Spasticity Management in Multiple Sclerosis

Evidence-Based Management Strategies for Spasticity Treatment in Multiple Sclerosis

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Multiple Sclerosis Council for Clinical Practice Guidelines

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FOREWORD

Professional organizations from all sectors of the healthcare community have embraced the development, use, and evaluation of practice guidelines through which they collate and evaluate empirical evidence and expert opinion. Generally, the goals of these practice guidelines are to reduce inappropriate care and improve patient outcomes, reduce healthcare costs, enhance quality assurance, and improve medical education. Their benefit is in documenting clinical research as well as the advice of clinical experts, and assessing the clinical significance of conflicting research findings. Recognizing that many persons with MS employ complementary and alternative medicine (CAM), these treatments are included in this guideline. Many public and private healthcare organizations are involved in developing practice guidelines, and the scope of topics researched and methodologies used is quite diverse. The decision to produce a guideline on spasticity reflects its importance to the member organizations of the Multiple Sclerosis Council for Clinical Practice Guidelines. Whenever possible, this and the other guidelines produced by the MS Council, are based on empirical evidence and the recommendations are graded on the quality of evidence. Nonetheless, expert opinion remains an integral part of guidelines development because “reliable scientific evidence is lacking for most clinical practices” (S.H. Woolf, 1992. Practice guidelines: a new reality in medicine. II Methods of development guidelines. Archives of Internal Medicine 152:946-52).

We are pleased to present this updated version of the clinical practice guideline on Spasticity Management in Multiple Sclerosis to the healthcare community. As this guideline demonstrates, spasticity is a common consequence of MS. When properly treated, the immediate symptoms as well as secondary complications can be avoided. This guideline synthesizes the currently available literature and identifies many key questions that remain to be investigated. It will need to be updated as evidence from on-going studies becomes available.

This guideline, and the others developed by the MS Council for Clinical Practice Guidelines, reflect both the published research on this topic as well as the expert consensus of the panel members that has been supported, by the consensus of a broad range of clinicians with MS expertise. We encourage researchers to consider those recommendations that are based on expert consensus as an important area of investigation.

These guidelines are written for healthcare professionals to assist them in clinical decision-making. We anticipate that the document will be useful in discussing spasticity with their patients and in making treatment decisions. We also expect the publication will be useful to individuals and organizations responsible for allocating healthcare resources.

People with MS come from all walks of life and live with a broad range of disability. Many healthcare professionals in varied settings provide their care. For this reason, the guidelines have been developed for a range of patients, clinicians, and treatment settings. Adaptability has been a guiding principle of the MS Council for Clinical Practice Guidelines, whose members represent the major professional and consumer MS groups, and of the members of the Guidelines Development Panel, who also reflect this provider and consumer diversity.

This guideline will be of benefit only if it is studied, implemented, evaluated, and updated. The MS Council welcomes the responsibility of ensuring the current and future value of this guideline as part of its ongoing activities. However, we will be successful in this effort only with the participation of the healthcare providers who use this document.
We are grateful to the Paralyzed Veterans of America (PVA) for convening and supporting the Spasticity Panel and to PVA and the Consortium of MS Centers for providing ongoing support to the representatives of the 20 organizations that constitute the Multiple Sclerosis Council for Clinical Practice Guidelines. The concern of these two organizations for the well-being of people with MS, and their commitment to ensuring that appropriate care is available to every person with MS, is an example to us all.

Deborah M. Miller, PhD
Chair, MS Council for Clinical Practice Guidelines
ACKNOWLEDGEMENTS

The chair and members of the Spasticity Management Guideline Development Panel express their appreciation for the leadership and encouragement given by the representatives of the organizations that make up the Multiple Sclerosis Council for Clinical Practice Guidelines. In addition, we acknowledge the efforts of the 15 professionals who provided expert review of the final draft. The efforts of the organizations and their members are central to the development of this guideline.

The guideline depended on the expert assistance of the Center for Clinical Health Policy Research at Duke University for the able literature review and synthesis. We especially thank David B. Matchar, MD, Douglas C. McCrory, MD, MHSc, Olivier Rutschmann, MD, MPH, and Jane Kolimaga, MA.

The panel is indebted to the leaders and staff of the Paralyzed Veterans of America and the Consortium of Multiple Sclerosis Centers for providing the organizational, administrative, and financial support to conduct this effort. In particular, the panel recognizes the efforts of John Carswell and Thomas Stripling, former and present Associate Executive Director of the Health Policy Department of the Paralyzed Veterans of America for championing the cause of veterans who have MS. June Halper, Executive Director of the Consortium of Multiple Sclerosis Centers, Tina Trott and the Board of Governors of the Consortium of Multiple Sclerosis provided support, critique and encouragement that was instrumental to the development of this guideline. This work has been presented as it progressed at the annual meetings of the Consortium of MS Centers. We appreciate the rich input of the members of this organization.

In addition, the panel is grateful to the United Spinal Association for their ongoing dissemination of this document and their educational programs on the effective management of spasticity in MS and Spinal Cord Injury.

Last, but certainly not least, the panel recognizes the commitment and fortitude of Deborah Miller, PhD, in nurturing this guideline from conception to publication.

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<table>
<thead>
<tr>
<th>Rating of recommendation</th>
<th>Translation of evidence to recommendations</th>
<th>Rating of Therapeutic Article</th>
</tr>
</thead>
</table>
| **A** = Established as effective, ineffective, or harmful for the given condition in the specified population | **Level A** rating requires at least one convincing class I study or at least two consistent, convincing class II studies | **Class I**: Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required:
- a. primary outcome(s) is/are clearly defined
- b. exclusion/inclusion criteria are clearly defined
- c. adequate accounting for drop-outs and crossovers with numbers sufficiently low to have minimal potential for bias
- d. relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. |
| **B** = Probably effective, ineffective, or harmful for the given condition in the specified population | **Level B** rating requires at least one convincing class II study or at least three consistent class III studies | **Class II**: Prospective matched group cohort study in a representative population with masked outcome assessment that meets a-d above OR an RCT in a representative population that lacks one criterion a-d. |
| **C** = Possibly effective, ineffective, or harmful for the given condition in the specified population | **Level C** rating requires at least two convincing and consistent class III studies | **Class III**: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment. |
| **U** = Data inadequate or conflicting. Given current knowledge, treatment is unproven. | | **Class IV**: Evidence from uncontrolled studies, case series, case reports, or expert opinion. |
Spasticity is a disorder characterized by increased resistance of muscle to an externally imposed stretch, often with more resistance to rapid stretch. Spasticity in MS is due to changes in the central nervous system from lesions in either the brain or spinal cord. Spasticity can be nothing more than an annoyance or it can cause significant disability and result in a chain of secondary complications that result in unnecessary morbidity and mortality.

For instance, spasticity can result in muscle fibrosis and joint contracture that can lead to skin breakdown, osteomyelitis, sepsis, and death. Alternatively, spasticity can result in pain, reduced mobility, and reduced quality of life that can lead to social isolation and depression. Spasticity can be diagnosed and treated effectively to minimize impairments, disability, loss of social participation, and altered quality of life.

Spasticity may change depending on position. For instance, an individual may have more flexor spasms when positioned in the wheelchair with the hips and knees flexed. Another individual may have difficulty clearing his foot when ambulating due to an increase in extensor spasms involving the quadriceps and gastrocnemius that occurs predominantly when s/he is upright, but not when sitting on an examination table or in a wheelchair. Thus, an individual may have valid complaints of spasticity that limit function that are not apparent during a routine office examination.

Spasticity often occurs with effort exerted during activity. During an examination, the clinician may not observe a marked increase in deep tendon reflexes or resistance to passive range of motion. However, when that individual tries to voluntarily activate the muscles around a joint, both the flexors and extensors co-contract involuntarily resulting in great difficulty or an inability to move the joint through its range of motion. When postural stability is challenged or a task becomes more complex, spasticity often increases. Spasticity can also increase at night making sleep difficult, resulting in daytime fatigue.

Spasticity of particular muscles may also correlate with the presence or absence of spasticity in the muscles that are part of the same synergistic pattern. For instance, reducing spasticity in the finger flexors, may decrease or inhibit the spasticity in the more proximal elbow flexors. Similarly, reducing spasticity in the muscles that plantarflex the foot may reduce an overall extremity extensor synergy.

Spasticity is associated with noxious stimuli, such as a full bladder or colon, an infection, renal or bladder stones, a bone fracture, extreme physiological or environmental temperature, other physiological stressors, menses, tight clothing, and some medical treatments.

