

## THERAPEUTIC OPTIONS

### NONBEHAVIORAL AND BEHAVIORAL THERAPIES FOR SPASTICITY

Treatment/Class/Agent*	Advantages	Disadvantages
<b>Pharmacotherapy</b>		
<b>Oral Medication</b>		
<b>Muscle Relaxants</b>		
Baclofen	<ul style="list-style-type: none"> <li>Most effective in treatment of spasticity caused by multiple sclerosis or other diseases of the spinal cord<sup>1</sup></li> <li>Decreases frequency and severity of painful spasms, especially flexor spasms in spinal cord lesions<sup>1,2</sup></li> <li>Reduces increased muscle tone<sup>1</sup></li> <li>Improves range of joint movement<sup>3</sup></li> <li>Decreases frequency and severity of sudden painful spasms<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>Weakness<sup>1-3</sup></li> <li>May impair the patient's ability to walk or stand<sup>1,2</sup></li> <li>Sedation<sup>2,3</sup></li> <li>Fatigue<sup>2,3</sup></li> <li>Nausea<sup>2,3</sup></li> <li>Dizziness<sup>1,3</sup></li> <li>Mental confusion<sup>1,2</sup></li> <li>Sudden withdrawal may cause hallucinations,<sup>3</sup> anxiety,<sup>1</sup> tachycardia,<sup>1</sup> or seizures<sup>3</sup></li> <li>Benefits less clear on functional skills, such as mobility or activities of daily living<sup>2</sup></li> </ul>
Dantrolene	<ul style="list-style-type: none"> <li>Exerts effects by direct actions on skeletal muscle<sup>1</sup></li> <li>Decreases clonus, hyperreflexia, muscle stiffness, and cramping<sup>3,5</sup></li> </ul>	<ul style="list-style-type: none"> <li>Generalized weakness, which often negates the functional improvement<sup>1,3,4</sup>; use may be limited to nonambulatory patients with severe spasticity<sup>3</sup></li> <li>Hepatotoxicity<sup>1-3,6</sup>; liver function testing required<sup>3</sup></li> <li>Drowsiness<sup>3</sup></li> <li>Diarrhea<sup>3</sup></li> <li>Malaise<sup>3</sup></li> <li>Photosensitivity<sup>6</sup></li> </ul>
<b>Anxiolytics/Benzodiazepines</b>		
Diazepam	<ul style="list-style-type: none"> <li>Reduction of muscle tone<sup>4</sup> and frequency of spasms<sup>3</sup></li> <li>Frequently used in combination with baclofen treatment; less commonly used alone<sup>3</sup></li> <li>Relieves skeletal muscle spasm due to reflex spasm to local pathology as well as spasticity caused by upper motor neuron disorders<sup>7</sup></li> <li>Causes general relaxation<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>Sedation<sup>2-4</sup></li> <li>Weakness<sup>4</sup></li> <li>Attention or memory impairment<sup>2,3</sup></li> <li>Reduced motor coordination<sup>2</sup></li> <li>Long-term use can cause dependence and tolerance<sup>3,7</sup>; true physiologic addiction can occur<sup>2</sup></li> <li>Abrupt cessation has been associated with seizures and other withdrawal symptoms<sup>2,3</sup></li> <li>Neutropenia and jaundice can develop during long-term therapy<sup>7</sup></li> </ul>
Clonazepam	<ul style="list-style-type: none"> <li>Suppresses nighttime spasms<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>Sedation,<sup>2</sup> drowsiness<sup>1</sup></li> <li>Confusion<sup>2</sup></li> <li>Fatigue<sup>1,2</sup></li> <li>Lethargy<sup>1</sup></li> </ul>
<b><math>\alpha</math>2-Adrenergic Agonists</b>		
Clonidine	<ul style="list-style-type: none"> <li>Reduction of muscle tone in patients with brain injuries<sup>3</sup></li> <li>Supplement to baclofen treatment<sup>3</sup></li> <li>Can be administered via a patch changed every 7 days<sup>3</sup></li> <li>Decreases vibratory inhibition index in patients with spinal cord injury<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>Dry mouth<sup>2,3,8</sup></li> <li>Sedation<sup>8</sup></li> <li>Bradycardia<sup>2,3</sup></li> <li>Hypotension<sup>2,3</sup></li> <li>Constipation<sup>2,3,8</sup></li> <li>Depression<sup>2,3</sup></li> <li>Dizziness<sup>2,3</sup></li> </ul>

\*Baclofen, dantrolene, diazepam, and tizanidine are currently approved for use in patients with spasticity.<sup>3</sup> Other compounds are being used off-label.<sup>3</sup>



