Downstream obstruction in the system could lead to a higher-than-expected volume.

The CAP must be checked using the specified kit to access the CAP. This is the only needle that can access the CAP – the refill needle cannot be used. A total of 2–3 mL of fluid should be aspirated, all the baclofen in the catheter will have been withdrawn after the first ~0.25–0.5 mL, and the system will be withdrawing cerebrospinal fluid (CSF). Inability to aspirate easily suggests obstruction downstream and the catheter MUST be replaced.

It is important to program a priming bolus if the system is flowing freely and drug/CSF are withdrawn. Forgetting to perform a priming bolus can lead to withdrawal since the spinal catheter will be empty.

Imaging is useful to confirm what components of the system are implanted. Some components (Medtronic Ascenda™ catheter) are less visible on plain films. A computed tomography (CT) myelogram/Dye Study may be necessary. It is important to make sure that the catheter is aspirated via CAP before instilling dye. Radiopaque dye may be instilled under fluoroscopy or dye may be instilled in the CT scanner immediately before scan.

When programming the bolus dose, the same dose as the test dose should be used if the patient is not currently receiving bolus medication. The clinical response to bolus administration should be assessed where soleus H-reflexes can be useful as they are sensitive to intrathecal baclofen.[18]

It must be remembered that the algorithm is only an example. Local resources must be employed and the algorithm modified to produce an acceptable way to troubleshoot the system. Consideration should be given to team members skill in accessing the CAP, who participates in managing baclofen pump patients, whether there should be baclofen pump clinic days and education for the local emergency department.

When "inheriting" a patient with a baclofen pump, it may be worth investing some time is checking the device, verifying dose concentration etc., and ensuring that the indication for intrathecal baclofen in the first place is clear; the information should be shared with the management team.[19]

Case History

Case 2

A 58-year-old male patient suffering from right sylvian ischemic stroke (right internal carotid artery dissection, happened at the age of 52) with left hemiplegia, left homonymous hemianopia, left neglect, and persistent anosognosia has been treated for severe hand spasticity with BoNT-A two times, 4 and 7 months after stroke.

He was lost at follow-up and came only 3 years later, due to a skin infection of the palm. His left hand had a severe clenched fist, and, after a new BoNT-A treatment and antibiotics, he recovered.

6 months after his treatment the patient comes back [Figures 7-9].

He was treated with incobotulinumtoxinA, under ultrasound guidance, to the following muscles:

- Interossei: 80 UI
- FDS: 190 UI
- FDP: 60 UI
- FPL: 20 UI.

Dilution was 1 ml 0.9% saline: 100 UI for interossei and FPL and 2 ml 0.9% saline:100 UI for the other muscles. The primary objective was hygiene ease (opening the hand alone to clean the palm).

Competency Assessment

The answers to the Competency Assessments can be found at the end of the module before the references.

1. Which are the most frequent reason for a suboptimal outcome following BoNT-A?
2. What conditions can mimic apparent increased spasticity in a patient treated with intrathecal baclofen?
3. In the case history discussed above, what are the possible explanations for the result seen at 4 weeks after the last BoNT-A treatment?

Competency Assessment Answers

1. Which are the most frequent reason for a suboptimal outcome following BoNT?

Expected content of answer:

The most frequent reasons can be summarized in 3 groups:

1. Goal-related: Revise goal appropriateness, formulation, and measurement
2. Procedure-related: Correct muscle selection, correct targeting, correct dose
3. Patient-related: Patient motivation, cooperation, concomitant health problems

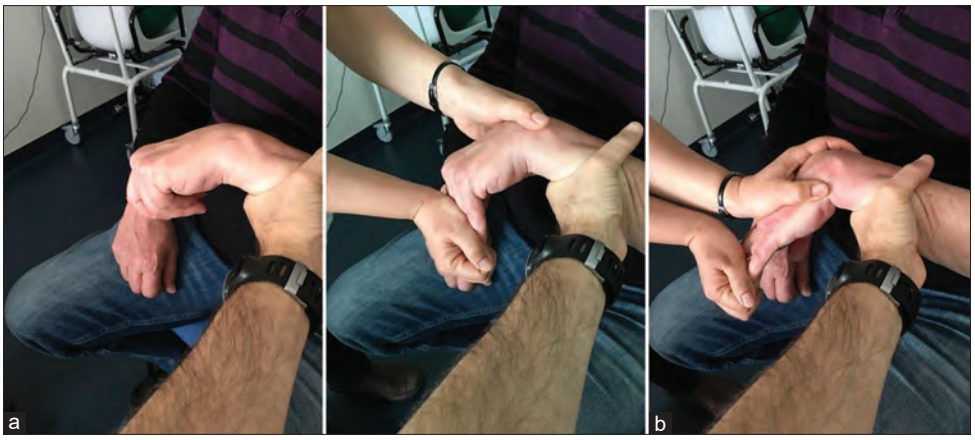

Figure 7: (a and b) Left-hand posture 6 months after last BoNT-A treatment

Figure 8: The result of this treatment 4 weeks after last BoNT-A treatment. The patient is quite disappointed about his hand posture

Figure 9: Four months after. The same patient, two weeks after having repeated the same BoNT-A treatment but this time with the addition of taping for 7 days

2. What conditions can mimic apparent increased spasticity in a patient treated with intrathecal baclofen?

Expected content of answer:

Withdrawal or increased spasticity may be mimicked by autonomic dysreflexia, serotonin syndrome, noxious stimuli, UTIs, or constipation.

3. In the case history discussed above, what are the possible explanations for the result seen at 4 weeks after the last BoNT-A treatment?

Expected content of answer:

Since the dose and dilution utilized are adequate, we should check for:

a. Goals: Is the goal realistic? If the patient had some contractures, the result achieved is the maximum possible. Anosognosia can make harder/impossible for the patient to evaluate his improvement
b. Procedure related: Did the patient have any adjuvant therapy?
c. Patient-related: Which was patient's compliance with correct positioning and how did he take care of his arm after the treatment?

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