The panel recommends that spasticity be evaluated as part of routine evaluation whether or not the person with MS makes a specific complaint. Documentation of baseline reflexes, range-of-motion, Ashworth Scale\(^1\), modified Ashworth Scale\(^2\) (Table 3), Spasm Frequency Score\(^3\) (Table 4) a clinical measure of pain intensity\(^4\), or other measures provide a useful baseline for subsequent follow-up. (Expert Consensus)

The following two sections present an algorithm and associated recommendations to be used as tools for evaluation, monitoring, and treatment of spasticity. The algorithm and recommendations are presented as a guideline not as rules. The authors appreciate that a sequential, linear approach may not apply to every individual. The guideline is intended to augment, rather than substitute for good clinical decision making.
Spasticity Management in Multiple Sclerosis

ALGORITHM

1. New onset or change in spasticity

2. Concurrent factors present?
   - Yes:
     2a. Treat
     2b. Spasticity resolves? Insufficient Resolution
        - Yes:
          2c. Monitor
        - No:
          5. Insufficient Resolution

3. Other impairments or functional changes

4. Health Promotion Strategies
   - Yes:
     4a. Spasticity resolves?
        - Yes:
          4b. Monitor
        - No:
          6. Assess Preferences, Complications, Social Support

5. Insufficient Resolution

6. Characterize Spasticity
   - Generalized
   - Focal: Limited muscle groups involving one extremity or the neck

7. Neumuscular Block

8. Skilled Rehabilitation Strategies

9. Oral Pharmacotherapy (Sequential Trials)
   - No:
     10. Tolerated/Effective

11. Yes:
    - Monitor

12. No:
    - Appropriate for Intrathecal Rx
      - Yes:
        13. Refer
        - Yes:
          13a. Effective?
          - Yes:
            13b. Monitor
          - No:
            14d. Continuing Care
        - No:
          14a. Appropriate for other surgical procedures?
          - Yes:
            14b. Effective?
            - Yes:
              14c. Monitor
            - No:
              14d. Continuing Care
          - No:
            14a. Appropriate for other surgical procedures?
1. **Identify New Onset or Change in Spasticity.**
   
   **Level U/Expert Consensus**
   
   **Goal:** To determine if spasticity is present.
   
   **Procedure:** Regularly assess for spasticity using history and physical examination, whether or not the person with MS makes a specific complaint. Document symptoms described in Table 2. Use range-of-motion, spasm frequency score, Ashworth Scale, and other impairment and disability instruments for baseline.
   
2. **Determine if Concurrent Factors are Present.**
   
   **Level U/Expert Consensus**
   
   **Goal:** To identify and appropriately manage treatable factors aggravating spasticity.
   
   **Procedure:** Screen for concurrent factors and disease progression (e.g. infection, mechanical disorders/problems, noxious stimuli, exacerbation, etc.). See Table 5.
   
2a. **Treat.**
   
   **Level U/Expert Consensus**
   
   Treat appropriately.
   
2b. **Determine if Spasticity has Resolved Sufficiently.**
   
   **Level U/Expert Consensus**
   
   Perform history and physical examination.
   
2c. **Monitor.**
   
   **Level U/Expert Consensus**
   
   Reassess spasticity at each visit.
   
3. **Determine if There Are Other Impairments or Functional Changes.**
   
   **Level U/Expert Consensus**
   
   **Goal:** To assess the impact of spasticity on function in order to determine the need for and effects of a treatment program.
   
   **Procedure:** Assess the functional consequences of spasticity. See Table 6.
   
4. **Provide Health Promotion Strategies.**
   
   **Level U/Expert Consensus**
   
   **Goal:** To limit future disability and enhance quality of life.
   
   **Procedure:** Recommend community-based exercise that promotes stretching, strengthening, endurance and function.
   
4a. **Determine if Spasticity has Resolved Sufficiently.**
   
   **Level U/Expert Consensus**
   
   Perform history and physical examination.
   
4b. **Monitor.**
   
   **Level U/Expert Consensus**
   
   Reassess spasticity at each visit.
   
5. **Assess Preferences, Complications, Social Support and Other Impairments.**
   
   **Level U/Expert Consensus**
   
   **Goal:** To optimize the person’s participation in an intervention, increase adherence, and minimize secondary complications associated with spasticity, especially pain, skin breakdown, and contracture.
   
   **Procedure:** Provide a treatment plan that is individualized for each person, taking into account the individual’s ability to adhere to the plan. (See Table 7 and Appendices A and B.)
   
6. **Characterize Spasticity.**
   
   **Level U/Expert Consensus**
   
   **Goal:** To offer the most targeted treatment appropriate for the individual.
   
   **Procedure:** Use information from the history and physical exam to determine if impairments are caused by spasticity that is focal or generalized.
   
7. **Perform Neuromuscular Block.**
Level A Recommendation

**Goal:** To relieve focal spasticity.

**Procedure:** Have appropriate specialists evaluate for and perform neuromuscular blocks. In practice, this is done in conjunction with referral for skilled rehabilitation therapies.

8. **Focal: Apply Skilled Rehabilitation Strategies.**

   Level A Recommendation

   **Goal:** To optimize function and to minimize secondary disability due to spasticity.

   **Procedure:** Provide a skilled rehabilitation program in conjunction with focal neuromuscular blocks.

Generalized: **Apply Skilled Rehabilitation Strategies.**

   Level A Recommendation

   **Goal:** To optimize function and to minimize secondary disability due to spasticity.

   **Procedure:** In the presence of generalized spasticity, refer to a skilled rehabilitation program. In practice, skilled rehabilitation strategies are often prescribed in conjunction with oral pharmacotherapy.

   In the presence of generalized spasticity, rehabilitation is an essential component of management.

Specific Modalities:

1. Range of Motion: Level U/Expert Consensus.5-11


5. Cold: Level B Recommendation.13, 14 There is insufficient evidence to support the use of cooling as an independent modality in the treatment of spasticity.


   The panel does not recommend the use of heat to treat spasticity in individuals with MS. Warm pools may be acceptable when a person's functional status is not adversely impacted by heat.


   **Education fosters informed decisions, active participation, and long-term transition from a skilled environment to the community.**

   8. Compensatory Strategies to Optimize Energy Effectiveness: (See Fatigue and Multiple Sclerosis: Evidence-Based Management Strategies, Kinkel, R. Philip et al., October 1998.)


Gait training used in conjunction with prescription of orthotics and aids enhances the safe use of assistive technology and mobility.

10. Upper and Lower Extremity Assistive Technology: Level U/Expert Consensus


12. TENS: Level U/Expert Consensus.15, 17 TENS may be useful in selected patients with painful spasms.


14. Magnetic Stimulation: Level U/Expert Consensus.18

   There is evidence that magnetic stimulation has a transient effect on spasticity, but insufficient evidence to support its use for routine treatment of spasticity.

9. **Prescribe Oral Pharmacotherapy.**

See Procedure for levels of recommendation.

**Goal:** To effectively treat spasticity.

**Procedure:** Initiate treatment with a single agent selected considering the person's preferences and the agent's efficacy, side effect profile, and cost. For spasticity that lasts most of the day, start with either baclofen or tizanidine: Level A Recommendation. In head-to-head studies between these two drugs, the evidence demonstrates no compelling difference in effect on spasticity: Level B Recommendation. A step therapy approach with individual agents should precede the
use of combination therapy: Level U/Expert Consensus (See Table 8). In practice, oral pharmacotherapy and skilled rehabilitation strategies are often done concurrently.

10. Determine if Treatment is Tolerated/Effective.

Level C Recommendation

Goal: To maximize effective treatment and, if necessary, to refer for surgical interventions.

11. Monitor.

12. Determine Appropriateness of Intrathecal Therapy.

Level U/Expert Consensus

Goal: To determine if the person’s impairments and disabilities can reasonably be addressed by the anticipated benefits of intrathecal therapy.

Procedure: Refer to specialist. This is an elective procedure where the individual benefits and risks need to be carefully assessed by specialists who have used it to manage spasticity in MS.

13. Refer for Intrathecal Therapy.

Level A Recommendation for patients with Expanded Disability Status Scale (EDSS) of 7 or above19

Level C Recommendation for patients with EDSS of 5.0-6.5

Goal: To treat those individuals whose spasticity is not adequately responsive to oral and rehabilitation strategies.

Procedure: Refer to center with extensive experience for baclofen pump evaluation, implantation, and management.

Intrathecal therapy is effective for patients with MS for whom oral therapy alone has failed (See Table 8).

13a. Determine Effectiveness of Intrathecal Therapy.

Level U/Expert Consensus

Goal: To assess functional benefits from intrathecal therapy.

13b. Monitor


Level U/Expert Consensus

Goal: To determine if the person’s impairments and disabilities can reasonably be addressed by the anticipated benefits of other procedures including:

- Paravertebral Spinal Nerve Block with Phenol or Ethyl Alcohol
- Intrathecal Nerve Root Block with Phenol or Ethyl Alcohol
- Dorsal Rhizotomy
- Tenotomy
- Myelotomy
- Cordotomy

Procedure: Refer to appropriate specialists. These approaches may be beneficial for people with MS who are not appropriate candidates for or who do not respond to other therapies.

There is insufficient evidence to recommend either dorsal column or spinal cord stimulation in MS for spasticity relief: Level C Recommendation20–24.

15. Refer for Other Palliative Procedures.

Level U/Expert Consensus

Goal: To improve comfort and to prevent secondary complications.

Procedure: Refer to appropriate specialists. These are elective procedures in which the individual benefits and risks need to be carefully assessed by specialists who have used them to manage spasticity in MS.

15a. Utilize Rehabilitation to Maintain or Augment Other Procedures.