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Treatment/Class/Agent*	Advantages	Disadvantages
Tizanidine	<ul style="list-style-type: none"> <li>Reduction of muscle tone and frequency of spasms<sup>3,4</sup></li> <li>Reduces spasticity without altering muscle strength<sup>3</sup></li> <li>Short-acting muscle relaxant<sup>4</sup></li> <li>Potentially useful option in treating spasticity of spinal and cerebral origin in patients in whom weakness is more of a concern than potential sedation<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>Sedation<sup>2</sup></li> <li>Drowsiness<sup>3,4</sup></li> <li>Dry mouth<sup>2,4</sup></li> <li>Dizziness<sup>2,3</sup></li> <li>Muscle weakness<sup>2,4</sup></li> <li>Hepatotoxicity reversible with dosage reduction<sup>3</sup></li> <li>Risk of potential hypotension; avoid concomitant antihypertensives<sup>2,3</sup></li> <li>Hallucinations<sup>2,3</sup></li> </ul>
<b>Anticonvulsants</b>		
Phenytoin	<ul style="list-style-type: none"> <li>Stabilizes the threshold against hyperexcitability caused by overstimulation<sup>9</sup></li> </ul>	<ul style="list-style-type: none"> <li>Decreased coordination<sup>9</sup></li> <li>Confusion<sup>9</sup></li> <li>Slurred speech<sup>9</sup></li> <li>Abrupt withdrawal can cause seizures in patients with epilepsy<sup>9</sup></li> </ul>
Carbamazepine	<ul style="list-style-type: none"> <li>Reduces nerve pain<sup>10</sup></li> <li>Reduces polysynaptic responses<sup>10</sup></li> <li>Blocks posttetanic potentiation<sup>10</sup></li> </ul>	<ul style="list-style-type: none"> <li>Drowsiness<sup>1</sup></li> <li>Blurred vision<sup>1</sup></li> <li>Nausea<sup>1</sup></li> <li>Ataxia<sup>1</sup></li> <li>Vertigo<sup>1</sup></li> <li>Aplastic anemia and agranulocytosis<sup>1,10</sup></li> </ul>
Topiramate	<ul style="list-style-type: none"> <li>Anticonvulsant activity<sup>11</sup></li> </ul>	<ul style="list-style-type: none"> <li>Metabolic acidosis<sup>11</sup></li> <li>Somnolence<sup>11</sup></li> <li>Psychomotor slowing<sup>11</sup></li> <li>Difficulty with concentration<sup>11</sup></li> <li>Speech, language problems<sup>11</sup></li> <li>Mood disturbances, depression<sup>11</sup></li> </ul>
Gabapentin	<ul style="list-style-type: none"> <li>Reduces spasticity<sup>4</sup></li> <li>Decreases pain<sup>4,12</sup></li> </ul>	<ul style="list-style-type: none"> <li>Somnolence<sup>12</sup></li> <li>Decreased concentration<sup>4</sup></li> <li>Dizziness<sup>12</sup></li> <li>Nausea<sup>12</sup></li> <li>Peripheral edema<sup>12</sup></li> <li>Long-term use for spasticity not established<sup>4</sup></li> </ul>
Ethosuximide	<ul style="list-style-type: none"> <li>Antagonistic activity in inhibitory neural systems<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Drowsiness<sup>1</sup></li> <li>Dizziness<sup>1</sup></li> <li>Nausea, vomiting<sup>1</sup></li> <li>Lethargy<sup>1</sup></li> <li>Headache<sup>1</sup></li> </ul>
<b>Chemodenervation</b>		
Phenol	<ul style="list-style-type: none"> <li>Produces a temporary nerve block lasting up to several months<sup>4</sup></li> <li>Helps control muscle spasticity<sup>4,13</sup></li> <li>Acts as a local anesthetic with no long-term effects at concentrations below 1%<sup>13</sup></li> <li>Affects all neural tissues between 1% and 7%<sup>13</sup>; may cause permanent injury at concentrations &gt;5%<sup>14</sup></li> </ul>	<ul style="list-style-type: none"> <li>Local soft-tissue injury can result<sup>13</sup></li> <li>Highly variable duration of action<sup>13</sup></li> <li>Muscle necrosis<sup>13</sup></li> <li>Postinjection pain<sup>13</sup></li> <li>Dysesthesia<sup>13</sup></li> <li>Vascular complications may include peripheral edema and rarely deep vein thrombosis<sup>13</sup></li> <li>Location of injection should be verified with electrical stimulation technique<sup>15</sup></li> <li>Pain of injections may require local anesthesia<sup>13</sup></li> </ul>

