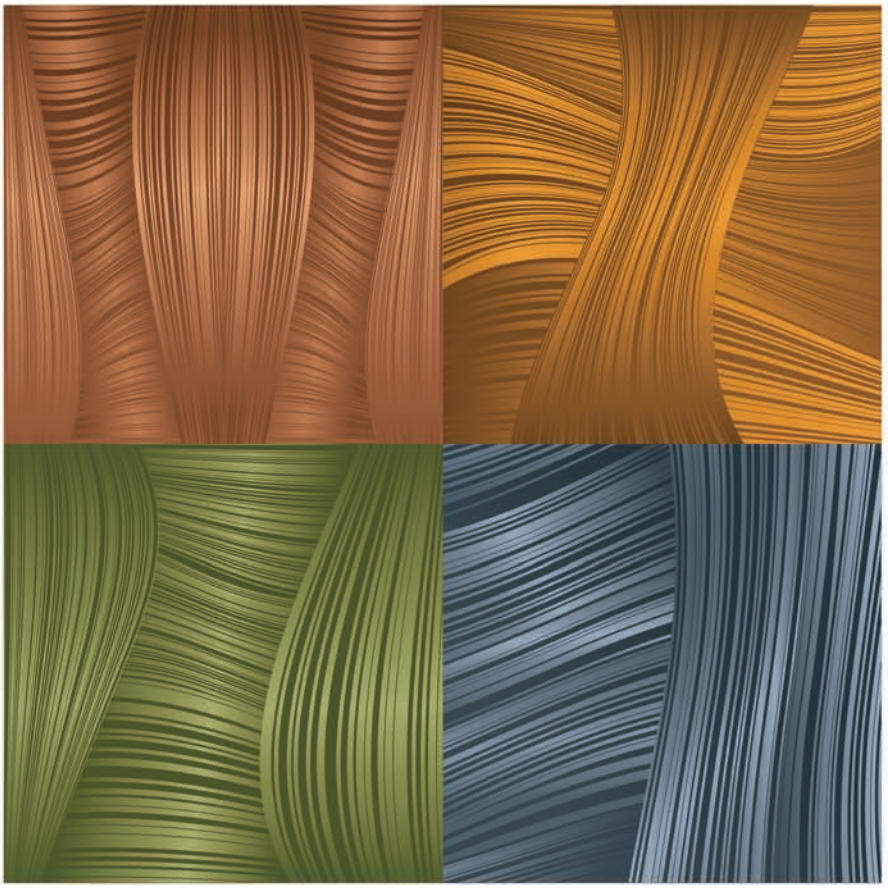
Optimizing Spasticity Outcomes

Throughout the Patient Continuum: Individualized Assessment, Therapy, and Follow-up



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Faculty Biography

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Dr Odderson received a medical degree from Vanderbilt University, in Nashville, Tennessee, and a doctorate from Indiana University, in Bloomington. He held a visiting fellowship at the National Institute of Mental Health, in Bethesda, Maryland.

Dr Odderson helped pioneer the treatment of hyperhidrosis with botulinum toxins. He has written articles on reduction of saliva production with rimabotulinumtoxinB and served as guest editor for a journal on the use of botulinum toxins. He authored the book *Botulinum Toxin Injection Guide*, and his work appears in such journals as *Neurorehabilitation and Neural Repair*, *Annals of Neurology*, and *Physical Medicine and Rehabilitation Clinics of North America*.

Dr Odderson is a Fellow of the American Academy of Physical Medicine and Rehabilitation. He is a member of several organizations, including the American Association of Electrodiagnostic Medicine, the American Academy of Neurology, and the American Paraplegia Society. Dr Odderson has been identified as one of Seattle's top doctors in *Seattle Magazine* and *Consumer's Checkbook* several times.

Intended Audience

This educational activity is intended to educate neurologists, primary care physicians, nurses, case managers, and other healthcare professionals who are involved in the treatment of patients with spasticity.

Needs Assessment

Spasticity is a serious medical condition that can cause severe disability, pain, immobility, contractures, and skin problems and negatively affects quality of life. Once incompletely treated through surgical means and oral medications, the treatment of spasticity has been revolutionized with the advent of botulinum toxins that afford targeted aggressive management.