Level U/Expert Consensus

Goal: To combine medical, surgical, and rehabilitative approaches to optimize comfort and positioning and to minimize the risk of secondary complications associated with spasticity, such as skin breakdown and contractures. Some functional benefits may occur.

15b. Monitor

16. Continued Anti-Spasticity Medication and Rehabilitation.

Goal: To provide ongoing treatment to minimize secondary complications and disability. (See Table 6.)
ANALYSIS OF THE EVIDENCE

Following is a summary of the expert panel’s clinical consensus and the literature relevant to key recommendations and elements of the algorithm.

Identify New Onset or Change in Spasticity

Initially, a person with spasticity may have no complaints or concerns related to spasticity. S/he may accept this problem as “part of MS” not realizing that it is treatable. However, history may reveal a “heaviness” of the upper or lower extremity or the inability to move a joint. The person may also report of “jumping of the limbs,” “spasms,” “painful involuntary movements,” or “sudden thrusting of the limbs or the trunk in the wheelchair.” The provider may observe negative findings (those less than the normal resting state), such as muscle weakness, along with positive findings (those in excess of the normal resting state) associated with spasticity, such as increased tendon reflexes, clonus, extensor spasms, flexor spasms, mass reflex, dysynergic co-contraction and associated reactions. (See Table 2.)

Spasticity can be graded using a variety of scales. The Ashworth Scale, Modified Ashworth Scale, and the Spasm Frequency Scale are useful in the clinical setting. (See Tables 3 and 4.) The Ashworth scale and modified Ashworth are very similar. The modified Ashworth scale is preferred by clinicians and researchers.

Are Precipitating Factors Present?

A new onset or change in spasticity may signify the presence of visceral and other noxious stimuli due to treatable, precipitating factors. An exacerbation of MS, progression of MS, treatment with interferon-beta 1b, treatment with a serotonin reuptake inhibitor, the presence of a skin lesion, a fracture, an infection, a renal or bladder stone, an overly full bladder or colon, excess fatigue, extremes of body or ambient temperature, menses, psychological stress, tight clothing, hunger, and other noxious stimuli may increase an individual’s spasticity. (See Table 5.)

The panel recommends that the clinician assess for an underlying cause of the spasticity, and if found, treat appropriately. (Level U/Expert Consensus)

Does Spasticity Result in Other Impairments or Functional Limitations?

The presence of a minor level of spasticity does not warrant treatment. In fact, some spasticity may be beneficial. For instance, spasticity in the lower extremities may prevent dependent edema and deep venous thrombosis in individuals who have paraplegia. Extensor spasticity may permit standing for transfers or assist with ambulation in individuals whose voluntary motor control is too weak to allow these activities. As discussed above, a change in an individual’s “usual” spasticity may also assist in detecting a noxious stimulus in the absence of pain or light touch sensation.

However, complaints or physical findings of spasticity should alert the clinician to a need for assessment and possible intervention. Untreated spasticity may result in any of the consequences outlined in Table 6. The presence of any of these impairments or limitations in activities suggests the need for intervention and ongoing monitoring.

The Panel recommends a thorough assessment of the impact of spasticity on function in order to determine the need for and effects of a treatment program. (Level U/Expert Consensus)
Table 2.  **Symptoms and Signs Associated with Spasticity**

<table>
<thead>
<tr>
<th>POSITIVE</th>
<th>NEGATIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spasms: flexor, extensor, adductor</td>
<td>Weakness</td>
</tr>
<tr>
<td>Velocity dependent increase in resistance to</td>
<td>Reduced dexterity</td>
</tr>
<tr>
<td>stretch</td>
<td></td>
</tr>
<tr>
<td>Clasp knife phenomena</td>
<td>Reduced speed of movement</td>
</tr>
<tr>
<td>Hyperactive deep tendon reflexes</td>
<td>Fatiguability</td>
</tr>
<tr>
<td>Clonus</td>
<td></td>
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<tr>
<td>Abnormal cutaneous reflexes</td>
<td></td>
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<tr>
<td>Co-contraction of antagonist muscle groups</td>
<td></td>
</tr>
<tr>
<td>Associated reactions</td>
<td></td>
</tr>
<tr>
<td>Stiffness</td>
<td></td>
</tr>
<tr>
<td>Heaviness</td>
<td></td>
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<tr>
<td>Pain</td>
<td></td>
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<tr>
<td>Frequent waking from sleep</td>
<td></td>
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</table>

Table 3. **Modified Ashworth Scale**

<table>
<thead>
<tr>
<th>Score</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No increase in tone.</td>
</tr>
<tr>
<td>1</td>
<td>Slight increase in tone. Affected part gives a “catch” when moved in flexion or extension at the end of ROM.</td>
</tr>
<tr>
<td>1+</td>
<td>Slight increase in tone, manifested by a “catch”, followed by minimal resistance throughout the remainder (less than half of the ROM).</td>
</tr>
<tr>
<td>2</td>
<td>More marked increase in tone, but affected part is easily moved.</td>
</tr>
<tr>
<td>3</td>
<td>Considerable increase in tone. Passive movement is difficult.</td>
</tr>
<tr>
<td>4</td>
<td>Affected part is rigid in flexion or extension.</td>
</tr>
</tbody>
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Table 4. **Spasm Frequency Scale**

<table>
<thead>
<tr>
<th>Score</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No spasms.</td>
</tr>
<tr>
<td>1</td>
<td>No spontaneous spasms, but spasms induced with vigorous motor stimulation.</td>
</tr>
<tr>
<td>2</td>
<td>Infrequent spasms occurring less than once per hour.</td>
</tr>
<tr>
<td>3</td>
<td>Spasms occurring more than once per hour, but &lt; 10.</td>
</tr>
<tr>
<td>4</td>
<td>More than 10 spontaneous spasms per hour.</td>
</tr>
</tbody>
</table>
Table 5. Precipitating Factors Associated with Spasticity in MS

<table>
<thead>
<tr>
<th>Exacerbation of MS</th>
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<tbody>
<tr>
<td>Progression of MS</td>
</tr>
<tr>
<td>Disease modifying therapy</td>
</tr>
<tr>
<td>Antidepressant therapy with SSRIs</td>
</tr>
<tr>
<td>Fracture</td>
</tr>
<tr>
<td>Skin lesion</td>
</tr>
<tr>
<td>Renal or bladder stones</td>
</tr>
<tr>
<td>Bladder or colon distension</td>
</tr>
<tr>
<td>Excessive fatigue</td>
</tr>
<tr>
<td>Extremes of ambient or body temperature</td>
</tr>
<tr>
<td>Psychological stress</td>
</tr>
<tr>
<td>Menses</td>
</tr>
<tr>
<td>Tight clothing</td>
</tr>
<tr>
<td>Other noxious stimuli</td>
</tr>
</tbody>
</table>

Table 6. Functional and Activity Limitations Associated with Spasticity in MS

**Functional Limitations (Impairments)**

<table>
<thead>
<tr>
<th>Pain</th>
</tr>
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<tbody>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Poor quality and reduced sleep</td>
</tr>
<tr>
<td>Soft tissue shortening</td>
</tr>
<tr>
<td>Joint contracture</td>
</tr>
<tr>
<td>Cardiopulmonary deconditioning</td>
</tr>
<tr>
<td>Bladder and bowel dysfunction</td>
</tr>
<tr>
<td>Decubitus ulcers</td>
</tr>
<tr>
<td>Poor body image and reduced self esteem</td>
</tr>
<tr>
<td>Difficulty swallowing</td>
</tr>
<tr>
<td>Impaired sexual function</td>
</tr>
<tr>
<td>Poor skin hygiene and/or skin breakdown</td>
</tr>
</tbody>
</table>

**Limitations in Activity and Participation (Disability and Handicap)**

<table>
<thead>
<tr>
<th>Inappropriate positioning in bed or wheelchair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired walking or wheelchair propulsion</td>
</tr>
<tr>
<td>Inability to drive</td>
</tr>
<tr>
<td>Difficult transfers from bed, toilet, bathtub, automobile, etc.</td>
</tr>
<tr>
<td>Falls</td>
</tr>
<tr>
<td>Difficult toileting</td>
</tr>
<tr>
<td>Increased care provider effort</td>
</tr>
<tr>
<td>Difficulty eating</td>
</tr>
<tr>
<td>Difficulty dressing</td>
</tr>
<tr>
<td>Difficulty writing or keyboarding</td>
</tr>
<tr>
<td>Reduced intimacy</td>
</tr>
<tr>
<td>Vocational disability</td>
</tr>
<tr>
<td>Social isolation</td>
</tr>
</tbody>
</table>
HEALTH PROMOTION STRATEGIES

No research evidence directly addresses the effects of community-based exercise programs or general exercise on spasticity in persons with MS. One Class IV study found that bicycle ergometry for 30 minutes three times per week increased passive range of motion (PROM) in the hip adductor/abductor muscles and decreased PROM in hip extension, ankle dorsiflexion, and ankle plantarflexion muscles. However, this finding may have been due to the generalized neurological decline in 6 of the 18 subjects rather than a direct effect of the exercise program.