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Treatment/Class/Agent*	Advantages	Disadvantages
Alcohol	<ul style="list-style-type: none"> <li>Quick onset of action (&lt;1 hour)<sup>13</sup></li> <li>Acts as local anesthetic at concentrations of 5% to 10%<sup>13</sup></li> <li>Higher concentrations (&gt;45%) cause neural destruction<sup>13</sup></li> <li>In adults, use of up to 100% in intramuscular injections is safe<sup>15</sup></li> <li>In children, use of 50% to 60% of alcohol is preferred<sup>15</sup></li> </ul>	<ul style="list-style-type: none"> <li>Associated pain; conscious sedation or general anesthesia is usually required<sup>13</sup></li> <li>Skin irritation<sup>13</sup></li> <li>Muscle discomfort<sup>13</sup></li> <li>Muscle and soft-tissue damage may occur<sup>13</sup></li> <li>Location of injection needs to be verified with electrical stimulation technique<sup>15</sup></li> </ul>
Botulinum neurotoxin	<ul style="list-style-type: none"> <li>No anesthetic required<sup>14,16</sup></li> <li>Results in localized decrease in spasticity symptoms<sup>14</sup></li> <li>Effective for reducing spasticity-related pain<sup>14,19</sup></li> <li>Injection can concentrate on the relevant overactive muscle groups without causing systemic side effects<sup>18</sup></li> <li>Injections can be guided into the appropriate muscle using electrical stimulation<sup>15,20,21</sup> or electromyography<sup>15,17,20,21</sup></li> <li>Effect is reversible<sup>14,18,22</sup></li> </ul>	<ul style="list-style-type: none"> <li>Transient weakness of muscles can occur due to local diffusion of botulinum neurotoxin, especially when large volumes are injected at one site<sup>17</sup></li> <li>Tolerance can develop because of immunoresistance<sup>17,18</sup></li> <li>Repeated injections are often required because effect is reversible<sup>18</sup></li> <li>Should be complemented by rehabilitation therapy, splinting, and other therapies<sup>18,20,21</sup></li> </ul>
<b>Physical Therapy</b>		
	<ul style="list-style-type: none"> <li>Treatments designed to reduce muscle tone and improve range of motion, functional mobility, and muscle strength may reduce pain<sup>20</sup></li> <li>Stretches muscles; helps prevent muscle shortening<sup>14</sup></li> <li>Response to therapy improves when complemented by chemodenervation<sup>3,14,21</sup></li> </ul>	<ul style="list-style-type: none"> <li>Direct effects of muscle relaxation are short-lived<sup>3</sup></li> <li>Physiotherapy alone is often insufficient to treat symptoms<sup>3</sup></li> <li>Pain may interfere with treatment<sup>14,23</sup></li> </ul>
<b>Occupational Therapy</b>		
	<ul style="list-style-type: none"> <li>Treatments designed to reduce muscle tone and improve range of motion, functional mobility, and muscle strength may reduce pain<sup>20</sup></li> <li>Stretches muscles; helps prevent muscle shortening<sup>14</sup></li> <li>Response to therapy improves when complemented by chemodenervation<sup>21</sup></li> </ul>	<ul style="list-style-type: none"> <li>Direct effects of muscle relaxation are short-lived<sup>3</sup></li> <li>Pain may interfere with treatment<sup>14,23</sup></li> </ul>
<b>Surgery</b>		
Intrathecal administration of baclofen (pump implantation)	<ul style="list-style-type: none"> <li>Direct administration of baclofen into the spinal cord allows a continuous supply of baclofen to the site of action<sup>3,4</sup></li> <li>Useful for severe cases of spasticity that do not respond to other less invasive treatments,<sup>3</sup> as well as for nonambulatory patients<sup>2</sup></li> <li>Less central adverse effects as compared to oral baclofen because of reduced dose required<sup>3,16</sup></li> <li>Reduces painful spasms<sup>4</sup></li> <li>Reduces spasticity in terms of both muscle tone and frequency of spasms<sup>3,4</sup></li> </ul>	<ul style="list-style-type: none"> <li>Surgical technique to install pump, reservoir, and intrathecal catheter<sup>4</sup></li> <li>Risk of complications due to catheter or pump failure<sup>3,4</sup> and infection<sup>3</sup></li> <li>Drowsiness<sup>2,3</sup></li> <li>Headache<sup>2,3</sup></li> <li>Weakness<sup>2,3</sup></li> <li>Risk of drug withdrawal<sup>2,15</sup></li> <li>Risk of death due to overdose or withdrawal in cases of pump dysfunction<sup>24-27</sup></li> </ul>
Neurosurgery	<ul style="list-style-type: none"> <li>Useful for severe cases of spasticity that do not respond to other less invasive treatments<sup>3,14,19</sup></li> <li>Reduces painful spasms<sup>4</sup></li> </ul>	<ul style="list-style-type: none"> <li>Complications due to surgery</li> </ul>
Surgical lengthening, transfers, and releases of individual muscles <sup>28</sup>	<ul style="list-style-type: none"> <li>Fixed contractures may be better managed by surgical releases<sup>20</sup></li> <li>May provide long-term muscle rebalancing<sup>28</sup></li> </ul>	<ul style="list-style-type: none"> <li>Complications due to surgery</li> </ul>

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### REFERENCES

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