Spasticity is caused by an upper motor neuron dysfunction, such as various diffuse or focal cerebral and spinal pathologic conditions. This complex disorder is characterized by a velocity-dependent increase in muscle tone that can lead to considerable motion restriction and, eventually, to serious disability. Often poorly treated and mismanaged, spasticity may result in a range of undue medical complications, negatively impacting and challenging patients and their caregivers.

Epidemiologic figures vary and are specific to associated conditions and their etiology. Rough estimates have suggested that 12 million people worldwide are affected by spasticity. In a 2008 Swedish study, Lundstrom et al noted that the observed prevalence of spasticity 1 year after first stroke was 17% and that of disabling spasticity was 4%. An even higher estimate was found at 12 months after stroke by Watkins et al, who reported a prevalence of spasticity of 38% of patients. It has been noted that spasticity may be underreported because patients with mild spasticity require little or no treatment.

Pain may be the primary complaint in patients with upper- and/or lower-limb spasticity who also have other symptoms related to spasticity. Clinicians need to be sensitive to the fact that, if left untreated or suboptimally treated, spasticity may lead to major long-term health consequences, including muscle shortening, limb deformity, painful muscle spasms, and depression.

Treatment for spasticity is necessary when clinical problems or symptoms are disabling for daily function. Management of expectations for long-term treatment is necessary, and goal setting is critical. Patient-specific goals should be regularly assessed and revised to achieve and measure effective treatment outcomes. Combination therapeutic interventions to treat spasticity may be appropriate to optimize outcomes through greater efficacy and tailoring to the needs of the patient.

Educational Objectives

At the conclusion of this activity, participants should be better able to…

1. Define and differentiate spasticity from other neurologic conditions, and incorporate improved differential diagnosis skills into the clinical practice setting
2. Explain the natural history and progression of spasticity, namely, the breakdown of neural insult, the relative immobilization of the paretic body part, and the chronic disuse of the paretic body part
3. Weigh the benefits of localized versus systemic treatment to optimally manage spasticity
4. Compare the fundamental biochemistry, formulations, and interactions of and indications for botulinum toxins
5. Carefully monitor and follow patients with spasticity by using assessment scales and a multidisciplinary team approach.

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This activity is an enduring material and consists of an online case study. Successful completion is achieved by viewing the material, reflecting on its implications in your practice, and completing the assessment component.

The estimated time to complete this activity is 1.0 hour.

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Part 1. An Integrative Team Approach to Early Diagnosis of Spasticity: Increasing Awareness

Spasticity is a complex condition that requires a multidisciplinary team of specialists—neurologist, rehabilitation physician, occupational therapist, orthopedic surgeon, and general practitioner—collaborating to achieve goals set at the onset of treatment. Early diagnosis and treatment are essential to mitigate the severe complications of the condition and to address related disabilities and morbidity.[1-3]

Spasticity management strategies include rehabilitation techniques in conjunction with pharmacotherapy.[4,5] Spasticity management may be optimized with combination therapy. This may include targeted, localized treatment focused on specific functions that are responsive to treatment.[5] Spasticity severity, time since injury, number of limbs involved, and patient preference should be considered when tailoring treatment to an individual.[6]

With greater stress on healthcare providers to improve efficiency and closely synchronize their efforts in a continuum of care, it is important to train and educate healthcare providers to recognize the early signs of spasticity and understand the need for prevention and appropriate treatment to improve outcomes.[7,8]

Epidemiologic figures vary and are specific to associated conditions and their etiology. Rough estimates have suggested that 12 million people worldwide are affected by spasticity. Despite the prevalence of spasticity, many cases are suboptimally treated or may go unrecognized, for instance, in patients with multiple sclerosis, traumatic brain injury, and cancer, who can suffer from spasticity due to a disease and its treatment.[2,3] Although more than a third of stroke patients experience spasticity and intensive stroke-rehabilitation programs are in place, it remains unclear who is at greatest risk for spasticity to develop and who is the most likely to respond to treatment.[9]

Healthcare professionals in public residential facilities for adults with intellectual disability recognize the importance of treating residents for potentially life-threatening medical conditions, such as epilepsy, but other conditions, such as spasticity, often are unrecognized and remain untreated.[10,11] The undertreatment of spasticity may be due to limited availability of physicians in institutions who specialize in its treatment, reluctance of specialists to evaluate people living in public residential facilities for adults with intellectual disability, or a lack of knowledge among caregivers about remediable conditions.[11,12] These factors may result in a failure to bring medical issues to an appropriate physician's attention.