There has been a dramatic increase in the use of health promoting complementary/alternative medicine strategies (CAM). The many CAM therapies available include those that focus on physical alignment, flexibility, strength, balance, movement, energy flow and relaxation. Studies indicate that CAM use is higher in people with MS than the general population.

CAM use is likely to grow as individuals explore additional strategies when traditional treatments are not available, are not adequately effective, have undesirable side effects, or are unaffordable. Some widely used examples of CAM are: multivitamin therapy, bee sting therapy, T’ai Chi, biofeedback and acupuncture. The effectiveness of CAM therapy in the management of spasticity of MS has not yet been well documented.

Providers should be aware of the commonly used treatments so that the prescribed treatment program is well-integrated with individual’s preferences.

With or without spasticity, people with MS should be encouraged to participate in low to moderate intensity aerobic and strengthening exercise programs to actively stretch muscles, maintain joint range of motion, increase muscle strength, and enhance cardiopulmonary function. Exercise programs must be paced to avoid fatigue and should be conducted in cool environments particularly for those individuals with heat sensitivity. This goal can be achieved through referrals to community-based MS exercise programs or through individualized exercise programs in the home. If the individual requires guidance to begin an exercise program or if he or she encounters difficulty participating in a community based program, referral to a physical therapist for exercise instruction may be appropriate.

While research is needed to assess the benefits of general exercise programs and frequently used complementary/alternative medicine strategies, the panel recommends the use of health promotion strategies for individuals with MS who have mild spasticity without functional changes, and to augment prescribed or non-prescribed interventions for those who have more severe spasticity. (Level U/Expert Consensus) Health promotion strategies include home and community-based programs that promote safe stretching, strengthening, endurance and sustaining of function.

Assessment of Preferences, Complications, Social Support and Other Impairments

If a person with MS has spasticity that is resulting in impairments or limitations in function, serious consideration should be given to treatment. Effective long-term treatment depends not only on an effective management strategy, but also on personal and social factors that promote adherence or self-regulation.

Self-regulation is the active, voluntary, and collaborative involvement of the person and treatment team in the selected intervention. Self-regulation can be increased through careful attention to the factors outlined in Table 7.

Begin to guide treatment by identifying symptoms and functional concerns from Table 6 that are most important to the individual. Spasticity is an impairment that can have a dramatic negative impact on an individual’s ability to perform usual activities, to participate in work and society, and overall perception of quality of life. As stated earlier in this document, spasticity can impact every aspect of an individual’s life and untreated can result in undue morbidity and even mortality.
Unfortunately, spasticity treatment can also be associated with side effects that are undesirable. For instance, individuals may experience sedation, reduced cognition and weakness when treated pharmacologically. In addition, there may be decreased functional status due to the loss of spasticity that was useful in walking or transferring. The clinician and the person with MS must identify the most important and most frequent adverse impact of spasticity, select an appropriate outcome, and choose an intervention that has the best risk benefit profile, and monitor indicators or intervals for follow-up. For example, it may be useful to select functional concerns from Table 6 and the Spasm Frequency Score in Table 4 and have the person keep a diary to assess outcomes of treatment. Side-effect of treatment and impact on function can also be documented.

Individual preferences can also impact self-regulation, such as the desire and ability to exercise. An individual with restricted mobility or poorly managed fatigue or depression may not be able to commit to and follow through with an exercise program. Other preferences that impact adherence include tolerance of medications and the extent of the use of CAM therapy. Strategies to facilitate self-regulation, listed in Appendix B, include a therapeutic partnership, fostering the treatment team-patient relationship, educating the person and care partners, enhancing the patient’s support network, and setting realistic goals.

Joint contracture and skin breakdown are complications associated with spasticity. These are potentially life-altering complications. For example, in the presence of contracture skin is at high risk to break down due to pressure and shear over bony prominences such as the sacrum, medial and lateral malleoli, medial femoral condyles, greater femoral trochanters, lateral and medial epicondyles, and occiput. Also at risk are sites that are difficult to access for appropriate hygiene such as the palmar surfaces of the hands, the antecubital fossae, and the perineum. Therefore, spasticity that is associated with these complications requires aggressive management and monitoring.

Social and economic factors also can alter a person’s ability to self-regulate and may benefit from a comprehensive treatment regimen. These factors include the availability of a care partner, financial resources, the distance from a care provider, and access to transportation.

Other MS related impairments, especially altered cognition, can limit the ability of an individual to self-regulate and participate in a treatment program. Cognitive deficits may be detected in 40-70% of individuals with MS. When considering treatment options, the clinician must take into account that the individual with spasticity and MS may also have decreased attention and concentration, decreased processing speed, diminished comprehension, poor recall, and reduced problem solving. One must recognize that treatment may have additional negative impacts on cognition (i.e. sedating medications). These deficits may alter accurate assessment of outcomes due to poor patient self-report. (Appendix A lists strategies to help recognize and compensate for cognition change.)

The panel recommends that clinicians assess individual preferences, secondary complications associated with spasticity, level of social support, and other impairments that may limit or worsen the effectiveness of treatment. Strategies that promote adherence (self-regulation) are associated with optimal treatment outcomes.

(Level U/Expert Consensus)

<table>
<thead>
<tr>
<th>Table 7. Factors to Consider in Selecting a Management Strategy for Spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferences:</strong> Exercise, Medication, Complementary therapy</td>
</tr>
<tr>
<td><strong>Complications:</strong> Pain, Joint contracture, Skin breakdown, Infection</td>
</tr>
<tr>
<td><strong>Social and economic:</strong> Availability of a care partner, Financial resources</td>
</tr>
<tr>
<td><strong>Other Impairments:</strong> Mobility, Cognition, Fatigue, Depression, etc.</td>
</tr>
</tbody>
</table>
Characterization of Spasticity as Predominantly Focal or Generalized

It is useful to characterize the impact of spasticity as predominantly focal or generalized. Spasticity that is causing primarily focal problems can frequently be treated with skilled rehabilitation strategies alone or neuromuscular blockade plus skilled rehabilitation strategies. Spasticity that is causing primarily general problems is likely to require more intense interventions. The panel recommends using information from the history and physical examination to characterize spasticity as either focal or generalized in order to plan and implement targeted interventions (Level U/Expert Consensus.) The following sections review the evidence in MS for neuromuscular block and skilled rehabilitation strategies before moving on to a discussion of pharmaceutical and surgical procedures.

Neuromuscular Blocks

Spasticity that affects focal functional muscle groups such as the cervical extensors, elbow flexors, wrist flexors, thumb and finger flexors, hip adductors, ankle plantar flexors, and ankle invertors may be effectively managed with alcohol, phenol, or botulinum toxin blocks. Two derivatives of botulinum toxin, Botulinum Toxin Type A and Botulinum Toxin Type B, are available for focal neuromuscular blockade of spastic muscles.

One Class Ib study of Botulinum Toxin Type A met the criteria for inclusion in this guideline. In this small randomized crossover study, the Ashworth Scale and the hygiene score improved significantly after injection of 400 MU botulinum toxin into the adductor muscles. There was no statistical difference in the Spasm Frequency Score. Duration of blockade lasted approximately three months and there were no significant side effects.

Similar improvements in spasticity were reported in a randomized, double-blind, placebo-controlled study of 74 individuals with MS using Botulinum Toxin Type B in the thigh adductors. Studies that assess the effectiveness of alcohol and phenol blocks were not included in this guideline. Supporting studies came from older literature and often included subjects with other central nervous system disorders such as a cerebrovascular accident, brain, or spinal cord injuries.

The panel recommends that focal neuromuscular blocks be done by appropriate specialists (i.e. trained in the use of these blocks to treat spasticity in MS) and repeated as necessary. (Level A Recommendation) Blocks should be done in conjunction with other appropriate skilled rehabilitation strategies. (See below.)

Skilled Rehabilitation Strategies

Skilled rehabilitation strategies are a mainstay of a treatment program whether spasticity is resulting in focal or generalized impairment or functional problems. A comprehensive review of the literature revealed few scientific studies of the effectiveness of rehabilitation in MS (three Class I studies, and in particular of the effectiveness of specific rehabilitation interventions for persons with MS (two Class II studies, ten Class IV studies). One Class I b study evaluated the effects of an inpatient rehabilitation program on 50 people with MS. Twenty-seven individuals were assigned to an inpatient rehabilitation intervention that included twice daily skilled therapy (stretching, mobilization and active intervention) for three weeks and education on a home program. Twenty-three participants were in the comparison group. This group received a one-day training session on a home exercise program and written instructions. At three weeks, there was no statistically significant change in impairments in the inpatient group as assessed by the EDSS. However 48% of this group did demonstrate improvement on two or more steps on the motor domains of the FIM compared to only 9% of the comparison group. These improvements were still apparent in 44% of the inpatient group at week 9 and in only 4.5% of the comparison group. It should be noted, however, that no compliance data was included for the comparison group, nor were direct measures of spasticity recorded.

Another Class I b study compared the effects of a short-term (20 day) inpatient rehabilitation stay.
on 70 individuals with MS. Thirty-six individuals in the inpatient group participated in two physical therapy sessions and one occupational therapy session daily. The interventions provided by the therapists were not specified. The control group (n=34) received no rehabilitation for the duration of the study. At six weeks, both disability and handicap were reduced in the treatment group as compared to the control group.