Diagnosis

Spasticity is a complex motor disorder characterized by exaggerated deep tendon reflexes and a velocity-dependent increase in muscle tone.[13] Although the precise pathophysiology of spasticity remains to be elucidated, it is suggested that spasticity develops from an imbalance between the excitatory and inhibitory input to alpha motor neurons, leading to hyperexcitability of the stretch reflex as one component of upper motor neuron (UMN) syndrome.[14]

Spasticity is caused by various diffuse or focal cerebral and spinal pathologic conditions (UMN syndrome), including but not limited to spinal cord injury, stroke, multiple sclerosis, traumatic brain injury, and cerebral palsy.[15] When voluntary movement through pyramidal and corticospinal tracts is disrupted by a UMN lesion, an imbalance in spinal reactivity occurs as a direct result of the descending input received by spinal neurons. As this is sustained over time, spinal circuits undergo progressive plastic rearrangement that leads to spasticity characterized by abnormal muscle contractions and reflex responses.[14]

Commonly associated negative features of UMN syndrome include weakness, fatigue, and loss of dexterity and selective control of segmental muscle groups.[14] Spasticity and other muscle overactivity are clinical signs of UMN syndrome that are considered positive symptoms of UMN. Spasticity is characterized by a velocity-dependent increase in muscle tone, an increase in tonic stretch reflexes, exaggerated tendon reflexes, and repetitive stretch reflex discharges.[13] Within the clinical setting, spasticity is diagnosed according to the velocity-dependent resistance felt during passive examination of joint range of motion and increased tonic stretch reflexes.

Patients are usually impaired by weakness and muscle shortening. Joint deformity is common in patients with spasticity and can significantly impede gait, balance, and body image.[14] Depending on the age at onset of UMN syndrome and location in the central nervous system, presentation may vary. Paresis and increased muscle tone can cause fatigue, muscle spasms, and joint stiffness leading to contractures. In patients with limb spasticity, pain may be the primary presenting complaint.[16] Limb spasticity may impede activities of daily living, hygiene, ambulation, and in some cases, function.

Assessment

A patient's pain perception, overall quality of life, and capacity to groom and manage basic hygiene are important considerations. The extent to which spasticity affects these parameters and function are significant. Therefore, qualitative and quantitative measures of the amount of spasticity and the degree of weakness in each limb are key. Various scales to quantitate clinical outcomes include the commonly used modified Ashworth scale (0-4) and a physician assessment scale.[17] The Tardieu scale appears not to be in widespread clinical use for spasticity assessment.[18,19]

Management

Spasticity is generally treated when clinical symptoms are disabling. Although not all spasticity cases require treatment, if left untreated or suboptimally treated, spasticity may lead to major long-term functional and health consequences, including contracture, limb deformity, painful muscle spasms, skin breakdown, and depression.[20]

Part 2. Local and Systemic Therapies for Spasticity: Choosing Appropriate Treatment Options

Factors that determine treatment choice include distribution (ie, focal or diffuse), duration, and severity of the spasticity[21]; coexisting medical issues (eg, seizures, allergies); and current medications and potential interactions. Commonly, the most conservative treatments with the fewest adverse effects are used to treat spasticity.[22]

Nonpharmacologic Therapies

Nonpharmacologic treatment options for muscle overactivity include physical and occupational modalities (eg, stretching; resistance; orthotic devices; casting; cold and electrical stimulation; biofeedback, ultrasound, and infrared therapy) and surgical interventions (eg, tendon lengthening, tendon transfer, osteotomy, arthrodesis).[23] Neurosurgical procedures (eg, rhizotomy, neurostimulation, deep brain stimulation) are performed for the relief of spasticity and may improve function.[24] Surgical procedures can be helpful but are limited in scope and not effective for all joints and muscles, and outcomes vary.