The panel recommends the use of skilled rehabilitation strategies for both focal and generalized spasticity. (Level U/Expert Consensus)

The following text reviews the existing evidence relating to specific skilled rehabilitation strategies in the management of spasticity in MS.

**Range of Motion**

Range of motion exercise is necessary for maintaining optimum joint mobility and minimizing the risk of joint contracture. The risk for complications associated with muscle and joint tightness and compromised range of motion is far greater for persons with spasticity than those without. Range of motion exercise should be initiated as early as possible for those joints at risk for restriction of full movement.

One Class IV study\(^9\) evaluated the effects on spasticity of therapy using a motorized exercise-cycle. Thirty-five subjects, 31 of whom had a diagnosis of MS, received treatment involving a 30-minute session where the participant operated an exercise cycle at a speed of 40 revolutions per minute. EMG studies completed immediately prior to and post treatment demonstrated a decrease in the mean F-wave amplitude / M-response ratio in 46 legs tested, demonstrating a reduction in motoneuron excitability. As with the previous study, direct measures of spasticity were not recorded. (Level U/Expert Consensus)

**Stretching**

Stretching is crucial in minimizing the risk for muscle shortening secondary to spasticity. Shortening of the soft tissues inevitably results in decreased range of motion, and may result in pain and loss of function (increased disability). It may be efficient to focus on commonly shortened muscles (e.g. iliopsoas which may contribute to low back pain and gait disorders, and biceps which may limit coordinated upper extremity function) and those muscles that cross two joints (e.g. rectus femoris, and gastrocnemius). For optimal effect, stretching must be performed daily. A stretch must be sustained in order to impact spasticity; some practitioners suggest holding a stretch for >1 minute, while others suggest that a prolonged stretch (hours) must be maintained by using a splint or a brace. (Level U/Expert Consensus)

**Strengthening**

There is a risk of progressive weakening of spastic muscles due to inactivity. As a result, it is important that strengthening programs are initiated early, and that strength in spastic muscles is optimized. There is no existing literature to suggest one form of strengthening exercise over another, however care must be taken to avoid programs that increase an individuals overall fatigue. (Level U/Expert consensus)

See also Fatigue and Multiple Sclerosis: Evidence-Based Management Strategies, Kinkel, R. Philip, et al., October 1998.

**Light Pressure/Stroking**

Light pressure or stroking may be an adjuvant to enhance muscle stretch and joint range of motion. One Class 4 study of stroking\(^33\) evaluated 10 subjects with MS out of a cohort of 22. Stroking decreased the alpha-motoneuron excitability. Light pressure or stroking may be used to facilitate an inhibitory response, but there is insufficient evidence to support its use as an independent modality.

**Cold Therapy**

Six studies of various cold treatments for persons with MS were included.\(^13, 14, 32, 34, 35, 37\) One level 2b study\(^12\) had 14 participants rest in a cold-water bath (24°C) for 20 minutes and measured spasticity with a modified Ashworth scale immediately following the cold bath. Core body cooling assessed by tympanic temperature was not obtained. The researchers observed that tone was increased during the bath but there were no objective measurements either during or after bathing.
A Class 4 study\textsuperscript{32} had subjects actively move their limbs while in a cold-water bath (80°F/27°C) for 10 minutes. No specific measures of spasticity were collected, however 10 of 10 subjects reported a feeling of relaxation and less muscle tension following the cold-water bath and 3 of 10 showed an immediate and remarkable increase in their ability to ambulate following the bath. Another Class 4 study\textsuperscript{36} found that decreasing core body temperature by 0.6-1.2°F by submersion in cold-water baths (70-80°F) improved “spastic paraplegia/paraparesis” while the body was cool in 5/6 subjects with spasticity. The method of assessing spasticity was not specified. This study also observed that exposure to cold without core body temperature reduction elicited no change in spasticity.

In summary, evidence to support cold-water baths as an effective treatment for spasticity in persons with MS is equivocal.

Several other studies examined the effects of applying cold locally to the skin. A level 2b study\textsuperscript{14} applied cold packs (16°F) to the axillary region, posterior and lateral neck, groin, and popliteal fossa for 20 minutes. In this study, oral temperature was reduced only 0.2-0.7°F. Indirect measures of spasticity, speed of hand and foot movements, the Quantitative Evaluation of Neurological Function did not improve significantly secondary to cold pack application.

A Class 4 study\textsuperscript{35} applied towels soaked in ice water to the lower extremities for 7 minutes, with cold towel exchanges every 30 seconds. Following cold towel application, skin temperature decreased from a mean of 88°F to 66°F. In 10 of 10 subjects, spasticity as measured by EMG recordings during a stretch reflex decreased during application of the cold towels. However, when the cold towel treatment was discontinued, the reflex response returned quickly to baseline levels.

A more recent Class 4 study\textsuperscript{34} applied a cooling vest and head cap with channels for circulating cooling fluid to 14 ambulatory and 6 wheelchair dependent individuals with MS. The cooling garments were worn for 40 minutes twice weekly for two weeks. Rectal temperature was decreased by 0.2°C in those who were ambulatory and by 0.29°C in the individuals using a wheelchair. Spasticity, as measured on the Ashworth scale, was reduced in 5/6 of those in the ambulatory group and in 6/6 of those using a wheelchair. Strength and gait skills were also improved in many of the individuals following cold treatment. Participants in this study subjectively reported a persistent positive effect of cooling for up to 12-24 hours following treatment.

In summary, evidence to support local cold applications is once again equivocal. Temporary relief may be gained by use of cold towel application whereas cooling garments may provide relief for hours.

The panel recommends the use of swimming/exercising in cool pools (80-82°F) to actively stretch spastic muscles and maintain/build endurance. Local applications of cold, e.g. cold towels or cold packs, may be recommended for temporary relief of localized muscle spasms and spasticity. Initial research on cooling garments is promising in terms of reducing spasticity and cooling garments should be considered as a treatment to provide at least short-term reductions in spasticity. There is insufficient evidence to support the use of cooling as an independent modality in the management of spasticity. In any application of heating or cooling modalities, intactness of the individual’s sensory system should be considered to minimize the risk of tissue damage. (Level B Recommendation)

Heat Therapy

Many people with MS are heat sensitive and experience a temporary worsening of their symptoms, including spasticity, when exposed to warm environments. A Class IV study\textsuperscript{36} examined the effects of induced hyperthermia on neurologic diseases. In this study, one hundred participants, 12 of whom had a diagnosis of MS, were exposed to warm (110°F) water for 20 to 30 minutes. All of the individuals with MS developed neurological changes following exposure. When compared to people from other diagnostic groups, these changes were found to occur more frequently and at a lower elevation in body temperature.

The panel does not recommend the use of heat to treat spasticity in individuals with MS. The use of
warm pools may be appropriate for carefully selected individuals. (Level U/Expert Consensus)

**Education**

When utilizing any first line rehabilitation strategies in the management of spasticity, interventions must carry over into a person’s daily routine. Adherence to home exercise programs is crucial. Education equips individuals to make informed decisions regarding their healthcare. Education fosters investment of people in their own treatment plans, and also facilitates active participation in the ongoing treatment process. (Level U/Expert Consensus)

**Use of Compensatory Strategies to Optimize Energy Effectiveness**

Individuals with disability due to spasticity may need to utilize compensatory strategies and/or adaptive equipment to minimize the effort associated with completion of a task, or to ensure their safety. See *Fatigue and Multiple Sclerosis: Evidence-Based Management Strategies*, Kinkel, R. Philip, et al., October 1998.

**Gait Training**

The panel does not recommend gait training as a specific treatment for spasticity, but does recommend that this modality be used in conjunction with orthotics and mobility aids. The goal is to enhance the safe use of assistive technology and to develop a safe mobility program. (Level U/Expert Consensus)

**Orthotics and Mobility Aides**

No research evidence is available regarding the effectiveness of assistive technology as a specific treatment for spasticity in persons with MS. However, it is widely recognized that persons who have MS with spasticity benefit from the use of orthotics and mobility aids to maintain safe mobility. As with other personal assistive technology such as hearing aids and eyeglasses, there is some role for “off-the-shelf” equipment, but customized options should be considered for long term use when the person with MS has specific needs (muscle atrophy, instability, or body height or weight that is not “average”). Orthotics can provide support to joints and maintain musculotendinous extensibility to facilitate proper postural alignment. Orthotics should also be considered for use in conjunction with neurolytic blocks when indicated. Use of mobility aids may reduce energy costs and improve balance and functional mobility, allowing the individual to participate more fully in activities of daily living and employment. Referral to a qualified therapist for training on the safe use of orthotics and mobility aids may be appropriate. The panel recommends the prescription of training in and use of upper and lower extremity assistive technology to optimize function in individuals whose spasticity has resulted in treatable impairments and disability. (Level U/Expert Consensus)

**Wheelchairs**

When gait is no longer energy efficient or safe, wheeled mobility aids should be considered. While manual wheelchairs may suffice for a limited number of persons with MS, many will require motorized scooters or power wheelchairs to avoid excessive fatigue. Motorized scooters are recommended for those individuals with adequate trunk and upper extremity control. Customized seating options may be necessary to prevent skin breakdown by avoiding pressure and sheer of skin over high-risk areas (described on page 10). Referral to a qualified, experienced therapist is appropriate to assess the abilities and needs of the individual with MS and to determine the most appropriate wheeled mobility device. (Level U/Expert Consensus)

**Transcutaneous Electrical Nerve Stimulation (TENS)**

TENS is used to control pain for a wide variety of disorders. Two Class 4 studies were reviewed on the effectiveness of TENS with MS spasticity. Both found that TENS decreased pain associated with painful muscle spasms in some of the subjects. One study applied TENS electrodes directly over painful muscles during nighttime sleeping and found pain “completely controlled” in 4/8 and “significantly reduced” in 2/8 individuals. Sleep disturbance was also significantly reduced. The other study applied TENS (similar to TENS) along the lumbar spine for at least 8 hours/day and found a reduction in
painful spasms in 5 of 9 participants. The panel recommends the use of TENS for painful spasms, especially if the spasms significantly disrupt sleep. (Level U/Expert Consensus) TENS should be prescribed on a trial basis and purchase of a unit is reserved for those individuals who complete a successful trial period. Referral to a physical therapist for effective instruction in application of TENS units is appropriate when TENS treatment is indicated. (Level U/Expert Consensus)

**Electrical Stimulation**

Electrical stimulation is applied to spastic muscles to cause muscle fatigue. When applied to antagonistic muscles, the intent is to inhibit the spastic muscle through a spinal reflex loop with reciprocal inhibition. Only one study\(^\text{16}\) has examined the effectiveness of surface electrical stimulation on spasticity in persons with MS. In this Class IIb study, 37 persons with MS received surface electrical stimulation to the quadriceps and hamstring muscles for 30 sessions during a 6-week period (2 minutes at 3Hz, 5 minutes at 10 Hz, and 5 minutes at 35 Hz with active movement). Spasticity, measured by verbal report of the subjects, did not change significantly during the 6-week period.

A number of other studies that were unclassified because they did not include subjects with MS\(^\text{38-44}\) were reviewed. These articles examine surface electrical stimulation applied to either the spastic muscle or its antagonist in persons with spinal cord injury or cerebral vascular accidents. They have found electrical stimulation to be relatively effective in reducing spasticity. Based on this evidence, the panel neither recommends nor discourages use of surface electrical stimulation as a treatment of spasticity in persons with MS. Surface electrical stimulation may be of benefit in reducing spasticity in persons with MS, but there is currently no evidence to support this supposition at this time. (Level U/Expert Consensus)

**Magnetic stimulation**

One Class Ib study\(^\text{18}\) evaluated noninvasive transspinal repetitive magnetic stimulation in 21 individuals with MS with spasticity \(\geq 2\) on an Ashworth scale and who were able to ambulate at least 10 meters. Spasticity was evaluated using the Ashworth score, reflex activity, and participant’s rating of ease of daily activity. The treated group’s clinical score improved by 18%, a statistically significant improvement compared to no change in the group of 17 individuals who received sham treatment. The threshold of the stretch reflex also increased in the treated group compared to the sham group and remained improved for eight days. Ease of self-care improved in both groups. Side effects in the intervention group included brief dizziness and a short lasting “tight feeling” around the midthoracic level.

Use of magnetic stimulation is not commonly used in the clinical setting to treat persons with MS and only one study has been conducted to establish its effectiveness in this population. Therefore, while the panel does not recommend magnetic stimulation for routine treatment, it may be considered when other therapies are either not effective or desirable. (Level U/Expert Consensus)

**Oral Pharmacotherapy**

Oral agents are effective in the treatment of spasticity in MS. Treatment should be individualized based on consideration of efficacy, side effects, cost, and ability to follow up with a care provider. Table 8 summarizes the factors to be considered when selecting an oral agent. Based on these factors, the panel recommends starting with one agent, either baclofen or tizanidine, for spasticity that lasts most of the day. (Level A Recommendation) A step therapy approach with individual agents should precede the use of combination therapy. (Level U/Expert Consensus) Head-to-head studies of baclofen and tizanidine fail to demonstrate any compelling differences between the two agents in their effects on spasticity. (Level B Recommendation) The following text summarizes the literature included in this guideline.
### Table 8: Synthesis of Commonly Used Oral Anti-Spasticity Agents

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Levels of Evidence</th>
<th>Efficacy</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Adverse Events</th>
<th>Precautions</th>
<th>Dose</th>
<th>Cost ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baclofen (Lioresal®)</td>
<td>1 lb², 4 lb 10, 46-62, 7 lb 7, 49-54, 1 lb 55, 56</td>
<td>3+</td>
<td>- sedation</td>
<td>- withdrawal</td>
<td>- seizures</td>
<td>Abrupt discontinuation has resulted in muscle rigidity and exaggerated rebound spasticity, severe high fever, altered mental status, and has progressed in rare instances to rhabdomyolysis, multiple organ system failure and death.</td>
<td>5mg orally 3 times a day; increase dosage by 15 mg/day every 3 days to a maximum dose of 80 mg/day (5-4 divided doses)</td>
<td>TAB, PO, 100mg, 100s, $ 61.91 20mg, 100s, $109.62</td>
</tr>
<tr>
<td>Tizanidine (Zanaflex®) tablet capsule</td>
<td>5 lb 57, 61</td>
<td>3+</td>
<td>- sedation</td>
<td>- dizziness</td>
<td>- hepatitis</td>
<td>Concomitant use of oral contraceptives (clearance is reduced by approximately 50%) congestive heart failure or cardiac arrhythmias hypotension or concurrent antihypertensives liver disease renal impairment</td>
<td>Initial: 4 mg/day orally and gradually increase 2-4 mg over 2-4 weeks Maintenance: 8 mg orally tid-qid (maximum dose 36 mg/day)</td>
<td>TAP, PO, 2mg, 150s, $183.65 4mg, 150s, $219.50</td>
</tr>
<tr>
<td>Baclofen vs. Tizanidine</td>
<td>1 lb 62, 5 lb 63-67</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CAP, PO, 2mg 4mg 6mg,</td>
</tr>
<tr>
<td>Dantrolene sodium (Dantrium®)</td>
<td>4 lb 69, 70, 71, 74</td>
<td>2+</td>
<td>- weakness</td>
<td>- lightheadedness</td>
<td>- hepatitis</td>
<td></td>
<td>25 mg orally once daily for 7 days, then 25 mg 3 times a day for 7 days, then 50 mg 3 times a day for 7 days, then 100 mg 3 times a day (maximum dose 100 mg 4 times a day); use lowest effective dose</td>
<td>TAP, PO, 25 mg, 100s, $100.50</td>
</tr>
<tr>
<td>Diazepam (Valium®)</td>
<td>2 lb 72, 73</td>
<td>2+</td>
<td></td>
<td></td>
<td>- withdrawal</td>
<td>Avoid abrupt withdrawal Concomitant use of other psychotropic or anticonvulsant agents Elderly and debilitated patients Hepatic insufficiency Patients with limited pulmonary reserve Pregnancy Severely depressed patients Simultaneous ingestion of alcohol</td>
<td>-2-10 mg orally 3-4 times a day Discontinuation dosing: Gradually taper dosage after extended therapy; avoid abrupt discontinuation</td>
<td>TAP, PO, 2mg, 100s, $10.65 5mg, 100s, $16.65 10mg, 100s, $31.55</td>
</tr>
<tr>
<td>Gabapentin (Neurontin®)</td>
<td>1 lb 75</td>
<td></td>
<td>- little drug interaction</td>
<td>- drowsiness</td>
<td>- titration</td>
<td>Abrupt discontinuation may precipitate status epilepticus renal insufficiency</td>
<td>Initial: 100 mg orally 3 times daily Daily maximum: 600-800 mg qid</td>
<td>CAP, PO, 100mg, 100s, $33.15 300mg, 100s, $112.96 400mg, 100s, $159.53</td>
</tr>
<tr>
<td>Tizanidine vs. Gabapentin</td>
<td>1 lb 65, 5 lb 63-67</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dantrolene vs. Diazepam</td>
<td>1 lb 74</td>
<td></td>
<td></td>
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<tr>
<td>Baclofen vs. Diazepam</td>
<td>2 lb 56, 47</td>
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<tr>
<td>Baclofen vs. Dibenzepam</td>
<td>1 lb 52</td>
<td></td>
<td></td>
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</tbody>
</table>
Baclofen

There are fourteen studies evaluating baclofen: one Ia systematic review,8 four Ib,10, 46–48 seven Ib7, 49–54 and two IV.55, 56 The findings demonstrate a consistent effect on change in spasticity as measured by the Ashworth Scale,8, 47, 52, 54–56 resistance to stretch,48, 49, 51, 76 spasm frequency,7, 10, 49 deep tendon reflexes, 10, 49, 50, 55, 56 clonus, 7, 8, 47, 49, 50, 54, 55 subjective improvement in function,59–51, the Barthel Functional Assessment7 or other measures of daily living,8, 49 pain,8, 10, 49, 50 gait,8, 47, 54 and on electrophysiologic measures of H-reflex modulation during walking.55