Oral Medications

Various pharmacologic agents are available for the treatment of spasticity. The possible cognitive effects (eg, sedation, confusion, and dizziness) are important to consider.

Tizanidine, baclofen, diazepam, and dantrolene are generally considered first-line therapy for treating spasticity but can have specific disadvantages and cause adverse effects.[25] Tizanidine has been associated with weakness, sedation, drowsiness, dry mouth, and dizziness. Baclofen has caused sedation, weakness, nausea, dizziness, and hallucinations upon sudden withdrawal. Dependence with long-term use has been reported with diazepam. Dantrolene has been connected to drowsiness, diarrhea, malaise, generalized weakness, and hepatotoxicity.

Intrathecal Baclofen

Intrathecal baclofen is commonly used in cases of severe spasticity that are unresponsive to less invasive treatment options, such as chemodenervation and neurolysis, or when adverse effects cannot be tolerated.[26] After the patient has responded favorably to a test dose of intrathecal baclofen, a programmable pump system comprising a catheter and a medication reservoir is surgically implanted subcutaneously or subfascially in the anterior abdominal wall. In contrast to the oral formulation, intrathecally administered baclofen delivers the drug directly to the site of action, thus requiring a smaller dose to be efficacious and lowering the potential for adverse effects. Patients and caregivers must consider the possible risks with intrathecal administration, namely catheter or pump failure or infection.[25] Patients and caregivers also must be educated about the signs of baclofen withdrawal and have a plan to respond to emergencies, such as abrupt discontinuation of intrathecal baclofen, which can cause seizures, severe spasms, or markedly increased tone.

Chemodenervation Agents

Injectable chemodenervation agents (eg, alcohol, phenol, botulinum toxin) act by interrupting nerve impulse pathways to the muscles.[26,27] Patient selection—primarily, patients with regional or focal spasticity—is critical to the success of treatment.[21]

Neurolysis with alcohol or phenol

Neurolysis is performed more commonly with phenol than alcohol, generally in more proximal than distal muscles, and when many muscles are involved. As with all treatment strategies for spasticity, neurolysis may be used in combination with other therapies, including oral medications, physical rehabilitation, and botulinum toxin injections.[28]

Phenol is used when treating large muscles, such as those of the anterior thigh.[29,30] Duration of treatment effect is inconsistent, and it may be associated with adverse effects (eg, dysesthesia) and destruction of non-targeted tissue.[27]

Chemodenervation with botulinum toxins

Botulinum toxins inhibit presynaptic exocytosis of acetylcholine at the motor neuron, leading to reduced motor nerve impulse transmission and inhibition of muscle contraction. In addition, botulinum toxin may prevent pain-stimulating neuropeptide release in peripheral nerves.[31,32]

Because of inherent differences in botulinum serotypes (A, B, C1, D, E, F, G), potencies vary considerably and toxins are not interchangeable.[33-38] Additional variables need to be considered, including spasticity severity, muscle location and size, and body

Table 1.
Doses of Various Botulinum Toxins in Treatment of Upper-Limb Spasticity

Treatment Doses	N	Mean Duration of Post-Stroke Spasticity	Injected Muscles	Results
AbobotulinumtoxinA[1] 350 U, 500 U, 1000 U	50	8.4 mo	BB, FCR, FCU, FDP, FDS	Significant reduction in muscle tone and pain with all 3 doses
IncobotulinumtoxinA[2] 40 U, 50 U, 80 U	148	55 mo	BB, FCR, FCU, FDP, FDS	Significant reduction in Ashworth scale score for wrist flexor treatment Significant improvement from baseline in disability assessment scale and global assessment scores No difference in adverse events between groups
OnabotulinumtoxinA 75 U, 150 U, 300 U[3]	39[3]	37 mo[3]	BB, FCR, FCU[3]	Significant reduction in Ashworth scale score with 300 U[3] Improvement in global assessment scores with 75 U and 300 U[3]
90 U, 180 U, 360 U[4]	91[4]	25.8 mo[4]	BB, FCR, FCU, FDP, FDS[4]	No difference between groups regarding adverse events[3] Dose-dependent response in muscle tone reduction but not in pain or global assessment measures[4]
RimabotulinumtoxinB[5] 10,000 U	15	Data not available	BB, FCR, FCU, FDP, FDS	No decrease in muscle tone in elbow, wrist, or finger flexors Dry mouth common

BB, biceps brachii; FCR, flexor carpi radialis; FCU, flexor carpi ulnaris; FDP, flexor digitorum profundus; FDS, flexor digitorum superficialis.