The systematic review done in 1972 included 343 people with MS who were involved in clinical trials of baclofen in 18 countries between 1968 and 1970. In approximately 70% of subjects with MS, therapeutic effect was seen in spasticity, clonus, flexor spasms, pain, ability to manage without assistance, and facilitation of active or passive physiotherapy. Not all subjects improved to the same extent. Forty-nine percent of subjects had a slight improvement in spasticity, 12.7% had a moderate improvement, and 6.8% a good to very good improvement compared with placebo. Improvements for pain were slight in 20.5%, moderate in 22.9%, and good/very good in 28.9%. Walking was slightly improved in 27.1%, moderately improved in 16.2% and good or very good in 15.2%. Doses in these studies ranged up to 225 mg, although side effects at the higher doses are more common than at 100 mg/day. The later dose results in similar therapeutic effects, but a lower frequency of side effects. The authors point out that doses vary individually and effective treatment can be seen in the 30-70 mg range.8

While laboratory changes are uncommon,8 other side effects can be expected in about 30% of individuals and usually can be managed by titration of dose.8, 53 The systematic review reported that side effects were bad enough to nullify the therapeutic value of the medication or to require withdrawal of baclofen in 4-5% of the individuals with MS.7, 10 The most common side effects are drowsiness,7 nausea, vertigo, and dry mouth. One study54 estimates that in MS, side effects that can be attributed to appropriately dosed baclofen are less than 10%, although another study60 suggests they are more common. Weakness is also reported,7, 53 and in one study48 3 of 21 subjects on baclofen experienced significant weakness associated with difficulty walking and falls. Prevalence of weakness associated with baclofen treatment was estimated at less than 0.5%.54 One small study54 attempted to measure the impacts of baclofen on gait unsteadiness and postural instability in mildly spastic individuals with MS. This underpowered study demonstrated a statistically significant improvement in the vertical unsteadiness during gait in the treated group and trends in improvement in almost all gait parameters. Careful titration is essential since the effective dose is highly variable. Too high a dose causes weakness and other side effects and too low a dose is ineffective.

The panel recommends baclofen as an effective agent to treat spasticity. (Level A Recommendation)

Tizanidine

There are five Ib trials of tizanidine versus placebo.57–61 Dose ranged from 2–36 mg in these studies. Three studies57, 59, 61 showed a statistically significant decrease in the Ashworth score, but one60 did not. One study60 showed a decrease in subjective spasms, but another61 did not. One study58 reported a decrease in ankle dorsiflexion tone, cumulative limb tone, ankle clonus, and improved scores on the Ambulation Index in the treated group.

Overall, all five studies demonstrated that tizanidine is an effective anti-spasticity agent. Tizanidine comes in tablet and capsule preparations. The capsule may be taken with food without a surge in plasma concentration levels. Both preparations require slow titration to manage the sedative side effects. Common side effects are dizziness, drowsiness, dry mouth, and fatigue.58, 61 Marked increases in transaminase levels were also seen.58, 60, 61 There was a single instance of drug-induced hepatitis.60 Isolated instances of hallucinations were also reported.60

The panel recommends tizanidine as an effective anti-spasticity agent.
agent to treat spasticity. (Level A Recommendation) Generally, laboratory changes are uncommon.58

**Baclofen versus Tizanidine**

There were six head-to-head trials of baclofen with tizanidine.62-67 Of these trials, one was a Ib study62 and the other five were IIb studies-. Both drugs proved effective; muscle strength improved with both agents. Tizanidine was associated with more sedation while more weakness was associated with baclofen.64, 66, 67 In one study,64 the use of baclofen was restricted because of muscle weakness and falls.

The evidence from trials of baclofen versus tizanidine does not overwhelmingly support the use of one agent over the other. The panel recommends an informed decision by the person in consultation with a knowledgeable provider. (Level B Recommendation)

**Other Pharmacotherapy**

While pharmacological management of spasticity in MS should be initiated with trials of baclofen or tizanidine, the panel recognizes a role for other agents. In selecting an agent, the individual and provider should consider both the level and amount of evidence demonstrating effectiveness, as well as perceived individual risks and benefits including side-effects, convenience, and cost. (See Table 8.)

**Carisoprodol:** There is one Class IV study of carisoprodol1 that demonstrated subjective relief in spasticity. The timeframe of assessment was not specified. The most common side effects included drowsiness. No additional studies on subjects were located.

**Dantrolene:** There are four Ib studies69-71, 73 that assessed dantrolene. Dantrolene was effective in managing spasticity by objective and subjective measures. Side effects were common including weakness, lightheadedness, nausea, dizziness, diarrhea, speech difficulty, drowsiness, incoordination, and lethargy. These side effects limited some people’s willingness to continue use of this agent. Due to the possibility of hepatotoxicity, appropriate monitoring of liver functions is essential.

**Diazepam:** There are two Ib studies72, 73 that demonstrate the effectiveness of diazepam using a 10 item exam evaluating spasticity, clonus, hyperreflexia, stiffness, and cramping68 and a clinical scale and EMG/force recordings.73 Doses in the two studies were 2 mg qid and 5 mg qid73 and 10 mg tid.72 Side effects included drowsiness and weakness.

**Gabapentin:** There is a single 1b short-term study75 of 15 patients using gabapentin which suggests this drug may be of value in treatment of spasticity. In this study, there was statistically significant improvement in the Ashworth Scale, clonus, and patient ratings at 48 hours. Side effects were mild drowsiness, reported in one patient.

**Tizanidine versus Diazepam**

One Ib study compared tizanidine to diazepam in 30 subjects.58 Subjects received an average of 14.3 mg/day in the tizanidine group and 15.0 in the diazepam group. Spasticity, measured by the Ashworth Scale, improved in 9 patients in each group and deteriorated in one patient in the diazepam group. All 4 dropouts were in the diazepam group. Muscle weakness and drowsiness was more common in the subjects treated with diazepam.

**Dantrolene versus Diazepam**

One Ib study compared dantrolene sodium 25 mg or 75 mg qid to diazepam 2 or 5 mg qid.74 Both agents were effective in reducing spasticity, stretch reflexes, and clonus. Both agents had commonly reported side effects. Drowsiness, imbalance and incoordination were statistically significant in the diazepam group. Dantrolene sodium was associated with muscle weakness at both doses, but diazepam was associated with weakness at the high doses only. Dantrolene increased postural stability while diazepam decreased it. Diazepam was associated with coordination and walking speed while dantrolene was not. At the conclusion of the study, subjects preferred dantrolene over diazepam, but at six-month follow up the numbers on dantrolene sodium and diazepam were equal.
Baclofen versus Diazepam

Baclofen has also been examined in two Ib head-to-head trials with diazepam\(^4\) and \(^5\) and a IIb head-to-head trial with clonazepam.\(^6\) In all three of these studies, baclofen resulted in an improvement in the Ashworth Scale but was not statistically different from the comparison agent. In one study,\(^7\) there was benefit in reducing spasm frequency and clonus, although not in bladder measures or ambulation. Side effect profiles were similar although there was more sedation with diazepam.

Baclofen versus Clonazepam

There is no individual study assessing baclofen versus clonazepam.

Delta-9-THC:

There are two IIb studies of Delta-9-THC with differing results.\(^7\) In one,\(^8\) patients on the active agent reported a significant reduction in their spasticity compared to placebo, but there were no differences in the five areas of motor function as assessed by a physician. In the second study,\(^7\) there were objectively measured decreases in DTRs, muscle resistance, and abnormal reflexes. In the first study, nearly all patients experienced side effects including weakness, dry mouth, dizziness, relaxation, and impairment of cognitive function, while in the second study side effects were minimal compared to placebo. The commercial preparation of Delta-9-THC is a Schedule 3 drug indicated for nausea and appetite stimulation in HIV patients. Its use for spasticity and pain is off-label.

Intrathecal Therapy

Implantable pumps for delivery of intrathecal medication to reduce spasticity have been generally available since 1992.\(^9\) Initially, treatment was oriented towards patients with severe spasticity, but recently patients with ambulatory function have received pumps for spasticity management (anecdotal evidence). In three Ib studies,\(^3\) \(^8\) \(^0\) \(^1\) intrathecal baclofen has been demonstrated to be effective in reducing spasms and spasticity as measured on the Spasm Frequency Scale and the Ashworth Scale. In one study,\(^1\) pain was also assessed and found to be managed effectively. Long-term patient benefits have also been found.\(^3\) Several other uncontrolled (Class IV) studies have confirmed the effectiveness of intrathecal baclofen in reducing both spasm frequency and resistance,\(^7\) \(^8\) \(^1\) \(^2\) \(^3\) \(^4\) \(^5\) \(^6\) reduced side effects due to discontinuation or reduction in oral medications, as well as reduced need for attendant care.\(^6\)

Intrathecal doses are titrated to the individual’s needs. In one trial,\(^3\) intrathecal doses ranged approximately from 62 ug to 749 ug/day with a mean dose of 340 ug/day while in another,\(^6\) were titrated from a minimum of 82 ug to a maximum of 570 ug over a ten month period. Pumps are refilled percutaneously in a simple, outpatient visit every 1-3 months depending on dose and concentration of medication.

Lightheadedness, confusion and headaches are reported side effects during the initiation of intrathecal treatment, but these effects resolve over time. The most frequent complications of long-term use of intrathecal baclofen have been tube-kinking, blocking with tissue at the tip, or cracking.\(^3\) \(^8\) \(^1\) \(^2\) \(^3\) \(^4\) \(^6\) Pump failures occurred more commonly with earlier models and are now rare.\(^3\) Pump battery life is about 5 years and the pump is replaced when the battery fails. Wound infections and erosion of the pump through the abdominal wall sometimes occur.\(^4\) Meningitis has occurred but is rare.\(^3\) Medication overdose and underdose can result in severe adverse events. Failure to obtain a refill on schedule can result in withdrawal. Other problems with dosage are most often due to human error and risk can be reduced by scrupulous detail in pump management. (See Table 9.)

Other medications have been considered for use in intrathecal therapy, particularly morphine and clonidine. Morphine has been used to control spasticity, usually when individuals develop tolerance to baclofen,\(^6\) but it is not used routinely to treat spasticity except during brief periods of time when the person is taken off of baclofen in an attempt to decrease the likelihood of tolerance. Clonidine has also been used with only anecdotal reports of benefit.

The panel recommends that individuals with an EDSS (Expanded Disability Status Scale\(^1\)) of 7 or
greater can be successfully managed with intrathecal baclofen. (Level A Recommendation)
In addition, selected individuals with EDSS 5.0 – 6.5 can be successfully managed with intrathecal baclofen. (Level C Recommendation) These individuals should be referred to a center with extensive experience for baclofen pump evaluation, implantation, and management. (Level U/Expert Consensus)

**Palliative Surgical Procedures**

Many palliative procedures have been developed for treatment of severe spasticity of multiple sclerosis that is unresponsive to health promotion strategies, physical modalities and oral medications.\(^87, 88\) Such ablative procedures are usually indicated only for those spastic limbs with no functional voluntary movement. These procedures include tenotomies, paravertebral spinal nerve blocks or intrathecal nerve root blocks with either phenol\(^87\) or alcohol. Open ablative procedures include posterior rhizotomy or lumbar myelotomy to disrupt spinal reflex pathways and thus reduce spasticity. The panel recommends that these procedures be considered only in carefully selected individuals who are refractory to other management strategies. (Level U/Expert Opinion)

**Conclusion**

The algorithm and associated recommendations presented here, supported by currently available evidence in the literature, provide a coherent plan and set of guidelines for the treatment and management of spasticity in individuals with MS. Further research focusing on the anatomical and physiological basis for spasticity is likely to increase the availability of more selective therapeutic approaches.

Published research of interventions to manage spasticity in MS will benefit from explicit discussion of the research design and methodology including:

1. Use of valid and reliable measurement of spasticity, 2. assessment of associated secondary impairments, 3. recruitment and description of an appropriate number of individuals with MS who are willing to be randomized, 4. specification of the randomization procedure, 5. efforts to retain the recruited population and appropriate handling and discussion of drop-outs, 6. use of placebo control, sham procedures, or appropriate cross over designs, 7. observer blinding, 8. clear description of the intervention and measures to assess adherence, 9. a prior assignment of primary and secondary outcomes, 10. recruitment of sample size necessary to address the primary outcome and analysis of statistical power, 11. solid statistical analyses including multi-variate analysis if possible, 12. thorough discussion of biases and limitations.

This guideline and its future enhancements can facilitate behavioral changes in practice and in research to minimize the often devastating impacts of spasticity associated with MS.
## Table 9: Synthesis of Commonly Used Other Anti-Stretch Agents

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Levels of Evidence</th>
<th>Efficacy</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Adverse Events</th>
<th>Precautions</th>
<th>Dose</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botulinum Toxin Type A (Botox®)</td>
<td>1 B, 11</td>
<td>3+</td>
<td>-Useful in focal spasticity or in combination</td>
<td>-Electromyographic guidance</td>
<td>-Weakness</td>
<td>-Peripheral motor neuropathic diseases or neuromuscular junctional disorders due to increase risk of significant systemic side effects compared to oral</td>
<td>30-400 Units, divided among affected muscles</td>
<td>IM, 100 Units $552.50</td>
</tr>
<tr>
<td>Botulinum Toxin Type B (Myobloc®)</td>
<td>1 B, 12</td>
<td>3+</td>
<td>As above</td>
<td>As above</td>
<td>-Weakness</td>
<td>-Use lower doses if no history of tolerating botulinum toxin injections</td>
<td>2500-5000 Units IM divided among affected muscles</td>
<td>IM, 5000 Units $362.50</td>
</tr>
<tr>
<td>Alcohol, 100% Phenol 3-5%</td>
<td>11b, 17</td>
<td>3+</td>
<td>As above</td>
<td>-Electromyographic guidance</td>
<td>-Weakness</td>
<td>-Peripheral motor neuropathic diseases or neuromuscular junctional disorders due to increase risk of significant systemic side effects compared to oral</td>
<td>30-400 Units, divided among affected muscles</td>
<td>IM, 100 Units $552.50</td>
</tr>
<tr>
<td>Baclofen (Lioresal® 17)</td>
<td>4 B, 5, 20, 31, 39</td>
<td>3+</td>
<td>-Potential for reduced systemic effects compared with oral</td>
<td>-Cost</td>
<td>-Hypotonia</td>
<td>-Intake</td>
<td>Same as for oral baclofen</td>
<td>Refills 0.5 mg/mL, $49.99</td>
</tr>
<tr>
<td></td>
<td>7 IV, 7, 9, 32, 90</td>
<td></td>
<td>-Titratable</td>
<td>-Surgical/procedural complications</td>
<td>-Dizziness</td>
<td>-Intake</td>
<td></td>
<td>2 mg/mL, $103.94</td>
</tr>
</tbody>
</table>

**Spasticity Management in Multiple Sclerosis**

**Table Notes:**
- Levels of Evidence: 1 A, 2 B, 3 C, 4 D
- Efficacy: 1 Strong, 2 Moderate, 3 Weak
- Advantages: - Usefulness in focal spasticity or in combination
- Disadvantages: - Peripheral motor neuropathic diseases or neuromuscular junctional disorders due to increase risk of significant systemic side effects compared to oral
- Adverse Events: - Weakness
- Precautions: - Use lower doses if no history of tolerating botulinum toxin injections
- Dose: - 30-400 Units, divided among affected muscles
- Cost: - IM, 100 Units $552.50
- Refills: - 0.5 mg/mL, $49.99
- 2 mg/mL, $103.94
REFERENCE LIST


50. Basmajian JV, Yucel V. Effects of a GABA—


71. Sheplan L, Ishmael C. Spasmyolytic properties


APPENDIX A

STRATEGIES TO ENHANCE COGNITIVE FUNCTION

- Make lists
- Use calendars for appointments and reminders
- Develop a memory notebook to log daily events, reminders, diary of medication effect
- Organize environment so that items used regularly remain in familiar places
- Modify the clinical environment for learning and recall (e.g. heat, light, seating, etc.)
- Schedule teaching session for early in the day and limit to a short period of time to minimize fatigue
- Conduct conversations in quiet places to minimize distractions
- Repeat information and write down important points
- Use simple, step by step instructions—include the “obvious” (i.e. if medication is not effective at the prescribed dosage call the physician for titration instructions)
- Follow verbal instructions with written back-up and use “visuals” (i.e. titration chart or diagram) when possible
- Involve care partners in instructions (i.e. follow-up phone calls to care partner, family at home)
- Teach basic organizational skills
- Openly discuss concern about cognitive dys function
- Have the care partner monitor for safety
- Introduce change slowly, one step at a time
- Refer for formal cognitive evaluation
APPENDIX B

STRATEGIES TO FACILITATE ADHERENCE/SELF REGULATION

• Foster a collaborative relationship
• Take the time to empathize and sympathize
• Establish a trusting relationship
• Establish a sense of support (availability and accessibility)
• Be sensitive to and provide necessary support for cultural differences, body image and gender concerns
• Educate and reinforce learning
• Provide understandable information regarding benefits/side effects, risks of therapy
• Give simple, structured instructions
• Provide care partners with instruction
• Encourage use of tape recording, memory note book, etc
• Furnish a non-distracting environment
  Offer reinforcement
• Enhance the support network
• Sustain access to health care system
• Facilitate access to home health care agencies
• Involve care partners/home-care nurses
• Refer to physical/occupational therapist
• Involve family and friends in care
• Suggest phone contact with other professionals
• Provide community referrals (e.g., National MS Society, Church groups, etc.)

• Interact with case managers, insurance providers, pharmacies, and access programs
• Refer to social worker and vocational rehabilitation
• Contact pharmaceutical company-funded patient support programs
• Present realistic expectations
• Help prioritize interventions
• Use hopeful approaches
• Offer options
• Facilitate coping strategies (relaxation, deep breathing, visualization, etc)
• Consider concomitant illnesses (e.g., psychiatric disorders)