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weight.[39] Commercially available botulinum toxin types are type A (abobotulinumtoxinA, onabotulinumtoxinA, incobotulinumtoxinA) and type B (rimabotulinumtoxinB; Table 1).

Although only onabotulinumtoxinA is approved in the United States for the treatment of upper-limb spasticity, all botulinum toxins have been investigated.[35] Clinical effects are usually noted within 24 to 72 hours, reaching maximum efficacy at up to 2 weeks after injection and lasting approximately 12 weeks. Duration of effect may be increased to 16 weeks or longer when combined with adjunctive therapies (eg, casting, stretching). Follow-up is critical to gauge patient response and to adjust dosage and muscle selection.[40]

In a retrospective analysis of 137 patients receiving 1221 treatments, Mohammadi et al investigated the long-term (up to 12 y) treatment of spasticity of various etiologies with botulinum toxin type A—onabotulinumtoxinA or abobotulinumtoxinA—evaluating efficacy, dosage, safety, and adverse effects.[41] Although the two formulations are not interchangeable, the clinical benefit, latency, and duration of response were comparable, and adverse effects (eg, injection-site pain and transient weakness of muscles) were similar and generally mild.

A recent expert panel report suggested there is a need for further studies comparing the effectiveness of the available formulations for spasticity treatment.[42] For the treatment of upper-limb spasticity, the evidence supported a level A recommendation for onabotulinumtoxinA and abobotulinumtoxinA, with a level B recommendation for incobotulinumtoxinA. There was insufficient evidence to support a recommendation for rimabotulinumtoxinB. For lower-limb spasticity, there was sufficient clinical evidence to support a level A recommendation for onabotulinumtoxinA individually and botulinum toxin type A in aggregate. The clinical evidence for abobotulinumtoxinA supported a level C recommendation. There was insufficient information to recommend incobotulinumtoxinA and rimabotulinumtoxinB.

Treatment Selection and Optimization

Clinicians should carefully evaluate patients with spasticity for symptoms and functional impact and set clear and realistic therapy goals before initiating treatment. Outcomes are generally optimized through a combination of pharmacologic and nonpharmacologic therapies, such as stretching, orthotic devices, and electrical stimulation.[43] It is critical for clinicians to include effectiveness and cost in their considerations when selecting a treatment.[44-47]

Case Study

A 52-year-old man with a 7-year history of poorly controlled

Table 2. AbobotulinumtoxinA Dosing for Arm and Leg Muscles

Muscle	AbobotulinumtoxinA Dose, Units
Upper limb	
Flexor carpi radialis	100
Flexor carpi ulnaris	100
Flexor digitorum profundus	200
Flexor digitorum superficialis	150
Lower limb	
Soleus	200
Tibialis posterior	200
Flexor digitorum brevis	50
Flexor digitorum longus	200

hypertension and dyslipidemia experienced acute left hemiparesis and was admitted to the hospital, where he was found to have suffered a right brain stroke. Five days later, he began inpatient rehabilitation with intensive physical therapy, occupational therapy, and medical and nursing care. Over the next 3 weeks, the patient continued to improve to the point that he could be discharged home to the care of his wife. He received physical therapy and occupational therapy visits at home. He used a wheelchair and, for short-distance ambulation, an ankle foot orthosis, a broad-based quad cane, and contact guard by his wife or therapist. His neurologist then referred him for outpatient rehabilitation to continue therapy and spasticity management.

The patient was experiencing frequent spasms in his left arm and leg. The arm spasms were painful, especially at night, and the leg spasms turned his left foot in and down and curled his toes under. When walking without a brace, his foot could easily roll and cause him to lose balance. Toe spasms made walking uncomfortable. He was taking antispasmodic medication (baclofen 30 mg/d), which was not adequately controlling the spasms and pain.

The decision was made to increase his baclofen gradually to the maximum recommended dose of 80 mg/day. If that was inadequate or if adverse effects, such as sedation or fatigue, curtailed the dose increase, the next step would be to do

Table 3. Modified Ashworth Scale Score

	Before Injection	After Injection
Wrist flexion	3.0	2.0
Finger flexors	3.5	2.0
Ankle flexion	2.5	1.5
Toe flexors	3.0	1.5

Table 4. AbobotulinumtoxinA Dosing for Arm and Leg Muscles

Muscle	AbobotulinumtoxinA Dose, Units
Upper limb	
Biceps	100-400
Brachialis	250
Brachioradialis	100
Flexor carpi radialis	150
Flexor carpi ulnaris	100-150
Flexor digitorum profundus	150-200
Flexor digitorum superficialis	150-300
Lower limb	
Hip adductor group	500-1000
Gastrocnemius	250-1000
Soleus	200-500
Tibialis posterior	200-500
Flexor digitorum longus	150-300

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botulinum toxin injections to relax his spastic muscles. The patient continued outpatient physical and occupational therapy.

At the next visit 3 weeks later, the spasms were not significantly improved. He was receiving the maximum dose of the oral antispasmodic medications and felt mild fatigue. The decision was made to treat him with botulinum toxin. Although, the spasms were regional (hemiparesis), focal treatment with botulinum toxin injection is very effective for specific joints. He received injections into muscles of the left arm and leg as listed in Table 2.

Upon follow-up 4 weeks later, he was pleased with the effects of chemodenervation. He no longer needed a plastic tube to keep his left hand open. He could now flex his fingers somewhat, but he was unable to extend them. He felt no forearm pain at rest but did have pain with stretching during occupational therapy. His left foot was no longer turning in and down, but he still did not have full dorsiflexion at the ankle. His gait with the broad-based quad cane was improved.

Botulinum toxin treatment was repeated 3 months after the first chemodenervation with plans to continue at 3-month intervals for as long as needed. Occupational therapy and physical therapy were continued, because he was still making progress (Table 3).

Summary: Spectrum of Treatment Options

Generally, management of spasticity requires a multidisciplinary and multimodal approach, including physical therapy, occupational therapy, medications, injectable agents, implants, and orthopedic surgery. The number of treatment options employed will depend on the severity and extent of the muscle overactivity. Treatments do not require a laddered approach, and several therapies can be used concurrently. The literature shows that outcomes are better with combined therapies than with any separate treatment.[48-51]

Physical and occupational therapies are generally used in addition to other treatments to maximize benefits. Patients are not only treated but also taught how to independently continue to improve through a home therapy program.

Oral muscle relaxants are helpful for mild to moderate spasticity. However, some patients experience intolerable adverse effects before the optimal therapeutic dose is reached, which limits the usefulness of the medication. Adverse effects are primarily fatigue, drowsiness, and dizziness.

A sudden increase in treatment options occurred with the advent of injectable botulinum toxins. Their treatment applications span the range of spasticity, from mild to severe muscle overactivity, and injections target specific muscles (Table 4),

allowing joints to be relaxed to improve positioning and movement. Although functional improvement has not been convincingly demonstrated with the injectable botulinum toxins, the treatment may allow a patient to participate in therapies that will improve function.

Four botulinum toxins are available on the US market, and cost and insurance coverage vary. The toxins differ in potency according to the manufacturing process and assay method used; doses of one toxin cannot be converted to doses of another. Quarterly injections allow optimization of dose and injection site. Adverse events are temporary and primarily involve the potential spread of the toxin to neighboring muscles or beyond the injection site, as delineated in each medication's prescribing information.

A newer spasticity treatment is a surgically implanted intrathecal pump that infuses baclofen into the spinal fluid in the back. The intrathecal baclofen pump is deployed mainly in cases of severe and generalized spasticity. This therapy does not preclude the use of other treatment options in combination.

Finally, orthopedic surgical tendon transfer can permanently correct abnormal joint position. The procedure can minimize or eliminate the need for oral and injectable muscle relaxants and, possibly, an orthotic device.

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